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26th UEG Week 2018

Vienna, Austria, October 2018

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United European Gastroenterology Journal provides an international forum for research in gastroenterology, publishing original articles which describe basic research, translational and clinical studies of interest to gastroenterologists and researchers in related fields. Articles from across all fields of gastroenterology are be welcomed by the Editor-in-Chief, including luminal, liver and pancreatic diseases, gastrointestinal surgery, gastrointestinal oncology, paediatric gastroenterology and nutrition as well as endoscopy.

Published article types include original research, reviews, guidelines papers and news items. The journal is a member of the Committee on Publication Ethics (COPE).

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Letter of Thanks for UEG Week 2018 Reviewers

Dear Colleagues,

On behalf of the UEG Scientific Committee, I would like to take this opportunity to thank you most sincerely for your contribution as an abstract reviewer for the original programme of UEG Week Vienna 2018.

The abstract reviewing process has been again very important this year with a number of innovations introduced to improve especially the poster abstract presentations.

I know just how much time and effort reviewing abstracts takes, but without your expertise we would not have the quality that I believe we have achieved in the free paper and poster sessions, and UEG Week would not be the top international digestive diseases meeting that it has become today.

Thank you!

We received a number of 3,170 abstracts in total for UEG Week 2018. In total, 2,214 abstracts were accepted, giving an acceptance rate of 69.84%. 337 abstracts will be delivered as oral presentations and 1,877 as posters. I am even more pleased to tell you that standards have again reached a very high level and we can expect to be exposed to most interesting research and great presentations.

This high volume and high standard confirm that UEG Week is the most important forum at which to present your best research. We have received 88 video cases and 254 clinical cases which were formally evaluated by the Scientific Committee for presentation in Vienna. As in previous years, late breaking abstracts have been scored by the Scientific Committee for presentation in Vienna.

The quality of reviewing this year was excellent, but if you have any further (positive or negative) comments, please do let us know!

Finally, but most importantly, thanks to all investigators both within and outside Europe who have submitted their research to the meeting, and who are clearly contributing to making UEG Week Vienna 2018 such a great success!

Herbert Tilg
Chair of the UEG Scientific Committee, Vienna 2018
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Disclosure: There is an important heterogeneity among Crohn’s disease patients including clinical presentation and severity, disease location, disease behavior, presence of extra-intestinal manifestations or not, duration of symptoms and response to therapies. There is also a huge number of genetic combinations and expositions to environmental factors. At the molecular level, transcriptome performed on mucosal samples exhibit a striking heterogeneity. A molecular classification could prove more relevant to predict disease course, response to treatment and to identify new drug targets.

Aims and Methods: Our aims are to identify shared and unique molecular features, clinically significant subtypes, and potential therapeutic targets. We conducted an integrated analysis of several cohorts from the IBD Over Time (IBD OT) consortium, including surgical samples of ileal disease and endoscopic samples of both ileal and colonic disease. We also searched for data available in the public domain. We performed molecular clustering (ConsensusClusteringPlus) using mRNA from microarray and RNA-seq, after correcting for batch effect. Cibersort was used to impute immune cells fractions from bulk transcriptome. Finally, KEGG pathway analysis was performed to characterize identified clusters.

Results: We included in the analysis 580 samples of the IBDOT consortium (all by microarray) and 971 samples available in the public domain (508 by RNA-Seq and 736 by microarray). We saw a clear batch effect between the different platforms and cohorts. Colonic and ileal samples were well clustered together in each cohort. After correction for batch effect using biopsy location as a covariate, we identified 4 robust clusters of Crohn’s disease samples. Colonic clusters were dominated by inflammatory disease, ileal samples clustered mainly in 2 groups, APOA1-low highly inflammatory (C1), the other APOA1-high less inflammatory (C2). The fourth group (C4) was smaller and contained ileal samples only. Immune cells fractions showed a neutrophilic infiltration in C1, and a higher proportion of CD8 T cells and Gamma-Delta T cells in C2. Pathway analysis confirmed a typical IBD-like inflammation in C1, and a more subdued inflammation in C2.

Conclusion: We performed the first molecular classification of Crohn’s disease using more than 1500 gut samples from 6 different cohorts. 4 robust disease groups were identified, representing both disease location and levels of inflammation. Some limitations were the high heterogeneity of disease stage and limited data on disease characteristics for the data collected in the public domain. Future work could look at the disease course of these 4 clusters and determine their persistence over time.

Disclosure: Nothing to disclose.
Aims and Methods: NLPR6 is highly expressed by epithelial and goblet cells, but its function in hematopoietic cells is rather unknown. Here, we determined the expression of NLPR6 in vitro differentiated T cells, and in T cells after coculture of wt and NLPR6-deficient T cells to elucidate the influence of different microorganisms on NLPR6 expression by T cells. Results: NLPR6 is not expressed by naïve CD4 and CD8 T cells, B cells and bone marrow-derived macrophages in contrast to epithelial cells. When naïve T cells were differentiated to Th1 cells, Th1 cells express NLPR6, whereas only a minority of differentiated Th2 cells and Th17 have NLPR6. Promoter analysis of the human and mouse NLPR6 starting revealed binding regions for STAT1, STAT5a and Tasb2 (T-bet). T-bet induced NLPR6 expression in differentiated Th1 cells because NLPR6 was not detected in Tbx21-deficient T cells. The production of IFNγ by NLPR6-deficient Th1 cells is reduced compared to wt T cells, which is independent of inflammasome assembly, because in ASC-deficient T cell differences in IFNγ production was not observed. Moreover, differences in IL-13 and IL-17 production by in vitro differentiated Th2 and Th17 cells and differences in Foxp3 Treg cells between wt and NLPR6-deficient T cells were not observed. Transfer of wt CD45RBhigh T cells into RAG hosts resulted in somewhat increased body weight loss and increased disease scores compared to RAG hosts receiving NLPR6-deficient T cells two weeks after transfer. Conclusion: the expression of NLPR6 by differentiated Th1 cells is rather intrinsic and independent of different microorganisms because NLPR6 expression was observed by in vitro differentiated T cells. As consequence increased apoptosis was observed after transfer of NLPR6-deficient T cells in RAG hosts. NLPR6 facilitates the survival of CD4 T cells.

Disclosure: Nothing to disclose.

References


MONDAY, OCTOBER 22, 2018 10:30–12:00
Endoscopic resection of polyps – Room B

OP005 ASSISTANCE OF A REAL-TIME AUTOMATIC COLON POLYP DETECTION SYSTEM INCREASES POLYP AND ADENOMA DETECTION DURING COLONOSCOPY: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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Introduction: Screening colorectal cancer can reduce the incidence and mortality of colorectal cancer through detection of polyps. However, a miss rate of up to 27% has been reported for adenomas.

Aims and Methods: The aim of this study was to investigate whether an automatic polyp detection system during colonoscopy increased the polyp and adenoma detection rate. Consecutive patients were prospectively randomized to undergo routine colonoscopy with or without assistance of real-time automatic polyp detection system providing a simultaneous visual notice and sound alarm when a polyp was detected. The automatic polyp detection system used in this study was a previously validated deep-learning polyp detection software.

Results: Out of 1,058 patients, 536 were randomized to a colonoscopy (control group) and 522 to a colonoscopy with computer-aided diagnosis (CAD group). There is no statistical difference between 2 groups in demographics and adenoma risk factors, including age (p = 0.16), gender (p = 0.19), BMI (p = 0.99), family/ personal adenoma history (p = 0.34/0.8), and family colon cancer history (p = 0.34). A total of 767 polyps, 422 adenomas and 31 serrated adenomas were detected. The polyp detection rate (PDR) of the control and CAD groups were 29.10% and 45.02% respectively (OR = 1.995, 95% CI 1.532-2.544, p < 0.001). The adenoma detection rates (ADR) were 20.34% and 29.12% respectively (OR = 1.61, 95% CI 1.23-2.135, p < 0.001). The average number of polyps detected were 0.50 and 0.95 respectively (Change Folds 1.89, 95% CI 1.63-2.192, p < 0.001).
OP006 POTENTIAL ACCEPTABILITY OF A WATCH-AND-WAIT APPROACH FOR DIMINUTIVE COLORECTAL ADENOMAS: FIVE-YEAR INDEPENDENT RISK FACTORS OF ADVANCED NEOPLASIA IN INDIVIDUALS WITHOUT UNEARTHED DIMINUTIVE ADENOMAS

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Introduction: Removal of all colorectal adenomas during colonoscopy (CS) is recommended; however, the increasingly frequent detection of diminutive adenomas raises the question as to whether the removal of all is mandatory, balancing benefit and harms. The increasing use of antithrombotic drugs and smoking raises the question as to whether the removal of all is mandatory, balancing benefit and harms. Although the watch-and-wait approach is allowed in Japan, evidence is lacking for its acceptability for diminutive adenomas.

Aims and Methods: This study aimed to evaluate the cumulative incidence of advanced colorectal neoplasia (ACN) in individuals with untreated diminutive adenomas. To compare this with the incidence in those without adenomas.

The incidence was also evaluated after identifying and adjusting for risk factors for the incidence of ACN. Data from 1,378 consecutive asymptomatic individuals who underwent first screening CS and at least one follow-up CS without polypectomy at the Cancer Screening Center, National Cancer Center, Tokyo, between February 2004 and March 2013 were analyzed. Those with no adenomas or only non-advanced diminutive adenomas (<5 mm) confirmed by image-enhanced magnifying endoscopy were scheduled to undergo follow-up CS within 5 years after the initial CS without treatment. Thus, participants were classified into two groups: those with untreated diminutive adenomas (group A) and those without any adenomas (group B). The cumulative incidence of ACN in both groups was assessed in March 2018, using Gray’s test with consideration of competing risk situations. Multivariate analysis using the Fine and Gray model was performed to identify independent risk factors for the incidence of ACN in each group A and B. The cumulative incidence in ACN in both groups was assessed in March 2018, using Gray’s test.

Results: There were 361 and 1,017 participants in groups A and B, respectively. Only 18 and 14 were 76-untreated diminutive adenomas in each group A participant, and 355 participants (92.8%) had less than 3. During a median follow-up of 60.9 months (interquartile range 40.6-64.2), 21 ACNs, including one T1 colon cancer, were detected in 18 individuals. The number of endoscopies performed per individual was two in both groups (p = 0.93), and the 5-year cumulative incidences of ACN in group A and B were 1.4% (95% CI 0.5-3.4) and 0.8% (95% CI 0.3-1.7), respectively, with no significant difference between the groups (p = 0.23).

Endoscopic findings showed that no ACN grew from an untreated adenoma. The only independent risk factor for the incidence of ACN was current smoking (hazard ratio 5.7; p < 0.01); presence and number of untreated diminutive adenomas did not affect the incidence of ACN. After adjustment for smoking status, the 5-year cumulative incidences of ACN in groups A and B were 1.0% (95% CI 0.0-2.2) and 0.7% (95% CI 0.1-1.2), respectively.

Conclusion: The 5-year cumulative incidence of ACN in those with untreated diminutive adenomas was sufficiently low, and was similar to that in those without no adenomas, indicating the potential acceptability of a watch-and-wait approach for diminutive adenomas. The present findings may be useful for consideration of more practical screening and surveillance programs, although further assessment is required particularly for cases with many diminutive adenomas.

Disclosure: Nothing to disclose

References
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Disclosure: Nothing to disclose

Introduction: Non-alcoholic fatty liver disease (NAFLD) is strongly related with lifestyle. Advanced glycation end products (AGEs), derived also from diet, have been positively related with NAFLD, while its soluble receptor (sRAGE) acts as a decoy. The association of sRAGE with NAFLD has been scarcely studied. Moreover, little is known about lifestyle-related determinants of sRAGE levels.

Aims and Methods: The aim of this study was to test the association of sRAGE with lifestyle and NAFLD. A cross-sectional study among subjects 40-70 years old, participating in a screening study, undergoing abdominal ultrasonography to diagnose NAFLD and fasting blood tests. Nutritional index consumption was measured by food frequency questionnaire (FFQ) and lifestyle habits were measured by a structured questionnaire. Low sRAGE levels were defined as a level below the population lower tertile (5013 pg/ml).

Results: A total of 789 subjects had valid FFQ. High processed and/or red meat consumption (above the third tertile) was associated with higher odds of low sRAGE, adjusting for gender, age, abdominal obesity and caloric intake. Conversely, greater exercise time (above the median) was associated with reduced odds for low sRAGE (OR = 0.68, 0.49-0.94, p = 0.020). Subjects with low sRAGE had higher odds for NAFLD (OR = 1.51, 1.01-2.27, p = 0.045) and elevated ALT among NAFLD subjects (OR = 1.72, 1.12-2.64, p = 0.014) and among the entire sample (OR = 2.27 95%CI 1.28-4.04, p = 0.005).

Conclusion: Diet and exercise are associated with serum sRAGE levels and, in turn, low levels of sRAGE are associated with NAFLD and elevated ALT levels.

Disclosure: Nothing to disclose

Introduction: Hypoxia and hypoxia inducible factors (HIFs) are believed to significantly affect the progression of chronic liver diseases (CLD). Recently, we showed that hepatectomy HIF-2alpha activation is a key feature in both human and experimental NAFLD and significantly contributes to disease progression.
A4

United European Gastroenterology Journal 6(8S)

Aims and Methods: In the present study we investigated the contribution of
hepatocyte HIF-2alpha in promoting the development of NAFLD/NASH-associated hepatocellular carcinoma (HCC). The role of HIF-2alpha was investigated
in human HCC liver specimens from NAFLD/NASH patients and in mice carrying hepatocyte-specific deletion of HIF-2alpha (HIF-2alpha fl/fl/Alb-Cre mice)
receiving diethyl-nitrosamine (DEN) administration plus choline-deficient Lamino acid refined (CDAA) diet (DEN/CDAA protocol).
Results: HIF-2 alpha, as detected by mRNA transcript and immunostaining, was
expressed in HCC specimens from NAFLD/NASH patients, with higher expression in patients experiencing early tumour recurrence. Following the treatment
with the DEN/CDAA protocol, mice carrying hepatocyte specific deletion of
HIF-2 alpha showed a significant decrease in either the volume and/or the
number of neoplastic liver tumour masses in transgenic mice as compared to
control littermates. Liver tumours in HIF-2 alpha transgenic mice were also
characterized by: i) a decrease of tumour associated macrophages and fibroblasts/myofibroblasts, as evaluated by F4/80 and alpha-smooth muscle actin
immunohistochemistry, respectively; ii) a significant decrease in transcript
levels for critical and HIF2alpha-related target genes, including c-Myc and
CXCR4.
Conclusion: These results indicate that the activation of HIF-2alpha in hepatocytes has a critical role in the development of experimental liver carcinogenesis in
a dietary NAFLD/NASH-related environment.
Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018

10:30–12:00

IBD: From epidemiology to costs and outcome –
Room F1____________________
OP009 IS THERE A COST-SAVING EFFECT OF BIOLOGICAL
THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL
DISEASE? RESULTS FROM A PROSPECTIVE EUROPEAN
POPULATION-BASED INCEPTION COHORT
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Introduction: The introduction of biological therapy has influenced healthcare
expenditures in inflammatory bowel disease (IBD) significantly. However, no
prospective long-term analysis of healthcare costs in patients with IBD in the
era of biologic treatments exists in Europe.
Aims and Methods: The aim of this study was to perform a cost analysis of a
pan-European inception cohort with five years of follow-up. The Epi-IBD cohort
is a population-based inception cohort of IBD patients diagnosed from 31 centers
in 20 countries in Western and Eastern Europe in 2010. Clinical and direct
cost data (investigations, treatments, hospitalization and surgery) were collected
prospectively. Patient management was left to the discretion of the treating gastroenterologists. Data are expressed as mean costs (E/patient-year). PY0 represents the inception year, and PY1, PY2, PY3 and PY4 are the four follow-up
years.
Results: The cohort included 1,362 IBD patients (Western Europe: 1,104; Eastern
Europe: 258), of which 52% had ulcerative colitis (UC), 37% Crohn’s disease
(CD) and 11% IBD unclassified. The age structure was: 40 y 45%, 41-60 y
31%, and  61 y 24%.
The total expenditures per year in CD and UC patients as well as the proportion
of expenditure spent on different categories of direct costs is shown in Table 1.
Total expenditure was higher in CD than UC, as was the annual percentage
outlay on biological therapy. In Western Europe, total annual costs were highest
in PY0 at E4,964, and then decreased as follows: PY1 E1,687, PY2 E1,585, PY3
E1,492, and PY4 E1,113. Expenditure on biologic therapy increased in this time
period (PY0 E338, PY1 E410, PY2 E440, PY3 E504, and PY4 E516). In Eastern
Europe, while overall healthcare costs were lower, similar observations were
made. Total annual costs were highest in PY0 at E2,227, and then decreased:
PY1 E934, PY2 E758, PY3 E643, and PY4 E734. Cost of biologic therapy was
the following: PY0 E31, PY1 E233, PY2 E355, PY3 E308, and PY4 E292. In
both regions this was paralleled by a steady decrease of costs of non-biologic
treatment, hospitalization and surgery.
In all centers the expenditure on investigations was highest in the year PY0. No
gender differences in costs were observed, however, patients aged  40 years
engendered higher costs than older individuals. The overall outlay on biological
therapy, expressed as a percentage of total expenditure, varied by age group:  40
yrs. 29%, 41-60 yrs. 21%, and  61 yrs. 11%.

PY0

PY1

PY2

PY3

PY4

Crohn’s disease – total expenditure 5,579E 1,820E 1,714E 1,907E 1,669E
CD – Biological therapy
11%
46%
51%
48%
56%
CD – Other IBD-related medication
5%
13%
11%
11%
12%
CD – Hospitalization
20%
14%
11%
11%
6%
CD – Diagnostic procedures
34%
17%
11%
12%
10%
CD – Surgery
30%
9%
16%
18%
17%
Ulcerative colitis – total expenditure 3,612E 1,421E 810E 983E 674E
UC – Biological therapy
2%
7%
20%
19%
25%
UC – Other IBD-related medication
15%
23%
29%
21%
26%
UC – Hospitalization
35%
29%
21%
33%
17%
UC – Diagnostic procedures
38%
20%
19%
20%
19%
UC – Surgery
10%
21%
10%
8%
13%
[Table 1. Mean total expenditure (E/patient) and as well as the proportion of
expenditure spent on different categories of direct costs]
Conclusion: In this large population-based inception cohort of unselected IBD
patients, the overall direct expenditure on healthcare decreased over a 5-year
follow-up period. This period was characterized by remarkably increasing expenditure on biologics, particularly in CD patients, and decreasing expenditure on
standard medical treatments, surgery and hospitalization. Despite their known
high acquisition charges, these data indicate a cost-saving effect of biologic
medications.
Disclosure: Nothing to disclose

OP010 EFFICACY AND SAFETY OF THE SEQUENTIAL USE OF A
SECOND AND THIRD ANTI-TNF DRUG IN PATIENTS WITH
INFLAMMATORY BOWEL DISEASE
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The aim was to investigate the efficacy and safety of the sequential use of a second and a third anti-TNF agent after developing intolerance to an anti-TNF drug. Patients diagnosed with IBD from ENEIDA registry (a prospectively maintained registry from GETECCU) who switched to a second or a third anti-TNF after failure or intolerance to a previous anti-TNF drug were included. Efficacy, loss of response, and safety of the second and third anti-TNF were evaluated by logistic regression, Kaplan-Meier and Cox regression analyses.

Results: 1,022 patients that switched to a second anti-TNF were included (50% more severe age at diagnosis 31 years, 73% CD). The proportion of patients who became intolerant to the first anti-TNF were: primary failure (21%), secondary failure (51%), and intolerance (28%). A second attempt with an anti-TNF agent induced remission in 45% of patients in the short-term. 33% received concomitant immunosuppressive therapy. In the multivariate analysis, factors associated with a lower probability of achieving remission after a second anti-TNF were: type of IBD and combo therapy. Almost all patients who responded to a second anti-TNF subsequently lost response. Factors associated with loss of response of a second anti-TNF were: combo therapy (HR = 2.4; 1.8-3.2, p = 0.0001), to withdraw the first anti-TNF due to a primary failure (vs. intolerance) (OR = 1.6; 1.1-2.3, p = 0.007) and to withdraw the first anti-TNF due to secondary failure (vs. intolerance) (OR 1.5; 1.2-2.5, p = 0.003). The cumulative incidence of loss of response after achieving remission with the second anti-TNF (median follow-up of 19 months) was 45% (41-49%); 23% at 1 year, 38% at 2, 66% at 3, and 62% at 5 years. The incidence of loss of response to the second anti-TNF was 19% per patient-year of follow-up. The dose of the second anti-TNF was increased in 22% of patients during follow-up (median follow-up of 13 months); of these, 56% regained remission. At 1 year, 91% of these patients were in remission. The factors associated with a higher risk of loss of response were: UC vs. CD (HR = 1.6; 1.1-2.1, p = 0.005) and combo therapy (HR = 2.4; 1.8-3.2, p = 0.0001). The rate of adverse events after a second anti-TNF was 15%, and led to drug discontinuation in 61%. 71 patients switched to a third anti-TNF (55% IBD, mean age at diagnosis 32 years, 63% CD). The reasons for withdrawing the second anti-TNF were: primary failure (45%), secondary failure (39%), and intolerance (16%). Remission was achieved with the third anti-TNF in 55% of patients in the short-term. The incidence of loss of response was 22% per patient-year of follow-up (HR = 1.6; 1.0-2.6, p = 0.05). The cumulative incidence of loss of response was 38%: 18% at 1 year and 37% at 2 years. 7 patients (11%) had adverse events, but only one discontinued the therapy.

Conclusion: The efficacy of a second anti-TNF in IBD patients was associated with the reason for switching. Almost half of the patients who achieved remission with a second anti-TNF subsequently lost response. Factors associated with loss of response of a second anti-TNF were: type of IBD and combo therapy. Almost two-thirds of patients who received a third anti-TNF achieved remission; however, one-third of them lost response subsequently. The sequential use of a second and third anti-TNF is apparently safe.
Introduction: Studies comparing the characteristics of childhood-onset and adulthood-onset inflammatory bowel disease (IBD) in the biologic era are scarce. Aims and Methods: To compare the disease characteristics, the use of immunomodulators and biologic agents, and the need for surgery between childhood and adulthood-onset IBD.

IBD patients diagnosed from 2007 from the ENEIDA registry – prospectively maintained database promoted by GETECCU were included. Patients diagnosed at ≤16 years comprised the childhood-onset cohort (CC), and those diagnosed >16 years were the adult cohort (AC). Cox-regression analysis was performed to identify potential predictive factors to receive immunosuppressants, biological agents or surgery.

Results: From 21,200 patients, 96% comprised the AC and 4% the CC. Median follow-up was 54 months in the CC and 38 months in the AC (p < 0.001). The proportion of male gender, CD and family history of IBD was higher in the CC. CD patients in the CC had more extensive involvement while the proportion of patients with strictureing or fistulizing phenotype was higher in the AC. UC patients in the CC had more extensive involvement. Cumulative incidence of exposure to immunomodulators was higher in the CC: 54% at one year, 63% at 2 years, 70% at 3 years, 73% at 4 years and 87% at 5 years in the CC; and 34% at 1 year, 43% at 2 years, 48% at 3 years, 52% at 4 years and 53% at 5 years in the AC (p < 0.001). The cumulative incidence of exposure to biologic agents was higher in the CC: 25% at 1 year, 39% at 2 years, 45% at 3 years, 50% at 4 years and 65% at 5 years in the CC; and 16% at 1 year, 24% at 2 years, 29% at 3 years, 33% at 4 years and 37% at 5 years in the AC (p < 0.001). The proportions of patients and the cumulative incidence of surgery were similar in the CC and AC (17% vs. 15%, p > 0.05). Childhood-onset IBD was associated with higher risk of immunomodulator and biologic agents exposure. Childhood-onset IBD was not associated with higher risk of surgery (table 1).

Conclusions: Childhood-onset IBD patients diagnosed during childhood have differential characteristics (higher prevalence of CD, more extensive disease and more frequent family history). In addition, the use of immunomodulators and biologic agents is higher in childhood-onset patients. Despite of the higher burden of the disease in children, the rate of surgery is similar to that in the adulthood-onset IBD population.

Variable | Hazard ratio (95% confidence interval)
--- | ---
**USE OF IMMUNOSUPPRESSANTS**
Childhood-onset vs. adulthood-onset IBD | 1.6 (1.5–1.8)
Female gender | 0.94 (0.91–0.98)
Crohn’s disease (vs. ulcerative colitis) | 3.2 (3.09–3.4)
Family history | 1.08 (1.01–1.1)
Extraintestinal manifestations | 1.2 (1.1–1.3)
Smoking habit | 1.1 (1.05–1.16)
**USE OF BIOLOGIC AGENTS**
Childhood-onset vs. adulthood-onset IBD | 1.5 (1.4–1.7)
Female gender | 0.92 (0.85–0.95)
Crohn’s disease (vs. ulcerative colitis) | 2.5 (2.3–2.7)
Extraintestinal manifestations | 1.7 (1.6–1.7)
Smoking habit | 1.1 (1.04–1.18)
**SURGERY DURING FOLLOW-UP**
Childhood-onset vs. adulthood-onset IBD | 0.9 (0.8–1.2)
Female gender | 0.79 (0.73–0.86)
Crohn’s disease | 6.6 (5.8–7.4)
Immunomodulators before surgery | 0.36 (0.33–0.39)
Smoking habit | 1.2 (1.1–1.3)

[Variables associated with the risk of exposure to immunosuppressants, biological agents and surgery during follow-up.]

Disclosure: M. Chaparro has served as a speaker, or has received research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, and Amgen. J.P. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Kern Pharma, Biogen, Takeda, Janssen, Roche, Celgene, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotis Pharma, Chiesi, Casen Fleet, Gebro Pharma, Osuka Pharmaceutical, Vifor Pharma.
especially in the era of biologic therapy. To date, no study has assessed indirect costs in IBD and UC patients in a population-based setting.

Aims and Methods: Our aim was to assess the indirect cost of CD and UC patients in a population-based inception cohort with 10 years of follow-up. All incident patients, diagnosed with CD (213) or UC (300) year 2003-2004 in a well-defined Copenhagen County, were followed prospectively until 2014. Employment status, sick-leave and social benefits are automatically registered in national registries through the unique 10 digit personal identification number given at birth or immigration. With use of these national registries, indirect cost of unemployment, sickness- and/ or disability assessed. The loss of income for the Danish government during unemployment was calculated using the mean income for the Danish popu-
lization of 41,970 EUR (value of 2017). Data were compared with a population of healthy controls matched by age, sex and municipality at diagnosis with a ratio of 1:20 (n = 10,259). Using multiple linear regression models, associations between indirect cost and multiple variables (gender, age, smoking status at diagnosis, disease behaviour, -location, -extension and diagnostic delay) were assessed.

Results: During follow-up, 139 [65%] CD and 181 [60%] UC patients had at least one episode of paid sick-leave (HR [95% CI] = 1.62) (2.6-19.8) months for CD and 5.1 (1.6-15.9; p = 0.2) for UC. The median cost of sickness benefits during follow-up for CD was 10,230 (3,900, 32,100) and 8,800 (2,400, 28,500) EUR for UC. No significant difference was found between healthy controls and IBD patients regarding length of paid sick-leaves (5.7 months [1.2, 16.4], p = 0.08) or sickness benefits (9,700 [2,100, 30,200], p = 0.2). Regarding unemployment, a total of 279,193 (543%) (CD: 12,377 [58%]; UC: 156,116 [52%]) patients were unemployed at least once during follow-up. In CD, the median length of unemployment was 5.3 (2.3-12) and 6.6 (2.14-18) in UC (p = 0.55). The median cost for unemployment benefits was 13,301,700 (4,703,100, 55,800,600) EUR for CD, and 12,301,400 (3,102,400, 47,103,300) EUR for UC patients. These estimates did not differ significantly from the healthy controls (5.9 [1.8, 14.4]; p = 0.6 and 13,400,000 [24,000,000, 46,600,300] p = 0.23, respectively). The median loss of tax income for the Danish government because of unemployment was 6,900,020 (2,001,800, 7,001,021,800) EUR, with a range from healthy controls (17,005,300, 16,401,200, 30,06) to 0 p = 0.06). The total indirect cost accounted for 19,714.4 million EUR (CD: 9.16 million, UC: 10.67 million). No factors were associated with the indirect cost in CD. In UC, age 17-40 years (OR: 1.53 [1.01, 2.11] 6), being male (OR: 0.90 [0.8, 1.0]) and current smoker (OR: 1.31 [1.0, 1.62]) at diagnosis were significantly associated with the indirect cost of 100,000 EUR.

Conclusion: In this population-based inception cohort with ten years of follow-
up, indirect cost of IBD patients did not differ from the general population. Furthermore, no significant increased expenses were found between CD and UC patients. These data indicate that in a country with universal and free access to healthcare current treatment strategies keep patients with IBD on the job market. Except for higher direct costs due to health care utilization, IBD patients had a higher indirect cost. In CD, 70% of the indirect cost was due to sickness benefits and unemployment. In UC, 65% of the direct cost was due to health care utilization.

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OP013 IS CROHN DISEASE THE PRICE TO PAY TODAY FOR HAVING SURVIVED TO THE BLACK DEATH?
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Introduction: Nodular Oligomerisation Domain 2 (NOD2) is a key gene of immune recognition to the host defence toward pathogens. Several NOD2 variations associated with Crohn Disease (CD). Unexpectedly, these loss-of-function mutations are frequent in populations of European ancestry suggesting a model of balancing selection and thus a benefit to mutation carriers. NOD2 deficiency has been associated with a severe form of Yersinia pseudotuberculosis we hypothesized that NOD2 mutations have been selected during past plague outbreaks due to Yersinia pestis.

Aims and Methods: We performed a PubMed search looking for the frequencies of CD associated NOD2 mutations in healthy controls. Using historical data on plague outbreaks, we evaluated the rate of exposure to plague of the ancestors of the corresponding populations. Demography of cities and migration rates from the 14th century to the 19th century were also taken into account to evaluate the impact of putative confounding factors.

Results: The rates of the CD-associated NOD2 mutations in the general population were correlated with the intensities of plague outbreaks in Europe and the Mediterranean Basin. Statistical significance was obtained with the most frequent mutation (R702W, p = 0.03) and with the pooled three mutations (p = 0.023). The association remained significant when putative demographic biases were considered suggesting a robust finding.

Conclusion: This result argues for a selection of CD-associated NOD2 mutations by the various plague episodes which have occurred in Europe and the Mediterranean Basin since the Middle ages.

Disclosure: Nothing to disclose.

OP014 CROHN’S DISEASE: WHAT CAN WE EXPECT FROM THE COURSE OF THE DISEASE?
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Introduction: Crohn’s disease (CD) is a chronic and progressive disease that changes its behavior over time. Transmural inflammation in CD leads to stric-
turing and/or penetrating complications.

Aims and Methods: We aim to evaluate the frequency of the long-term progres-
sion of patients with CD by classifying them according to short term behavior and to determine the main factors associated with this evolution.

A retrospective study was conducted with a prospective follow-up. Patients included had a minimum follow-up of 12 months. Montreal classification was assessed at the moment of the diagnosis and at the end of the follow-up period.

Results: Included 290 patients, 53.8% female. The behavior at presentation was inflammatory (B1) in 64.5%, stricturing (B2) in 23.4%, penetrating (B3) 12.1% and perianal disease was present in 18.6%. Behavior at the end of the follow-up was: B1 in 51.4%, B2 in 30.3% and B3 in 18.3%, perianal disease was identified in 20%. Globally we observed a change in behavior in 46 patients (15.9%); from B1 to B2 in 30 patients, B2 to B3 in 16 patients and B1 to B3 in 10 patients.

Illeocolic location (60.9% vs 45.1%; p = 0.049), age at diagnosis < 16 (8.7% vs 2%; p = 0.017), the use of steroids at diagnosis (43.2% vs 27%; p = 0.031) and less exposure to biological therapy (15.9 months vs 41.3 months; p < 0.001) were the risk factors associated with changing phenotype.

Regarding surgery, 70 patients (24.1%) were submitted to intestinal resection. Smoking status (42.9% vs 24.8%; p = 0.004), B2 (47.1% vs 15.9%; p < 0.001), B3 (42.9% vs 2.3%; p < 0.001), hospitalizations in the first year of diagnosis (52.3% vs 12.4%; p < 0.001), use of steroids at diagnosis (61.4% vs 23.6%; p < 0.001) were more frequently observed in patients submitted to surgery. Patients submitted to surgery were less frequently treated with biological therapy (8.7% vs 23.4%; p < 0.025).

Conclusion: In our cohort we observed a behavior progression in about one-sixth of patients. The most frequent change in behavior was to strictureing pattern. Strictureting and penetrating behavior, higher number of hospitalizations in the first year of diagnosis, use of steroids at diagnosis, smoking status, age at diagnosis and ileocolic localization were factors associated with an unfavorable clinical evolution. Patients that were submitted to surgery were less treated with biological therapy.

Disclosure: Nothing to disclose.
**Introduction:** Surveillance programs on high-risk individuals (HRIs) can detect precancerous pancreatic lesions (PCL) not previously identified. We report the results of the first-round of screening of the Italian multicenter program supported by the Italian Association for the study of the Pancreas (AISP).

**Aims and Methods:** The multicenter surveillance program includes: a) individuals with hereditary pancreatitis (HP), the second highest risk group after individuals with at least 2 relatives affected by pancreatic cancer; b) patients with at least one first-degree relative affected by pancreatic cancer (FPC-HRI); c) patients with at least two second-degree relatives affected by pancreatic cancer (2, SDR) with at least 1 FDR; d) patients with Peutz-Jegher (PJ) syndrome; e) patients with 2 relatives affected by pancreatic cancer (2, FDR) with at least 1 SDR; and f) patients with 3 relatives affected by pancreatic cancer (3, SDR), 1 of whom is a first-degree relative. These groups were combined into one cohort advised by FPC-HRI, HP, or probands with at least 2 relatives affected by pancreatic cancer. To evaluate the population-based screening, we included the cohort of HRIs suffering from PJ syndrome. To evaluate the population-based screening, we included the cohort of HRIs suffering from PJ syndrome.

**Results:** The first-round screening results in Italy report a high rate of pancreatic abnormalities. The rate of malignancies detected was higher in the cohort of FPC-HRI suffering from PJ syndrome than in the cohort of HRIs suffering from PJ syndrome (7.5% vs. 3.5%). The rate of malignancies detected was higher in the cohort of FPC-HRI suffering from PJ syndrome than in the cohort of HRIs suffering from PJ syndrome (7.5% vs. 3.5%). The rate of malignancies detected was higher in the cohort of FPC-HRI suffering from PJ syndrome than in the cohort of HRIs suffering from PJ syndrome (7.5% vs. 3.5%).

**Conclusion:** The first-round screening results in Italy report a high rate of pancreatic abnormalities. The rate of malignancies detected was higher in the cohort of FPC-HRI suffering from PJ syndrome than in the cohort of HRIs suffering from PJ syndrome (7.5% vs. 3.5%). The rate of malignancies detected was higher in the cohort of FPC-HRI suffering from PJ syndrome than in the cohort of HRIs suffering from PJ syndrome (7.5% vs. 3.5%). The rate of malignancies detected was higher in the cohort of FPC-HRI suffering from PJ syndrome than in the cohort of HRIs suffering from PJ syndrome (7.5% vs. 3.5%).

**References:**

OP017 SINGLE MOLECULE REAL-TIME SEQUENCING UNVEILS THE EVOLUTION OF MULTI-DRUG RESISTANT HEPATITIS C VIRUS CLONES DURING DIRECT-ActING ANTI-VIRAL THERAPY

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**Introduction:** The recent development of oral direct-acting antivirals (DAAs) has dramatically improved the efficacy of anti-hepatitis C virus (HCV) treatment, however, resistance-associated variants (RAVs) are associated with treatment failure in HCV-infected patients receiving DAA therapy. Although low- abundance RAVs are detected by real-time PCR as early as weeks after the start of therapy, it has been difficult to determine the clonal origin of RAVs using conventional short-read sequencing methods. Thus, in the current study, we investigated the viral dynamics in patients undergoing DAA therapy and explored the clonal origin of multi-drug resistant viral clones using single molecular real-time (SMRT) sequencing, so-called third generation sequencing, which can generate extremely long contiguous sequence reads.

**Aims and Methods:** Among 283 patients with genotype 1b HCV receiving DAAs therapy in our study group, 32 who failed to achieve a sustained virological response (SVR) were included in this study. First, conventional ultra-deep sequencing of NS3 and NS5A regions of HCV genome was performed in all patients using IonProton (ThermoFisher Scientific). Then, paired sera samples were collected before and after DAA therapy and from a cohort of 12 non-SVR patients, we applied SMRT sequencing using PacBio RSII (Pacific Biosciences) to determine the long contiguous sequences spanning >3000 bp of the NS3 to NS5A regions of each viral clone.

**Results:** Sixteen-deep sequencing detected representative RALs in all non-SVR patients at baseline, including NS5A-Y93H or L31M and NS5D-D168V. Importantly, at treatment failure, multi-drug resistant HCV clones were detected in all cases as the major population. Then, long contiguous sequences of each viral clone in 12 sera from 6 non-SVR patients (a total of 3601 clones) were determined by PacBio RSII. We found the substantial sequence diversity of viral isolates present at baseline in all cases, showing the high degree of genetic heterogeneity in HCV clones. All the nucleotide substitutions analyzed in each clone before and after treatment were compared, and we found significant linkage between some synonymous substitutions and major resistance-associated substitutions. For example, several synonymous mutations linked to NS5A-Y93H in a subpopulation of pre-existing viral clones at baseline were shared by multi-drug resistant viral clones at treatment failure. Phylogenetic analyses revealed a close genetic distance between pre-existing drug-resistant clones and multi-drug resistant viral clones at treatment failure. In addition, linkage analysis demonstrated that multiple drug-resistant mutations newly developed based on pre-existing RALs after DAA treatment in all non-SVR cases.

**Conclusion:** Comprehensive analysis of SMRT sequencing and conventional ultra-deep sequencing revealed that multi-drug resistant viral clones at treatment failure originated from a subpopulation of pre-existing RALs in HCV-infected patients. Those RALs were selected for and became dominant with the acquisition of multiple resistance-associated substitutions under DAA treatment pressure. These findings give us a clue to a better understanding of treatment failure mechanisms with anti-HCV therapy.

**Disclosure:** Nothing to disclose
Aims and Methods: The objective of this analysis was to use eDISH to determine if patients with NASH treated with OCA showed increased markers of liver injury or whole liver dysfunction. eDISH methodology was applied to 278 patients treated with placebo (n = 140) or 25mg OCA (n = 138) from FLINT and 84 patients treated with placebo (n = 21), 5mg OCA (n = 20), 10mg OCA (n = 21), or 20mg OCA (n = 22) from CONTROL. Individual CONTROL and FLINT patients were matched on the basis of baseline values of alanine aminotransferase (ALT) and total bilirubin throughout the double-blind treatment phase were plotted on an x-y chart as logarithm_{10} values of multiples of elevations above the upper limit of the normal reference range (S ULN).

Results: Overall, no OCA-treated patients were in the Hy’s law quadrant (>3x ULN for ALT and >2x ULN for total bilirubin) compared with 1 placebo-treated patient in FLINT. The proportion of patients with peak ALT and total bilirubin values in the lower left quadrant (representing normal or near normal range) was higher in OCA-treated patients compared with placebo (FLINT: 91% OCA vs 84% placebo; CONTROL: 91% OCA vs 86% placebo). 8% of OCA-treated patients from both FLINT and CONTROL presented in the Temple’s corollary quadrant (>3x ULN for ALT and <2x ULN for total bilirubin) vs 14% (in both studies) for the placebo-treated patients. Across both studies (N = 362), 4 patients were in the cholestasis quadrant (>2x ULN total bilirubin and <3x ULN for ALT); 1 placebo-treated patient and 3 OCA-treated patients, including 1 patient with Gilbert’s syndrome.

Conclusion: In these 2 placebo-controlled, double-blind NASH studies, the eDISH analysis showed no trend for liver injury with OCA at doses up to and including 25 mg.

Disclosure: This study was funded by Intercept Pharmaceuticals Inc.

Reference

Aims and Methods: The first study in this series aimed to evaluate the feasibility and safety of EUS-guided photodynamic therapy (EUS-guided PDT) with a second-generation photosensitizer for unresectable pancreatic cancer. Patients with unresectable pancreatic cancer were prospectively enrolled in a single tertiary center between December 2015 and January 2018. Patients were photosensitized with chlorin e6 derivatives (Photolon®). After endoscopic ultrasonography (EUS-guided PDT) with a second-generation photosensitizer for unresectable pancreatic cancer. Patients with unresectable pancreatic cancer were prospectively enrolled in a single tertiary center between December 2015 and January 2018. Patients were photosensitized with chlorin e6 derivatives (Photolon®). After endoscopic ultrasonography (EUS-guided PDT) with a second-generation photosensitizer for unresectable pancreatic cancer. Patients with unresectable pancreatic cancer were prospectively enrolled in a single tertiary center between December 2015 and January 2018. Patients were photosensitized with chlorin e6 derivatives (Photolon®). After endoscopic ultrasonography (EUS-guided PDT) with a second-generation photosensitizer for unresectable pancreatic cancer. Patients with unresectable pancreatic cancer were prospectively enrolled in a single tertiary center between December 2015 and January 2018. Patients were photosensitized with chlorin e6 derivatives (Photolon®).
Aim and Methods: Therapies based on biomarker profiles.

Results: 40 patients were enrolled, 35 tumor samples were analyzed and interpretable results were obtained from 31 patients. At least 1 relevant biomarker was found in all cases. We found mutations in KRAS (n = 24), TP53 (n = 17), SMAD4 (n = 3), BRCA1 (n = 4; 3 germline, 1 somatic), CDKN2A (n = 9; ATM n = 3; LOF), APC (n = 4), and MSH3 (n = 15; 1 germline). MH Guide made treatment recommendations in 30:31 cases: PARP-inhibitors (n = 26), MEK/RAF inhibitors (n = 20), CDK inhibitors (n = 9), other kinase inhibitors (n = 3), mTOR inhibitors (n = 2). The molecular tumor board (MTB) agreed in 26 cases: 2 patients received other second-line line therapy and 2 BSC. 3 patients died before and 2 during analysis, 1 prior to the MTB, 2 before start of therapy and 3 shortly after. Today, the major cause of death is disease progression. Chemotherapy for which they had a toxic effect was given to 13/27 patients and 7 had toxicity of grade 3 or above.

Conclusion: Evidence-based personalized treatment recommendation in PDAC is feasible and molecular stratification of PDAC patients routinely leads to recommendation of off-label use of registered drugs. Today, we have found tumors with HCC, 30-59 15.0 12.3–18.0 18.4 12.1–26.7 30-59 39.1 31.5–47.9 39.0 23.1–61.6 41.1–73 71.8–133 19.6–183 1.44–317 1.44–317 Ø.003, n = 5,578) and patients with missing information on cirrhosis status (7.6% vs. 0%, p = 0.048, n = 365), respectively.

Conclusion: Statin use was associated with reduced risk for HCC development in chronic hepatitis B patients, regardless of cirrhosis status. Statin treatment may decrease HCC risk, which warrants prospective validation.

Disclosure: Nothing to disclose

References
Disclosure: LCS and LAGR work for the Spanish Centre for Pharmacopoeiologic Research (CEIFE), which has received research funding from Bayer AG. LAGR has also served on advisory boards for Bayer AG. MS-G is a full-time employee of Bayer AG. AL has previously received a research grant from Bayer AG and has served as an advisory board member for Bayer AG and Bayer HealthCare.

OP025
ACUTE UPPER GASTROINTESTINAL BLEEDING IN PATIENTS USING ANTITHROMBOTIC AND NON-STEROIDAL ANTI-INFLAMMATORY THERAPY: CONTRIBUTING FACTORS AND OUTCOMES
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Introduction: The most common causes of acute nonvariceal upper gastrointestinal bleeding (AUGIB) are peptic ulcer bleeding and haemorrhagic gastritis. The use of non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose acetylsalicylic acid (LDA) are known risk factors for both COX-2 selective NSAIIDs are considered safer in terms of bleeding.

Aims and Methods: To identify patients with AUGIB who use LDA and NSAIDs, determine the severity of bleeding, outcomes and potential risk factors for adverse outcomes. Retrospective, prospective analysis of all patients over 18 years of age consecutively admitted for AUGIB in a tertiary centre in Latvia – Riga East Clinical University Hospital from November 2013 to December 2014. Data was collected regarding history of drug use, bleeding-related interventions, length of hospital stay and outcomes. Forrest classification was used to evaluate the severity of bleeding, data was entered into the database with consecutive statistical analysis using SPSS 20.0.

Results: 236 patients with AUGIB were enrolled (138 (58%) men, 98 (42%) women, mean age 62 ± 17.36 years). Peptic ulcer disease (PUD) was the most common diagnosis (n = 180, 73%). Out of all patients, 90 (38.1%) were NSAIDs users (more often women (46/44)), 27 (11.4%) used oral anticoagulants (mean past use of 10.8 years) and 52 (22.4%) used alcohol (mean age 47 ± 11.61 years). NSAIDs use was associated with more frequent PUD bleeding (r = 0.347, p < 0.001). Out of 26 patients with Forrest I type (IA and IB) peptic ulcer bleeding, 12 (46%) used NSAIDs, 9 (34.6%) were on LDA therapy, 3 (11.5%) were alcohol users. The most commonly used NSAIDs were diclofenac (n = 24, 26%) and ibuprofen (n = 8, 9%). There was only one patient on COX-2 selective NSAID therapy, who was admitted with Forrest II B bleeding. 108 patients (45.7%) were hospitalised in intensive care unit, most often with Forrest IIIB PUD bleeding – 36 (33.3%). Tranfusion of red blood cells was required in 133 (56.3%) cases, fresh frozen plasma in 106 (44%) cases and cryoprecipitate in 39 (16.5%) cases. Surgery was performed in 37 (15.6%) patients. Most of the patients requiring surgical intervention were on NSAID therapy (22/37, p = 0.004, Pearson Chi-Square). Bleeding-related in-hospital death occurred in 24 (10%) cases, mostly in patients with recurrent PUD bleeding. There was a statistically significant age difference between patients who recovered and those who died (n = 212, 61 ± 17.14 vs. n = 24, 78 ± 10.04, p < 0.001). The difference in length of hospital stay between NSAIDs users and non-users was marginally significant (p = 0.058, Mann-Whitney Test).

Conclusion: 1. LDA and NSAIDs remain the most common risk factors for AUGIB and are associated with the need for surgical intervention. 2. Bleeding-related mortality and need for surgery during hospitalisation remain high. 3. Important prophylactic measures should include patient education about risks, adequate gastroprotection and minimisation of alcohol use.

Disclosure: Nothing to disclose

OP026
NO DIFFERENCES IN GI BLEEDING RISK BETWEEN CLOPIDOGREL-, TicAGRELOR- OR PRASUGREL-BASED DUAL ANTIPLATELET THERAPY AFTER PERCUTANEOUS CORONARY INTERVENTION
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Background: Emerging evidence suggests that the benefit of dual antiplatelet therapy (DAPT) might be independent of the platelet inhibitor used. However, this approach has not been prospectively validated in registry data. DAPT has been associated with a higher risk of bleeding complications compared to single antiplatelet treatment. Methods: We performed a retrospective evaluation of patients who received a percutaneous coronary intervention (PCI) to estimate the risk of both any major bleeding (MB) and major bleeding complications (MBC) requiring urgent surgery or blood transfusion (BTT) in those receiving clopidogrel (CP), ticagrelor (TCA) or prasugrel (PSG). Results: A total of 44,091 patients were included in the study. MB was observed in 3,254 patients (7.4%) and MBC/BTT occurred in 883 patients (2%). There were no significant differences in the risk of MB (p = 0.61) or MBC/BTT (p = 0.52) between the three treatment groups. Conclusion: The use of CP, TCA, or PSG did not lead to differences in the rate of MB or MBC/BTT after PCI. The risk of major bleeding complications requiring urgent surgery or blood transfusion was similar in all three groups.
Introduction: Dual antiplatelet therapy (DAPT) decreases major adverse cardio-vascular events after a percutaneous coronary intervention (PCI). New and potentially more effective antiplatelet agents such as ticagrelor or prasugrel combined with aspirin (ASA) are being prescribed preferentially to younger and healthier patients based on the potential higher risk of GI bleeding. However, very few data are available concerning the occurrence of GI bleeding associated with these new compounds when compared to classical DAPT with clopidogrel in common clinical practice.

Aims and Methods: We aimed to determine the risk and type of major and minor GI events in patients with DAPT and type of DAPT, and to analyze PPI therapy regimens during and after DAPT withdrawal. This was a retrospective observational cohort study of patients who started DAPT after a PCI from January 2013 to December 2017. All patients underwent upper endoscopy, and were on DAPT with either clopidogrel, ticagrelor or prasugrel, respectively. There were statistically significant differences in baseline characteristics between the groups, indicating that younger and healthier people received therapy with the new antiplatelet agents (table 1). Most patients (661/710; 93.1%) received PPI therapy while DAPT was active and after withdrawal (582/661); 88%; 32 patients (4.5% (32/710)) developed a major GI bleeding and 18.9% (134/710) developed anemia. Lower GI bleeding was more frequent than upper GI bleeding (78.1% (25/32) vs 18.8% (6/32) and 3.1% (1/32) had obscure GI bleeding. There were no differences in the occurrence of major GI bleeding (5.1% vs 3.9%, 0.475), non-gastrointestinal bleeding (10.4% vs 10.5%, 0.001), ischemic events (13.6% vs 9.6%, 0.103) or death (4.8 vs 2.1%, 0.066) between patients on DAPT with clopidogrel or new antiplatelets; however, anemia was most common in the group of DAPT with clopidogrel (21.8% vs 15.6%, 0.035). After adjusting for major confounding factors, including age, comorbidities, anticoagu- lant therapy and GI risk, there was no differences in the risk of GI events between groups (clopidogrel vs new agents overall GI events HR: 0.839 (0.579–1.215), major GI events HR: 1.050 (0.448–2.461), minor GI events HR: 0.801 (0.531–1.207).

Conclusion: DAPT is more frequently associated with lower than upper GI bleeding. Prasugrel- or ticagrelor-based DAPT was not associated with increased risk of either GI (upper or lower) bleeding when compared to clopidogrel-based therapy. The potential benefits of the new antiplatelets might be extended to all patients undergoing PCI based on GI risk factors.

Results: 519 patients with a diagnosis of upper gastrointestinal bleeding were included in the study. 279 patients differed from the remaining 240 patients in comorbidity (82.1% vs 37.1%, p < 0.001) and in antipeptide (31.2% vs. 5.4%, p < 0.001), anticoaguclants (26.9% vs.5%, p < 0.001) and NSAIDs (16.1% vs. 30.8%, p < 0.001) use. No differences were found in the need for endoscopic, interventional radiology and surgery procedures; blood units transfusions, days of hos- pital stay, in-hospital rebleeding and in-hospital mortality. Independent predictors for in-hospital mortality in EPs were onset as hematemesis (HR 2.73; 95% CI 1.105–6.84; p = 0.030), rebleeding (HR 6.251; 95% CI 2.731–15.79; p < 0.001) and antiplatelets (HR 0.290%; CI 0.290–9.96; p = 0.046). However, elderly patients presented a higher rate of delayed 6-months mortality (15% vs. 7.7%, p = 0.016) and were related with GI bleeding. Independent predictors for this event in EPs were albumin (HR 0.426; 95% CI 0.236–0.712), and creatinine levels (HR 1.927; 95% CI 1.178–3.150; p = 0.009).

OP028 SHOULD WE BE USING THE SHOCK INDEX TO ASSESS PATIENTS PRESENTING WITH UPPER GI BLEEDING?

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Introduction: Upper GI bleeding (UGIB) is a common cause of hospitalisation. The admission Rockall (ARS), Glasgow-Blatchford (GBS) and AIMS65 scores are validated pre-endoscopy risk assessment tools. The UK NICEPOD report into UGIB used Shock Index (SI = pulse/systolic blood pressure) to assess risk of poor outcome. However existing data on SI are mostly from trauma settings. The limited data in UGIB suggest SI > 0.7, or SI > 1 may predict need for endoscopic therapy or mortality. Our aim was to assess the accuracy of SI to predict clinical outcomes after UGIB.

Aims and Methods: We collected demographic, clinical and laboratory data on consecutive patients admitted to 6 large hospitals across the UK, USA, Denmark, Singapore, and New Zealand over 12 months. We compared the SI, AIMS scores, GBS and AIMS65 and the new international bleeding risk score (IBRS) in their ability to predict need for endoscopic therapy, need for major transfusion (≥4 units PRBCs) and death. We also assessed score thresholds for identifying patients at low risk of death, and whether adding the SI as a parameter to the IBRS improved its predictive accuracy.

Results: 3012 patients (mean age 65yrs; 58% men) were studied. 574 (19%) required endoscopic therapy and 396 (13.3%) needed major transfusion. 30-day mortality was 7%. This table compares AUC/ROCs of the scoring systems for predicting outcomes.

References
**Aim and Methods:** Patients with manometric findings consistent with AC and no obstructive cause without prior therapy were randomly assigned to either LH or POEM from a single tertiary center. Demographic data, procedure info, Eckardt score, LES pressure, follow-up reflux esophagitis, adverse events and length of stay were collected. Student’s t-test, Chi square and Logistic regression analyses were conducted.

**Results:** 40 patients were enrolled (26 M, mean age 48.5) from Mar 16 to Jan 17. 29 patients performed POEM in 20 patients and LH in other 20. Both groups presented significant reduction in Eckardt scores compared to baseline (1.07 vs. 5.06 in POEM and 1.03 vs. 5 in LH, p < 0.001) and in LES pressure (7.89 vs. 7.01 in POEM and 7.03 vs. 6.73 in LH, p < 0.0001). Operative time was significantly lower for POEM (p < 0.001). There were no differences between POEM and LH in length of hospital stay (p = 0.173).

**Conclusion:** POEM as effective and safe as LH for the treatment achalasia but carries shorter duration of procedure. POEM patients present higher esophagitis rate.

**Disclosure:** Nothing to disclose.

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**References**


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**Outcome (AUROC)**

<table>
<thead>
<tr>
<th>Scoring System</th>
<th>Major Endoscopic Therapy (≥4-umits)</th>
<th>Transfusion (30-day)</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI</td>
<td>0.606</td>
<td>0.655</td>
<td>0.611</td>
</tr>
<tr>
<td>GBS 0.747*</td>
<td>0.836*</td>
<td>0.692*</td>
<td></td>
</tr>
<tr>
<td>AIMS65</td>
<td>0.621</td>
<td>0.692</td>
<td>0.785*</td>
</tr>
<tr>
<td>ARS</td>
<td>0.613</td>
<td>0.685</td>
<td>0.759*</td>
</tr>
<tr>
<td>IBRS</td>
<td>0.675*</td>
<td>0.726*</td>
<td>0.863*</td>
</tr>
</tbody>
</table>

\[ p < 0.001 and \ p > 0.001 when compared to SI \]

For predicting need for endoscopic therapy or major transfusion, SI had lower accuracy than GBS and IBRS, but similar to AIMS65 and ARS. In contrast to SI≥1, GBS≥7 correctly identified the majority of patients needing endoscopic therapy (80% vs 21%; p < 0.001). For predicting 30-day mortality, SI had lower AUROC than all other scores. GBS was superior to SI< 1.7 at predicting low-risk of death (mortality rate 0.35% vs 5.2%; p< 0.001). Patients with SI>1 had lower mortality than those with IBRS≥8 (15.3% vs. 31.4%; p< 0.001) and IBRS correctly identified a greater proportion of those who died as being high risk (49% vs 28%; p< 0.001). Adding SI to the IBRS did not improve its predictive accuracy (AUROC 0.864 vs 0.863).

**Conclusion:** Existing pre-endoscopy risk scores are superior to the SI in predicting need for endoscopic therapy, major transfusion or mortality after UGIH. Most patients who reach these important clinical endpoints are classified as low risk by SI.

**Disclosure:** Due to be presented at the British Society of Gastroenterology national meeting in June 2018.

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**References**


significantly higher health care cost. To date, there is no data regarding comparison between EUS-guided coils+CYA vs. EUS-guided coils alone. Aims and Methods: We aim to compare efficacy and safety of coils+CYA vs. coils alone in the EUS-guided management of GOV II and IGV I. Single-center, randomized, controlled trial (March 2016 – June 2017). Study protocol was approved by Institutional Review Board. Written informed consent was obtained. Selection criteria: 18-80 yo, hepatic cirrhosis with endoscopic evidence of GOV II or IGV I (Sarin classification), >50000 platelets/mL, INR ≤2, not into Hepatocellular Syndrome. After randomization, two groups were formed. EUS procedure was performed by a 1st endoscopist, blind to patients' history. EUS follow-up was performed 3 months later. CYA: 120 mg intrasophageal injection, 10% less re-bleeding, preventing 14% GV reappearance and saving 14% re-interventions rate, lower re-bleeding, and GV reappearance prophylaxis; compared with Coils alone, CYA represent an effective technique

Disclosure: Nothing to disclose

Results: Of all study participants 15% reported having IBS, 19% having BS-2w, and 47% being stressed. IBS and BS-2w were strongly correlated (r = 0.6), and these subjects were more often females, were younger, had lower physical activity level, were more often smokers and users of probiotics, were more likely to be stressed and suffered from worse psychological well-being, compared to the healthy subjects. The fecal samples of IBS were significantly enriched with Butyribibacterium (p = 0.030), Dorea (p = 0.039), Fusobacterium (p = 0.027), Streptococcus (p = 0.008) and Streptophyta (p = 0.015), and had significantly less Bacteroides (p = 0.018), Butyricimonas (p = 0.022), Christensenella (p = 0.010), Fecalibacterium (p = 0.048), Lachnobacterium (p = 0.043), Rikenellaceae (p = 0.009), and SH46 (p = 0.001). Individuals who reported having bowel symptoms last 2 weeks were significantly enriched with Blautia (p < 0.001), Dorea (p = 0.013), Ruminococcus (p = 0.008), and Streptophyta (p = 0.004), and had significantly less Christensenella (p = 0.003) and Lachnospiraceae on diarra (p for interaction = 0.002), where the association only occurred in stressed individuals.

Conclusion: This is to the best of our knowledge the first study to investigate relationship between gut microbiota and IBS in a general population. We observed that specific bacteria significantly differed between individuals with and without IBS and bowel symptoms. Diarrhea was the bowel symptom with most and strongest associations of different microbiota. Self-perceived stress was found to modify the composition of gut microbiota in relation to bowel symptoms.

Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018
Microbiota in IBS: From bench to bedside – Room N2

OP030 GUT MICROBIOTA CHARACTERISTICS ASSOCIATE WITH IRRITABLE BOWEL SYNDROME AND SPECIFIC BOWEL SYMPTOMS IN A POPULATION-BASED STUDY FROM SWEDEN

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Introduction: Abdominal pain in association with altered bowel habits, without any obvious organic changes, are called functional bowel disorders, with irritable bowel syndrome (IBS) being the most common entity. The etiology is unknown, but an altered gut microbiota has been observed in some studies, with incongruent results.

Aims and Methods: Our aim was to examine the gut microbiota composition in a large population-based cohort, the Malmö Offspring Study (N = 1888, mean age 40b, 53% with respect to presence or absence and severity of bowel symptoms and self-perceived stress. The participants completed questionnaires about socioeconomic factors, lifestyle and medical history, and were asked if they have (yes/no) 1) IBS, 2) experienced any bowel symptoms during the last 2 weeks (IBS-2w), 3) been commonly stressed during the last 12 months. Participants with BS-2w completed a Visual Analog Scale for Irritable Bowel Syndrome (VAS-IBS) including abdominal pain, diarrhea, constipation, bloating and flatulence, vomiting and nausea and psychological well-being. The 16S rRNA gene was sequenced (2300bp, V1-V3) from fecal samples. To identify OTUs at genus level the sequences were binned together by FLASH and QIIME and matched to the Greengenes (13.8) reference database. The OUT data was normalized using cumulative sum scaling, and rare- and low abundance OTUs were filtered out, resulting in 67 identified genus. Associations between the gut microbiota and IBS and BS-2w were analyzed by logistic regression, and items in VAS-IBS by general linear model, adjusting for age, sex, physical activity and smoking. We further studied if the associations were modified by self-perceived stress.

Results: Of all study participants 15% reported having IBS, 19% having BS-2w, and 47% being stressed. IBS and BS-2w were strongly correlated (r = 0.6), and these subjects were more often females, were younger, had lower physical activity level, were more often smokers and users of probiotics, were more likely to be stressed and suffered from worse psychological well-being, compared to the healthy subjects. The fecal samples of IBS were significantly enriched with Butyribibacterium (p = 0.030), Dorea (p = 0.039), Fusobacterium (p = 0.027), Streptococcus (p = 0.008) and Streptophyta (p = 0.015), and had significantly less Bacteroides (p = 0.018), Butyricimonas (p = 0.022), Christensenella (p = 0.010), Fecalibacterium (p = 0.048), Lachnobacterium (p = 0.043), Rikenellaceae (p = 0.009), and SH46 (p = 0.001). Individuals who reported having bowel symptoms last 2 weeks were significantly enriched with Blautia (p < 0.001), Dorea (p = 0.013), Ruminococcus (p = 0.008), and Streptophyta (p = 0.004), and had significantly less Christensenella (p = 0.003) and Lachnospiraceae on diarra (p for interaction = 0.002), where the association only occurred in stressed individuals.

Conclusion: This is to the best of our knowledge the first study to investigate relationship between gut microbiota and IBS in a general population. We observed that specific bacteria significantly differed between individuals with and without IBS and bowel symptoms. Diarrhea was the bowel symptom with most and strongest associations of different microbiota. Self-perceived stress was found to modify the composition of gut microbiota in relation to bowel symptoms.

Disclosure: Nothing to disclose

OP031 BACTERIA MODIFIED BILE ACIDS – A POSSIBLE MECHANISM FOR SYMPTOMS SEVERITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction: The intestinal microbiota has been implicated as an important factor in the pathogenesis of irritable bowel syndrome (IBS) however the mechanisms by which the intestinal microbiota affects the presence and/or severity of IBS symptoms are unclear. Recent advances suggest a role for bile acids in causing alterations in bowel functions including stimulating bowel secretion and increase in peristalsis and symptoms of diarrhea and watery stools that are commonly reported in patients with IBS. It is well known that the conversion of primary bile acids into (highly colonic irritant) secondary bile acids is entirely dependent on intestinal bacterial enzymes. However, the relation between the intestinal microbiota, bile salts composition and metabolism and IBS clinical symptoms.
Fresh fecal samples were collected from subjects who met the Rome III criteria for IBS, and non-IBS controls. IBS principal symptoms (abdominal pain, change in bowel movements and bloating) were assessed using validated measures on a daily diary. Overall IBS symptoms were assessed using the IBS symptom severity scale (IBS-SSS) and intestinal sensation by Visceral Sensitivity Index (VSI). The intestinal permeability was investigated by caecum supernatant and analyzed using an in-house validated, published pipeline (1), predicted metagenomics with PICRUSt(2) and concentrations of fecal bile acids by UPLC-MS system(3).

Mann-Whitney test was used for univariate analysis, and PERMANOVA(3) was used for between group comparisons. Pearson correlations were performed with log transformed bile acid concentration and clinical data.

Results: 3 Fecal samples from 25 IBS and 27 non-IBS subjects were analyzed. We identified 9 major phyla of which Firmicutes (58.22 ± 2.56%, mean ± SEM), Bacteroidetes (36.32 ± 2.84%), Actinobacteria (2.89 ± 0.66%) and Proteobacteria (1.37 ± 0.24%) were the most abundant in all subjects. There were no between groups-composition difference at the phylum and community levels. We identified 21 bile acids in stool, with no significant difference in concentration of individual bile acids between IBS and non-IBS samples. In patients with IBS, fecal conjugated primary bile acids (r = 0.62, p = 0.014) and conjugated secondary bile acids (r = 0.49, p = 0.074) and conjugated tertiary bile acids (r = 0.74, p = 0.022) showed a positive relationship with IBS-SSS. The 3rd conjugated bile acid also correlated with pain severity in IBS (positive correlation, r = 0.6809, p = 0.0435) and VSI score (negative correlation, r = 0.7905, p = 0.0195). No association was found between unconjugated bile acids and any of the clinical variables. Predictive metagenomic analysis of bile salt hydrolase (BSH) bacterial enzymatic activity showed negative correlation with glycine-conjugated primary bile acids (r = -0.473, p = 0.0305). More interestingly, an inverse trend was found between fecal BSH activity and IBS-SSS (r = -0.416, p = 0.0458).


Disclosure: The study was supported by NIH. JCS and BC are current employee of NIH and CLB is a former employee of NIH and other authors declare no conflict of interest.

References

OP032 RESTORING EPITHELIAL BARRIER IN IRRITABLE BOWEL SYNDROME: THE POTENTIAL ROLE OF ESCHERICHIA COLI NISSLE 1917

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Introduction: The intestinal barrier and epithelium play a key role in the pathogenesis of several gastrointestinal diseases, such as inflammatory bowel diseases and Irritable Bowel Syndrome (IBS). Among possible pharmacological interventions to restore epithelial barrier, an interesting perspective is represented by probiotics and prebiotics commonly used in clinical practice. Escherichia coli Nissle 1917 (EcN) is a probiotic effective in the maintenance of remission of ulcerative colitis, although the underlying molecular mechanisms remain unclear.

Aims and Methods: The aim of this study was to characterize the potential effect of EcN in reversing the increase of intestinal permeability caused by the media tors spontaneously released by IBS biopsies, by known inflammatory stimuli and to evaluate the molecular mechanisms involved. CaCo-2 cells were used as an in vitro model of intestinal epithelial barrier. Two concentrations of EcN (104 and 105) were applied to CaCo-2 with or without SLIGRL (a protease-activated receptor-2 activating peptide), tumor necrosis factor (TNF)-α, interferon (IFN)-γ and inflammatory mediators spontaneously released (SUP) by mucosal biopsies of patients with IBS and healthy controls (HC). Paracellular permeability was evaluated using sulfonic acid-conjugated to fluorescein (FITC). qPCR was used to assess mRNA expression of tight junction proteins, zonula occludens-1 (ZO-1), claudin-1 and occludin.

Results: EcN induced a dose-dependent reinforcement of CaCo-2 monolayer of 52% (104, p < 0.05) and 32% (105) compared to untreated CaCo-2 (CTR). SLIGRL 30uM and 200uM induced a significant increase in CaCo-2 permeability compared to CTR (p < 0.05); the co-incubation of SLIGRL and EcN induced a recovery of epithelial integrity compared to SLIGRL alone. TNF-α and IFN-γ strongly induced EcN sensitivity compared to EcN alone in Spontaneous PB of patients with IBS induced a significant increase of paracellular permeability compared to HC SUP (p < 0.05). The co-incubation of EcN with IBS-D or -C SUP induced a recovery of permeability rate compared to SUP alone (p < 0.05). No effect of EcN was observed with IBS-M SUP. qPCR analysis showed EcN induced a significant increase in Zo-1 and occludin expression compared to CTR. Permeability rate significantly correlated with severity and frequency of abdominal pain and distension.

Conclusion: EcN reinforces the intestinal epithelial barrier enhancing the expression of tight junction proteins. EcN reverses the increase of epithelial monolayer permeability induced by inflammatory stimuli and IBS SUP. These results pave the way to future studies to understand the potential application of EcN in IBS.

Disclosure: The aim of this study was to assess the effect of modulating the gut microbiota by faecal microbiota transfer (FMT) on visceral hypersensitivity in IBS patients. As part of a randomised, placebo-controlled, double-blinded clinical trial (registered at clinicalTrials.gov under NCT02092402), 16 IBS patients were randomly assigned to receive FMT either from a healthy donor (treatment group), or from their own faecal material (placebo group). The faecal material was administered into the caecum by whole colonoscopy after a bowel cleansing. In addition to completing questionnaires for assessing IBS symptoms (IBS-SSS, GSRS-IBS), the patients underwent a barostat procedure at baseline and 8 weeks after FMT. Before assessment, patients fasted overnight and were placed in a left lateral position. The barostat catheter (600 mL, Mui Scientific, Ontario, Canada) was placed 15 cm into the rectum. Rectal distensions were performed according to previous studies using an electronic distension barostat device (Distender series II, G&J Electronic Inc., Toronto, Canada) [2, 3]. In short, intermittent semi-random staircase distensions of 60 seconds duration were separated by intervals of 30 seconds of baseline pressure. During each distension, subjects reported their perception of pain, discomfort, and urge, respectively, using 100 mm visual analogue scales (VAS). VAS scores were fit to a logistic function for model and evaluated at fixed pressures of 40, 50, and 60 mmHg. The fitted baseline-corrected VAS values were then compared before and after FMT using Wilcoxon signed rank test, and between treatment and placebo using Mann-Whitney U-test.

Results: Evaluable barostat data was available from n = 14 participants. No statistically significant differences in the patients’ perception of pain and discomfort were found before and after FMT, neither in the treatment (n = 8) nor the placebo group (n = 6). The perception of urge was significantly lower in the placebo group compared to the treatment group at 20, 40, and 50 mmHg 8 weeks after FMT. Even though a relief in symptoms after FMT was found in the treatment group compared to baseline, this was not associated with decreased visceral hypersensitivity.

Conclusion: The beneficial effect of FMT from healthy donors on the symptom scores in IBS patients does not seem to be mediated by reduced hypersensitivity. The reduced perception of urge in the placebo group could be a result of the bowel cleansing prior to the colonoscopy. The absence of this effect on urge in the placebo group compared to the treatment group might be due to a reaction of the host mucosa to the introduction of a new, foreign microbiota. Further analyses need to be performed to study what contributes to the positive effect of FMT in IBS patients.

Disclosure: Nothing to disclose.

References
MICROBIOTA IN PATIENTS WITH IRRITABLE BOWEL SYNDROME: RESULTS FROM A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED STUDY

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Introduction: Irritable bowel syndrome (IBS) is associated with an intestinal dysbiosis, and fecal microbiota transplantation (FMT) has been hypothesized to have a positive effect in patients with IBS. We performed a randomized, double-blind placebo-controlled trial to investigate if FMT resulted in an altered gut microbiota and improvement in clinical outcome in IBS patients.

Aims and Methods: We performed this study in 52 adult patients with IBS (based on Rome III criteria) with moderate to severe disease activity based on a symptom score of at least 175 in the IBS-severity scoring system (IBS-SSS). Our primary endpoint was the difference in improvement in IBS-Score at 2 months. At the screening visit, clinical history and symptoms were assessed and fecal samples were collected. Patients were then randomized to FMT or placebo capsules for 12 days and followed for 6 months. Study visits were performed at baseline, 1 month, 3 months and 6 months, where patients were asked to register their symptoms using the IBS-SSS and IBS specific quality of life (IBS-QoL). Prior to each visit fecal samples were collected, inclusive of a sample 3 days after treatment was completed (day 15).

Results: A significant difference in improvement in IBS-SSS score was observed 3 months after treatment (p = 0.012) favoring placebo. This was similar for IBS-QoL data after 3 months (p = 0.003) favoring placebo. Patients receiving FMT capsules had an increase in biodiversity to the extent that this group wasn’t statistically distinguishable from the donors, and the placebo patients remained statistically indistinguishable from their pre-treatment state (Mann-Whitney U-test, p < 0.05). All participants completed the treatment and no severe adverse events were registered throughout the study period.

Conclusion: In a randomized double-blind placebo-controlled study, we found that FMT changed gut microbiota in IBS patients. But patients in the placebo group experienced greater symptom relief compared to the FMT-group. The gut microbiota is not enough to obtain clinical improvement in IBS. However, different study designs and larger studies are required to examine the role of FMT in IBS.

Disclosure: Nothing to disclose
analytical retrospective cohort study on all patients (178) with a distal pancreatectomy. The end point was clinical success of endoscopic treatment defined as a complete resolution of POPF discharge or fluid collection (PFC) or size < 2 cm, with association of symptoms resolution, without the need for percutaneous drainage or surgery. Secondary endpoints were technical success (feasibility and efficacy of stent placement), complication rate of endoscopic procedures, and reintervention rate. Categorical variables were compared using χ² test. Normally distributed continuous variables were analyzed by Student t-test and non-normally distributed variables by the Mann-Whitney U-test. Patients were divided in 3 groups (ERCP only, EUS drainage only, both EUS and ERCP).

Results: Out of 173 surgical patients, 58 POPF grade B and C were treated by both procedures (n = 31, 53.4%), EUS alone (n = 13, 22.4%) or both procedures (n = 14, 24.1%). There was a significant shift from ERCP alone (100% of cases between 2000-2005) to EUS alone and combined with ERCP (23% 2006-2010, and 48% 2011-2016). Technical success rates were similar in all groups (87%-100%). Clinical success in patients treated by ERCP only was 64.5% (20/31) and as high as 96.3% (26/27) in patients in whom EUS was performed at any points during endoscopic treatment (p = 0.003). The overall all re-intervention rate was 44.8%, significantly lower when EUS was part of the treatments (20 and 23% vs. 55%, p < 0.05). The complication rates in the ERCP, EUS and ERCP+EUS groups were respectively 20% (n = 6/30), 30.8% (n = 4/13) and 0% (p = 0.346), with a decrease to only 2 AE in the last 5 years.

Conclusion: Endoscopic treatment was highly successful in treating POPF after distal pancreatectomy, with a significantly better clinical success rate of EUS drainage resulting in less reinerventions when needed. We therefore suggest considering EUS as a primary approach, reserving ERCP for cases with pancreatic ductal strictures or inaccessible post-operative collections or fistulas.

Disclosure: Nothing to disclose

OP039 TECHNICAL ISSUES DURING EUS-GUIDED PLACEMENT OF LUMEN APPOSING METAL STENTS: DEFINITION AND CLASSIFICATION, INCIDENCE AND RISK FACTORS, ENDOSCOPIC MANAGEMENT AND EFFECT ON ENDOSCOPIC OUTCOMES

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Introduction: Lumen Apposing Metal Stents (LAMS) have been recently introduced into clinical practice. A variety of Technical Issues (TIs) can appear during LAMS placement but we lack a common terminology to address them and their consequences on clinical outcomes are unknown.

Aims and Methods: We define TI as any alteration in the normal sequence of LAMS placement (TI is not synonymous with adverse event). Consecutive patients undergoing an endoscopic procedure which included the placement of a transmural LAMS between May 2011 and June 2017 in a single tertiary center were included (table 1). Data were prospectively collected and retrospectively analyzed. We propose a novel classification of TIs, categorized in access failure, liberation failures, misplacements and dislodgment. We analyzed their rates, risk factors, endoscopic management and its effect on clinical outcomes.

Results: A total of 298 procedures (47.4% pancreatic fluid collections, 33.5% pancreato-biliary drainages including gallbladder drainages, 13.8% enteric anastomoses, 5.1% others) were analyzed. TI occurred in 27% of them, founding a significant higher rate in technical (99.5% vs 52.6%, p < 0.001), procedural (100% vs 82.1%, p < 0.001) and clinical success (88% vs 77.9%, p = 0.03) when compared with procedures without TIs. Distal (25.6%) and proximal flange misplacements (17.9%) and complete liberation failures (17.9%) were the most frequently encountered TIs. Forceps repositioning, placement of a new LAMS or another through-the-LAMS stent were the most frequent rescued techniques. 13 (16.7%) TIs could not be saved. Enterostomas (OR 3.42 (1.22-9.62) and malignant disease (OR 3.32 (1.05-10.56)) were risk factors associated to the development of TIs on multivariable analysis.

Conclusion: Even in expert hands, TIs are frequent during transmural EUS-guided LAMS placement, typically in distal flange misplacement. The knowledge of salvage techniques using other stents makes rescue possible in more than 80% of cases.

Basal Features N (%) [Characteristics of the study population and the procedure]

<table>
<thead>
<tr>
<th>Basal Features</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>71.5 (58.3-83.5)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>184 (63.7%)</td>
</tr>
<tr>
<td>Malignant disease, n (%)</td>
<td>75 (26%)</td>
</tr>
<tr>
<td>LAMS type, n (%)</td>
<td>170 (58.8%)</td>
</tr>
<tr>
<td>“Free-Hands” Technique</td>
<td>42 (14.5%)</td>
</tr>
<tr>
<td>Access, n (%)</td>
<td>215 (74.4%)</td>
</tr>
<tr>
<td>Jejunum Esophagus Missing</td>
<td>6 (2.1%)</td>
</tr>
</tbody>
</table>

Disclosure: Nothing to disclose

OP040 ROLE OF EUS-GUIDED TRANSMURAL DRAINAGE IN COMBINED MALIGNANT BILIARY AND GASTRIC OUTLET OBSTRUCTION

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In 7/29 PP cases, spontaneous resolution was observed; 3/29 PP and 3/31 WON were lost on follow-up, 19/19 PP and 10/10 WON underwent on EUS-guided stent placement, with 100% technical success. Time of procedure per stents as follows: Hot-AXIOS™ 5 (4-6) min, NAGI™ 19 (18-22) min, SPAXUS™ 20 (18-22) min (p = 0.01). In PP cases, a bleeding episode occurred 48 hours after a Hot-AXIOS™ placement (p = 0.58). In WON cases, an obstruction was reported with a Hot-AXIOS™, and a bleeding episode occurred 48 hours after a NAGI™ placement (p = 0.69). Both bleeding events required surgical management. Overall reintervention rate was 10% (3/29) with no reports from plastic stent cases. Overall 30-day mortality was 0%. All stents were finally removed. On this series, none of the cases needed percutaneous drainage. Overall median time from stent placement to complete drainage & removal was 8 (1-200) weeks. Overall median longest follow-up time was 41 (8-120) weeks. 3 cases (2 SPAXUS™, 1 NAGI™) cannot be released due to device failure, and no cases of Hot-AXIOS™ or plastic stent.

Conclusion: Neither stent material nor trademark present a significant impact on clinical outcomes, surgical and adverse events rate was 10% (3/29) with Hot-Axios™ seems to be more practical and faster for placement.

Disclosure: Nothing to disclose
Endoscopic ultrasound guided gastroenterostomy: What is the learning curve?

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Introduction: Endoscopic ultrasound guided gastroenterostomy (EUS-GE) is a minimally invasive option for patients with gastric outlet obstruction. It involves creating a gastroenterostomy fistula via EUS and deploying a lumen-apposing metal stent (LAMS) across the fistulous tract. It is a technically challenging procedure requiring combined intraluminal and EUS approaches.

The aim of this study was to determine the learning curve for EUS-GE.

Aims and Methods: Consecutive patients undergoing EUS-GE by a single operator were included from a prospective registry from Aug 2014 to Oct 2017. Data were collected at a median follow-up of 390 days. Non-linear regression and CUSUM analyses were conducted for the learning curve. Clinical success was defined as tolerating a diet.

Results: A total of 103 patients with a median age of 76.1 years (IQR: 61.3–84.3), 58 males, were included. Most frequent diagnoses were pancreatic adenocarcinoma (56.3%), ampulloma (10.7%), GOO and biliary obstruction were treated within the same week in 39/103 patients. Most biliary obstructions were distal (93/103). Initial management was performed with transluminal stenting in 69/103 patients and EUS-D in 34/103 (20 cholecodochoduodenostomies, 13 hepaticogastrostomies, 1 gallbladder drainage). Technical success was achieved in all patients undergoing EUS-D and in 67/69 of the transpapillary drainage group; clinical success was reached in 88.5% EUS-Ds and in 95.6% transpapillary drainages. Duodenal strictures were mostly Mutaginous types I (48.5%) and II (49.5%). GOO score at the time of treatment was ≤ 3 in 87.9% of cases. Initial management was performed with intraluminal SEMS in 100/103 cases and with EUS-GJ in 3 patients. Technical success was achieved in 96.8% and clinical success in 97.5%. Thus, initial management included intraluminal duodenal and biliary stents in 67/103 (65.1%) and EUS-D with intraluminal duodenal stents in 33/103 (32%). Follow-up was available in 89 patients, with a median time of 247 days (91-547), 60% of patients had 64+ follow-up, 4.4% completed the study period and 25% were lost after a median follow-up of 147 days (55-248). We observed a total of 79 biliary events (median 0 events/patients, IQR 0–1). Obstructive jaundice without cholangitis was the most common event (34/79) followed by cholangitis with and without hyperbilirubinemia (14/79). Biliary events were collected. Non-linear regression and CUSUM analyses was conducted for the learning curve. Clinical success was defined as tolerating a diet.

Conclusion: The role of EUS-guided transmural approaches in malignant biliary obstruction and GOO is expanding, but further data are needed before proposing management bundles. Our data suggest EUS-D reduces the need for further endoscopic procedures during follow-up, while EUS-GJ is being increasingly employed.

Disclosure: Dr. Manuel Perez-Miranda is a consultant for Boston Scientific and M.I. Tech and has lectured for Boston Scientific and Olympus. None of the remaining authors have potential conflicts of interests.

References
Introduction: The omega-3 polyunsaturated fatty acid (PUFA) eicosapentaenoic acid (EPA) and aspirin both have proof-of-concept for colorectal cancer (CRC) chemoprevention, aligned with an excellent safety profile.

Aims and Methods: We performed a randomised, blinded, placebo-controlled, 2×2 factorial trial to determine the effects of EPA and aspirin on preventing colorectal adenomas. We also assessed the safety and tolerability of EPA, in free fatty acid (FFA) or tri-gluceryl (TG) form, and aspirin. NHS Bowel Cancer Screening Programme (BCSP) patients (aged 55-73) identified as ‘high risk’ (≥5 small ≤10mm colorectal adenomas; or ≥3 colorectal adenomas, if one ≤10mm) at screening colonoscopy were randomly allocated to receive 99%EPA-FFA 2g or 90%EPA-TG 2780mg (equivalent to 2g FFA) daily, or identical placebo capsules; AND aspirin 300 mg daily, or an identical placebo

Results:
- There was no evidence of any difference in ADR between EPA users (62%) and non-users (61%) (risk difference [RD] -0.6% [-8.5, 7.2]). There was no evidence of an effect on advanced ADR among high-risk individuals (EPA vs. placebo: 18% vs. 20% [RD -1.5% [-4.7, 1.8]]).
- No significant effect was observed on the number of polyps identified. There was no evidence of any difference in ADR at between EPA users (62%) and non-users (61%) (risk difference [RD] -0.9% [95% CI -8.8, 6.9]). There was no evidence of an effect on advanced ADR of either EPA (RD -0.6% [-4.4, 3.1]) or aspirin (RD -0.3% [-4.1, 3.5]).

Conclusion: Neither EPA nor aspirin treatment was associated with a reduction in CRC, but both agents displayed evidence of chemopreventive efficacy, based on adenoma number reduction, which was adenoma type- and location-specific, and is compatible with the known anti-(right-sided) CRC activity of aspirin. Best use of EPA and aspirin may need a precision medicine approach to adenoma recurrence based on colorectal adenoma sub-types. ISRCTN59526847

Disclosure: This project was funded by the EME Programme, an MRC and NIHR partnership. The views expressed in this publication are those of the author(s) and not necessarily those of the MRC, NHS, NIHR or the DoH. MH has received an unretracted scientific grant for another project and also conference travel funding from SLA Pharma AG. MAH has provided paid consultancy for Bayer AG and Theris Pharma.
Aims and Methods: We collected clinical, endoscopic and histopathology data at index colonoscopy and we included both grown and stable lesions. Of the 19 endoscopically correctly diagnosed T1 CRCs, 17 (89.5%) were directly endoscopically resected. There were no correctly diagnosed T1 CRCs that were regressed after a surveillance interval of 3 years. Based on volumetric change, polyps were classified as having 30% regression (PCCRC-3yr), 30% growth (PCCRC-3yr), stable (PCCRC-3yr), or regressed (PCCRC-3yr) or regressed (PCCRC-3yr) or regressed (PCCRC-3yr). All samples were MMR proficient. No relation between growth and CIMP was observed. Based on the molecular definition of having ≥2 CAEs, 9% of all lesions were classified as being at high risk of progression. These lesions included both grown and stable lesions.

Conclusion: Molecular classification, together with adenoma to carcinoma progression are more frequent in growing polyps. The observation that high-risk lesions remained stable and grew, but not amongst regressing polyps, is relevant for screening and surveillance strategies.
Of the 78 endoscopically not as such recognised T1 CRCs, 36 T1 CRCs (46.2%) were resected endoscopically and had been followed up accordingly. Post-resection surveillance guidelines, 2 lesions showed recurrence within 3 years. (Table 1). 34 endoscopically not as such recognised T1 CRCs (45.6%) underwent surgery after an initial attempt at endoscopic resection. Histopathology of the resection specimen showed no residual submucosal invasion in 16 cases (47.1%). The remaining 8 endoscopically not as such recognised T1 CRCs (10.3%) were directly referred for surgery, because these lesions were too difficult to resect endoscopically due to their size and location. Logistic regression analysis showed that distant location (OR 3.83, 95% CI: 2.03–7.25), non-pedunculated shape (OR 2.03, 95% CI: 1.26–3.27) and estimated CRC based on microscopc appearance (OR 4.90, 95% CI: 2.11–11.35) were independent risk factors for submucosal invasion. Conclusion: Approximately 80% of the T1 CRCs in our national CRC screening program are not recognised as early CRCs. Uncertainty about diagnosis may lead to additional colonoscopies, delay in surgery and surgical over-treatment. Improvement in the recognition and treatment of early CRC is needed to further optimize the outcomes of our national CRC screening program.

For Table 1. Treatment strategies of T1 CRCs in the national screening program.

<table>
<thead>
<tr>
<th>Endoscopically not recognised T1 CRCs (n = 78)</th>
<th>Direct surgery</th>
<th>- Residual within 3 years</th>
<th>Surgery after initial attempt of endoscopic resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>18</td>
<td>2</td>
<td>34</td>
</tr>
</tbody>
</table>

Disclosure: R.M.G. Bogie and S. S-guarda-Duasascuela received an unrestricted research grant from Pentax Europe.

MONDAY, OCTOBER 22, 2018 14:00–15:30
Autoimmune hepatitis – Room F1

OP049 THE ANTI-INFLAMMATORY RECEPTOR TREM2 PROTECTS THE LIVER FROM CHOLESTATIC INJURY IN MICE
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Introduction: Cholestasis is a common feature of different cholangiopathies such as primary biliary cirrhosis (PBC). Cholestasis causes liver inflammation and induces centrilobular hepatocyte death, thereby inducing ductular reaction and activation of non-parenchymal liver cells [i.e. kupffer cells (KC) and hepatic stellate cells (HSC)] that ultimately result in biliary fibrosis. Liver injury leads to alterations in the intestine epithelial barrier, enabling the translocation of bacterial components from the gut via the portal vein. In the liver, these bacterial components bind to toll-like receptors (TLRs) expressed in KC and HSC promoting inflammation and progression of the wound-healing response. The triggering receptor expressed on myeloid cells 2 (TREM2) is an anti-inflammatory receptor that inhibits TLR-mediated signalling.

Aims and Methods: This study aims to evaluate the role of TREM2 in cholestasis. With this purpose, TREM2 expression was analyzed in the liver of PBC and PSC patients and normal controls. Wild type (WT) and Trem2-/- knock out (Trem2-/-) mice were subjected to bile duct ligation (BDL), or sham, for 7 days. Thereafter, sera were collected for the analysis of biochemical markers and livers were obtained for further histological and gene expression analysis. In vitro, KC’s were wounded from WT and Trem2-/- mice, treated with lipopolysaccharide (LPS) and cytokine and chemokine expression was assessed.

Results: TREM2 expression is upregulated in the liver of PBC and PSC patients as compared to healthy controls; this receptor was also upregulated in a BDL based model of murine cholestasis. After BDL, Trem2-/- mice showed exacerbated liver injury with increased hepatocyte necrosis and immune-cell infiltration compared to WT, as assessed by H&E staining. This was accompanied by augmented expression levels of cholangioyte (Cx-7 and Cx-19) and proliferation markers (Ki67 and PCNA), indicating that Trem-2-/-; animals suffered exacerbated ductular reaction. Likewise, Colta1 and α-Sma mRNA levels revealed enhanced fibrogenesis in Trem2-/-; mice compared to WT after BDL. In addition, the expression of proinflammatory cytokines (Il-6 and Tnfα) and chemokines (Mcp-1 and Cxcl1) were upregulated in these mice. The number of neutrophils infiltrating the liver was also increased in Trem2-/-; mice. LPS-treated Trem2-/-; KC displayed increased expression of pro-inflammatory (Il-6, Il-1B and Cxcl2), but not pro-fibrogenic (Ccl4) cytokines. In addition, Trem2-/-; mice showed a higher proliferation of KCs, suggesting an impaired autologous cell-recruitment and/or limited KC apoptosis.

Conclusion: TREM2 is overexpressed in the livers of PBC and PSC patients and during experimental cholestasis in mice. This receptor negatively regulates TLR4-mediated pro-inflammatory cytokine expression in KC, thereby protecting the liver from cholestatic injury in mice.

Disclosure: Nothing to disclose

OP050 TARGETING LIVER INFLAMMATION USING CD64-TARGETED LIPID NAPROTIALES AS A NOVEL DRUG DELIVERY SYSTEM
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Introduction: Inflammatory macrophages play a critical role in liver inflammation. Hepatocellular damage, instigated by viral infections, alcohol abuse or metabolic syndrome, results in the recruitment and activation of inflammatory cells mainly macrophages in the liver. The inflammatory macrophages initiates the process of liver injury progression from liver fibrosis to cirrhosis and hepatocellular carcinoma. Therefore, selective targeted inhibition of the inflammatory macrophages would be a promising approach to attenuate liver inflammation or inflammatory liver diseases. We identified CD6 receptor as a prospective target for pro-inflammatory macrophages.
Aims and Methods: In this study, we developed a novel delivery system i.e CD64-targeted EP to achieve M1-specific uptake and to selectively deliver anti-inflammatory drugs to inhibit M1 inflammatory macrophages thereby ameliorating liver inflammation. Specificity of CD64 receptor was evaluated in vitro in murine and human macrophages and in vitro in CCL4-induced acute liver inflammation mouse model. Novel CD64 targeting peptide was designed and CD64 targeting peptide coated liposomes were synthesized, characterized and evaluated for M1-specific uptake in murine and primary human macrophages using FACS. Prednisolone-encapsulated CD64-targeted liposomes were synthesized, characterized and investigated for efficacy in vitro in RAW macrophages, human THP1 monocytes, primary bone marrow derived macrophages (BMDMs), primary human monocytes, primary human Kupffer cells, and in vivo in acute CCL4-induced liver injury mouse model.

Results: Significant up-regulation of CD64 receptor was observed in murine and human LPS- and IFN-α-treated primary macrophages. CD64-targeted liposomes showed significant reduction in M1-specific inflammatory markers (i.e. iNOS, IL-6, IL-1β and TNFα) in vitro in RAW macrophages, human THP1 monocytes, primary murine BMDMs, primary human monocytes and primary human Kupffer cells. In vivo, prednisolone-encapsulated targeted liposomes demonstrated substantial liver uptake, highly significant attenuation of acute liver inflammation and fibrotic parameters as compared to free prednisolone and non-targeted liposomes.

Conclusion: This study presents a novel strategy to selectively target M1 macrophages therefore holds great promise for diagnosis and therapeutic treatment of liver fibrosis and inflammatory liver diseases.

Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 14:00:15:30

 Advances in pancreatic-biliary endoscopy – Room K

OP051 IMPACT OF ELECTRICAL PULSE CUT MODE DURING ENDOSCOPIC PAPILLECTOMY: A PROSPECTIVE MULTICENTER RANDOMIZED CLINICAL TRIAL

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2Tokyo Medical University, Gastroenterology and Hepatology, Tokyo, Japan

Aim: To compare the outcomes of endoscopic papillotomy (EP) using two different cutting modes (Endocut vs. Autocut) during EP, in terms of immediate bleeding and delayed adverse events.

Methods: We conducted a prospective, multicenter, randomized, single blind, parallel group, controlled clinical trial in patients with ampullary adenoma who were undergoing EP. Randomization was performed using a computer-generated randomization list. After EP, patients were randomized to undergo either EP with “Endocut” (EP-E) using a combined monopolar and bipolar stock tip or EP with “Autocut” (EP-A) with the same stock tip. The primary outcome was a composite of immediate bleeding and delayed adverse events at the time of the clinical follow-up assessment. Secondary endpoints were the time of follow-up, the rate of delayed bleeding, and the rate of delayed adverse events.

Results: From October 2016 to August 2018, 91 patients were randomized, 46 for EP-E and 45 for EP-A. The median age was 72 years (range 26 to 88). There were no significant differences between groups for age, gender, history of upper gastrointestinal bleeding, body mass index, and indication for EP. No significant difference was observed in the rate of immediate bleeding between groups (p = 0.44). Of the 91 patients, 80 (88%) had complete data. In the EP-A group, 8 patients (26.7%; 7 mild, 1 moderate) had acute liver injury that required hospital admission. In the EP-E group, the incidence of acute liver injury was 9 (30.0%; 8 mild, 1 moderate). The primary outcome did not differ between groups (p = 0.02). There were no cases of delayed bleeding and another adverse event were secondary endpoints.

Conclusion: EP-E mode demonstrated a trend toward higher success rate for EP (p = 0.02). However, the rate of delayed bleeding and delayed adverse events were similar between groups. EP-E mode therefore requires further study to confirm the efficacy and safety.

Disclosure: Nothing to disclose

Reference


OP052 LUMEN-APPOSING METAL STENTS (LAMS) FOR PANCREATIC FLUID COLLECTIONS: NEW INSTRUMENTS ARE SAFE AND ASSOCIATED WITH A LOW RATE OF DELAYED ADVERSE EVENTS AT THE TIME OF CLINICAL FOLLOW-UP: A MULTICENTER RETROSPECTIVE ANALYSIS

D. Yang1, Y. Peribam2, T. Kerdspirirat1, A. Prabhu1, A. Manvar1, S. Hoc1, D. Punn1, R. Kewsani1, D. Shah1, A. Wang1, E. Quintero1, J. Buscaglia1, J. Storms1, H. Alasian1, P. Dragnich1, A. Siddiqui2

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2University of Florida, Gastroenterology, Gainesville, United States

Aims and Methods: Evaluate clinical outcomes at the time of follow-up imaging and endoscopy after LAMS insertion for symptomatic PFC. Multicenter retrospective analysis of consecutive patients with EUS-guided LAMS placement for symptomatic PFC from January 2016 to December 2018.

Main outcomes included resolution of the PFC on follow-up imaging, and findings on follow-up endoscopy after initial LAMS placement, including the rate of adverse events (e.g. delayed bleeding, stent occlusion/migration, buried stent syndrome).

Results: A total of 122 patients (mean age 51 years; 68% male) underwent successful LAMS insertion for 56 WONs (88%) and 55 PPs (95%). The mean size of the PFC was 10.6 cm. Resolution of PFC on cross-sectional imaging was significantly higher for PP (96%; 50 of 52 patients) vs. WON (62%; 34 of 54 patients) at a median of 4 weeks after LAMS insertion (p = 0.001). There were no cases of delayed bleeding. There were no patients lost to follow-up. Size of PFC, diameter of LAMS (10 mm vs 15 mm), additional stents through LAMS (yes vs no), and debriement (yes vs no) were not associated with the likelihood of stent occlusion seen on follow-up endoscopy on multivariate analysis.

Conclusion: EUS-guided LAMS placement for PFC is safe, with serious adverse events encountered at the time of clinical follow-up and delayed adverse events. The rate of PFC resolution on imaging at a median of 4 weeks after LAMS insertion was significantly lower for WON vs. PP. Future large prospective studies are needed to better define the course of PFCs and optimize management protocol for patients with PFC treated with LAMS.

Disclosure: Nothing to disclose

Reference


OP053 OPTIMIZING OUTCOMES OF SINGLE OPERATOR CHOLANGIOSCOPY (SOC)-GUIDED BIOPSES: RESULTS OF A RANDOMIZED TRIAL

J.Y. Bang1, A. Navaneethan1, M. Hasan1, K. Krall1, R. Hawes1, S.S. Varadarajulu1,2,3,4,5

1Florida Hospital, Center for Interventional Endoscopy, Orlando, United States
2University of Florida, Division of Gastroenterology and Hepatology, Gainesville, United States
3University Of Florida, Gainesville, FL, United States
4Montefiore Medical Center, New York, United States
5Thomas Jefferson University Hospital, Philadelphia, United States

Aims and Methods: The aim was to determine the optimal method of specimen processing and to identify the number of biopsies required to establish a definitive diagnosis in patients undergoing SOC-guided biopsies. Patients with IBDS and presence of indeterminate bile duct strictures (IBDS) were randomized at ERCP to undergo specimen processing at single operator cholangioscopy (SOC).

Main outcomes were to compare the operating characteristics of onsite versus offsite specimen processing techniques. Secondary outcome measure was to determine the number of biopsies needed to establish definitive diagnosis. Final diagnosis was established at surgery or a minimum clinical follow-up of 12 months.

Results: 62 patients were randomized: onsite = 32, offsite = 30. Location of stricture was common bile duct (n = 19), common hepatic duct (n = 16), hilum (n = 18) and intrahepatic ducts (n = 9). Final diagnosis was benign disease in
35 and malignancy in 27. There was no significant difference in diagnostic accuracy (93.8 vs. 90.0%, p = 0.67), sensitivity (85.7 vs. 76.9%, p = 0.36), specificity (100 vs. 100%, p = 0.99), positive predictive value (100 vs. 100%, p = 0.99) or negative predictive value (90.0 vs. 85.0%, p = 0.99) between the on-site versus off-site cohorts, respectively. A diagnosis was established with a median of 1 biopsy (range 1-3) in the on-site cohort; false positives were encountered in 1 patient and false negatives in 2. The diagnostic accuracy was identical (90.0%) whether patients underwent 3 or 4 biopsies in the off-site cohort; false negatives were encountered in 3 patients.

Conclusions: For centers without onsite cytopathology support, performing three SOC-guided biopsies of the biliary stricture and processing the specimen offsite yields a diagnostic accuracy of 90%.

Disclosure: Shyam Varadarajulu and Robert Hawes are Consultants for Boston Scientific Corporation and Olympus America Inc. All other authors have no disclosures to declare.

OP054 APPLICATIONS OF INTRAOPERATIVE PANCREATOSCOPY FOR THE INVESTIGATION OF PANCREATIC IPMNS

R. Valente1,2, U. Arnelo1,2, R. Pozzi Mucelli3, M.H. Reuterwall1, E. Rangelova1, N. Fagerström1, M. Del Chiaro1

Aims and Methods: To assess the diagnostic yield and clinical impact of intraoperative pancreatoscopy in patients operated for suspect main pancreatic duct involvement IPMNs. It has changed the operative management strategy in 65.2% of patients involving IPMN. It has changed the operative management strategy in 65.2% of patients.

Conclusion: Intraoperative pancreatoscopy is a safe and feasible procedure and provides accurate and secure sampling of pathological tissue in the remnant pancreas.

Disclosure: Effective and safe alternative to PTBD after failed ERP, which can be performed under conscious sedation, often in the outpatient setting. Our technical success rate is comparable to published series. [3] Adverse event rates compared favourably with accepted rates from PTBD. [1] Experience and improved instruments should lead to further improved results. Definitive prospective, randomised studies are needed to compare outcomes for percutaneous versus EUS-guided drainage.

References
remaining indications, EUS-D was performed in 32/870 (3.7%) procedures, p < 0.001. 931 follow-up procedures were performed in 352 patients. Overall, the proportion of ERCPs among follow-up procedures was 85.7%, while ETCGs accounted for 7.4%, EUS-Ds for 4% and combined procedures for 2.9%.

Conclusion: EUS-D was performed overall in 6.9% of 2205 biliary and pancreatic duct drainage procedures (7.6% referred from high ERCP volume centers), whereas PTBD was required in 0.1%. The EUS-guided approach integrated with ERCP could be an optimal option of drainage at index and follow-up procedures.

Aims and Methods: We here designed 2 decellularization protocols to develop tissue in order to replace and regenerate dysfunctional tissue for improved life quality of the diseased patient but may also provide more sophisticated disease models. Engineering approaches to build human pancreatic tissue resembling acinar, ductal and endocrine tissue have been proposed by the complexity of the pancreas. Human pluripotent stem cells (PSCs) may provide the appropriate bioengineering platform for developmental and biomedical studies due to their capability to differentiate into every cell type in the human body.

Introduction: As one of the largest and most functionally complex organs of the body, the intestine is vulnerable to many disorders, which are burdened by high social costs. Options to investigate these functions with direct relevance to the human condition remain severely limited when using conventional two-dimensional (2D) cell cultures and animal models. The field of tissue engineering has extensively explored the development of engineered human gut as a natural 3D-platform for intestinal bioengineering. This approach yields virtually pure cultures of human pancreatic progenitor cells followed by spontaneous differentiation in a 3D-culture environment to allow acinar ductal commitment (Holwieder, GUT, 2017). These cultures are the basis of the current approach.

Results: We have implemented signals controlling embryonic lineage fate bifurcations to efficiently yield the desired cell types through exclusion of alternate fates. Specifically, we applied signaling molecules and growth factors inducing either acinar or ductal cells, while inhibiting the respective counter lineage with inhibitors. This approach yields virtually pure pancreatic acinar or duct-like cells generated from human PSCs resembling key features of adult human pancreatic counterparts as shown in an established test battery. Thereby, we provide a coherent roadmap to generate the 2 mature exocrine pancreatic cell types, acinar and ductal cells. Finally, we have applied this novel tool box to dissect the cell type of origin of pancreatic cancer.

Conclusion: The innovative model presented gives novel opportunities to study developmental processes in the pancreas and bears the unique chance to dissect the cell type of origin of pancreatic cancer.

Disclosure: Nothing to disclose

**OP057 DEVELOPMENT OF DECELLULARIZED HUMAN GUT AS A NATURAL 3-D PLATFORM FOR INTESTINAL BIOENGINEERING**

**Discipline:** Intestinal and colonic cancer

**Authors:** P. Giuffrida, M. Curti, W. Al-Akkad, C. Biel, C. Crowley, L. Frenquelli, A. Telese, A. Hall, D. Tamburro, G. Spletni, G. Fusii, F.P. Tinocci, A. Pietrabbina, G.R. Corazza, P. De Coppi, M. Pinzani, A. Di Battino,

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**Disclosure:** As one of the largest and most functionally complex organs of the human body, the intestine is vulnerable to many disorders, which are burdened by high social costs. Options to investigate these functions with direct relevance to the human condition remain severely limited when using conventional two-dimensional (2D) cell cultures and animal models. The field of tissue engineering has extensively explored the development of de novo tissue in order to restore diseased phenotype. A major opportunity exists to exploit these natural scaffolds as 3-dimensional (3D) models for the in vitro study of gastrointestinal diseases.

**Aims and Methods:** We here designed 2 decellularization protocols to develop acellular 3D scaffolds from both tubular and small scale cube human gut.

**Results:** The resultant scaffolds showed preservation of extracellular matrix (ECM) protein composition and 3D architecture. Decellularized human gut scaffolds were reseeded with human epithelial colorectal adenocarcinoma cells (Caco-2) and primary human intestinal myofibroblasts for up to 14 days. Engrafted cells showed excellent viability, motility, proliferation and remodeling of ECM. In addition, mRNA expression changed when comparing primary human intestinal myofibroblasts cultured in 2D versus 3D scaffolds. Compared to fibroblasts cultured in 2D, ACTA2 and COL1A1 mRNA expression were significantly downregulated whereas TGF-β1 and MMP-3 expression were increased in 3D-cultured myofibroblasts. Moreover, a long-term treatment with TGF-β1 and PDGF-BB, to mimic a diseased model, induced further gene expression in 3D whereas desensitization towards the stimuli was observed in 2D cell cultures.

**Conclusion:** Our results present 2 innovative and effective protocols for the decellularization of human gut. These human-derived intestinal scaffolds may represent an innovative platform for disease modelling, biomarker discovery and drug testing gastrointestinal fibro-carcinogenic disorders.

**Disclosure:** Nothing to disclose

**OP058 A COHERENT ROADMAP TO GENERATE EITHER PANCREATIC ACINAR OR DUCT-LIKE CELLS FROM HUMAN PLURIPOTENT STEM CELLS CHALLENGES PANCREATIC CANCER BIOLOGY**

**Discipline:** Pancreatic cancer

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**Disclosure:** Nothing to disclose

**Introduction:** Cell bioengineering approaches not only hold great promise to replace and regenerate dysfunctional tissue for improved life quality of the diseased patient but may also provide more sophisticated disease models. Engineering approaches to build human pancreatic tissue resembling acinar, ductal and endocrine tissue have been proposed by the complexity of the pancreas. Human pluripotent stem cells (PSCs) may provide the appropriate bioengineering platform for developmental and biomedical studies due to their capability to differentiate into every cell type in the human body.

**Aims and Methods:** PSCs typically yield heterogeneous populations, while certain disease models require homogenous populations. We previously succeeded in generating virtually pure cultures of human pancreatic progenitor cells followed by spontaneous differentiation in a 3D-culture environment to allow acinar ductal commitment (Holwieder, GUT, 2017). These cultures are the basis of the current approach.

**Results:** We have implemented signals controlling embryonic lineage fate bifurcations to efficiently yield the desired cell types through exclusion of alternate fates. Specifically, we applied signaling molecules and growth factors inducing either acinar or ductal cells, while inhibiting the respective counter lineage with inhibitors. This approach yields virtually pure pancreatic acinar or duct-like cells generated from human PSCs resembling key features of adult human pancreatic counterparts as shown in an established test battery. Thereby, we provide a coherent roadmap to generate the 2 mature exocrine pancreatic cell types, acinar and ductal cells. Finally, we have applied this novel tool box to dissect the cell type of origin of pancreatic cancer.

**Conclusion:** The innovative model presented gives novel opportunities to study developmental processes in the pancreas and bears the unique chance to dissect the cell type of origin of pancreatic cancer.

**Disclosure:** Nothing to disclose

**OP059 bifidobacterium animalis subspecies lactis ENGINEERED TO PRODUCE MYCOPRIN-LIKE AMINO ACIDS IN COLORECTAL CANCER PREVENTION**

**Discipline:** Gastroenterology

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**Disclosure:** Nothing to disclose

**Introduction:** Colorectal cancer (CRC) is the third common cancer and the third leading cause of cancer-related deaths in Western countries. The pathogenesis of CRC is a multi-step and multi-factorial process. Disruption of the gut microbiota has been associated with gastrointestinal diseases such as colorectal cancer [1]. The genus Bifidobacterium is considered an important component of the gastrointestinal microbiota. It has an important role in several aspects of gastrointestinal homeostasis: immunologic, neuro-hormonal, and metabolic. Bifidobacterium animalis subsp. lactis is a well documented probiotic form of Bifidobacterium. Mycoprin-like Amino Acids (MAAs) are low molecular weight amino acids. MAAs are unique components of red seaweeds and seaweed products are known as nutrional supplements in bowel diseases. Bifidobacterium animalis does not produce MAAs. If one could create a Bifidobacterium animalis producing MAAs via genetic engineering, it should exert more potent immuno-stimulatory properties and might become a more potent therapeutic agent in colorectal cancer.

**Aims and Methods:** Absynthetic gene cluster for MAAs has been demonstrated in the enteric cyanobacterium Bifidobacterium animalis subsp. lactis PCC 7937 (Cyano-bacterium) is able to synthesize MAAs [2]. Genome studies identified a combination of genes, YP_324358 (predicted DHQ synthase) and YP_324357 (O-methyl transferase), which were present only in B. animalis subsp. lactis PCC 7937 and missing in other Bifidobacterium species. Anaabaena sp. strain 7120 has been induced to produce MAAs after genomic transfer (YP_324358 and YP_324357) genes from Anaabaena variabilis PCC 7937 [3]. The comparative genome analysis revealed that the Bifidobacterium animalis subsp. Lactis. KLD2S 2.0603 strain has similar whole genome sequence to the BB-12 strain [4]. It seems that Cyano-bacterium is the source of MAAs and we hypothesize that the genes of Cyano-bacterium involved in MAAs biosynthesis could be transferred to the strain Bifidobacterium animalis subsp. lactis BB-12 [5].

**Disclosure:** Nothing to disclose

**MONDAY, OCTOBER 22, 2018 14:00–15:30**

**Novel technical developments in basic science - Room M**

- **OP057 DEVELOPMENT OF DECELLULARIZED HUMAN GUT AS A NATURAL 3-D PLATFORM FOR INTESTINAL BIOENGINEERING**
- **OP058 A COHERENT ROADMAP TO GENERATE EITHER PANCREATIC ACINAR OR DUCT-LIKE CELLS FROM HUMAN PLURIPOTENT STEM CELLS CHALLENGES PANCREATIC CANCER BIOLOGY**
- **OP059 bifidobacterium animalis subspecies lactis ENGINEERED TO PRODUCE MYCOPRIN-LIKE AMINO ACIDS IN COLORECTAL CANCER PREVENTION**
Results: Genetically modulated *Bifidobacteria* can modulate the immune system to induce inflammation and increase colonic mucosal stability. More decreased chronic inflammation and increased mucosal stability might have the promoting role in colorectal tumorigenesis at different stages including tumor initiation, promotion, progression and metastasis [6]. Also experimental data reveal the important role of NF-κB in colon tumor cells as well as in the surrounding “cancerous” and reactive microenvironment [7]. It can be predicted that this combination may be more effective in preventing colorectal cancer through NF-κB pathway. Elevated TBARS levels are associated with colon cancer initiation and progression and this combination can prevent cancer formation by lowering TBARS levels [8].

Conclusion: Significant progress has been made in recent years in recognizing the importance of gut microbiota to colorectal cancer. Key findings include the discovery of gut microbiota mechanisms that link the gut microbiome to colorectal cancer, including reduced SCFA production, chronic inflammation, altered transcription factors and the immune response. Creating *Bifidobacteria* species producing MAAs via genetic engineering could result in a bacterium that is more potent in its anti-cancer properties. This probiotic could be used not only as a probiotic, also as a pharmacological agent in CRC.

Disclosure: Nothing to disclose.

References


**OP060**

LONG-TERM EFFICACY AND SAFETY OF ALLOGENEIC BONE MARROW-DERIVED MESENCHYMAL STEM CELLS FOR PERIANAL FISTULAS IN PATIENTS WITH CROHN’S DISEASE: A 4-YEAR FOLLOW-UP STUDY

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Introduction: Perianal fistulae are regularly observed in patients with Crohn’s disease. Very few effective treatment options to accomplish closure of the fistula tract have been reported. The results from our dose-finding study (allogeneic bone marrow-derived mesenchymal stromal cell (MSC) therapy for perianal fistulae in Crohn’s disease) showed that local administration of MSCs in perianal fistulizing Crohn’s disease is safe and local injection of 1 x 10^6 MSCs and 3 x 10^6 MSCs is safe and feasible. In the current study we present the 4-year efficacy and safety data of 2 of the 3 dose cohorts.

Aims and Methods: All patients from cohort 1 (2 patients placebo; 5 patients 1 x 10^6 MSCs) and cohort 2 (2 patients placebo; 5 patients 3 x 10^6 MSCs) were invited for evaluation. The patients treated in cohort 3 (2 patients placebo; 5 patients 9 x 10^6 MSCs) will be seen in the next few months. Adverse events were registered and fistula healing (e.g. no fistula drainage) was evaluated. All MSC-treated patients were asked to undergo a pelvic MRI scan.

Results: From both groups of patients treated with MSCs, 4 out of 5 patients were available for long-term follow-up after 4 years. 1 of the patients in cohort 1 died because of an adenocarcinoma of the cecum and 1 patient in cohort 2 was lost to follow-up. With regards to therapy efficacy, fistula closure 4 years after MSC-therapy was observed in 3 out of 4 patients treated with 1 x 10^6 MSCs (75%) and in 3 out of 5 patients treated with 3 x 10^6 MSCs (60%). The single patient with an active fistula never experienced a closed fistula after treatment with MSCs. All 4 placebo-treated patients in cohort 1 and 2, still had draining fistulas at deblinding of the study and were offered post study treatment with MSCs. 2 of these 4 patients were indeed treated, now 2 years ago (both are not included in the current 4-year follow-up study). The 2 placebo-treated patients that denied the post study treatment still have fistula drainage after 4 years follow-up. A total of 6 out of 8 evaluated MSC treated patients were willing to undergo a pelvic MRI in the current 4-year follow-up visit. In all 6 patients, the original perianal fistula tract(s) were still seen on MRI.

Several adverse events were reported both in placebo and in MSC-treated patients. Most of the reported adverse events however are in line with the nature of the underlying disease and immunosuppressive medication (e.g., exacerbation of Crohn’s disease, pneumonia, uveitis). However, in the long-term follow-up in 1 patient treated with 3 x 10^6 MSCs, a superficial lesion in the distal rectum showed the presence of Epstein-Barr virus-associated B-cell lymphoma, a rare but currently occurring disease. This patient is currently being treated with chemotherapy.

Conclusion: After 4 years, 8 of 10 patients treated with 1 x 10^6 or 3 x 10^6 MSCs could be evaluated and 88% of these patients reported the absence of draining fistulas, compared to 0% of the patients treated with placebo after 3 years of follow-up. 2 serious adverse events have been reported in the long-term follow-up, but found not to be directly related to MSC therapy. The results of cohort 3 will become available in the summer of 2018. Our preliminary data show that long-term fistula closure can be achieved with a single MSC treatment. More long-term data are needed to further complete the safety profile of MSC therapy for Crohn’s fistulas.

Disclosure: Nothing to disclose.

Reference

Conclusion: This methodological approach with high concordance rate (80%), identified an overall 50% decrease of MP and SP neuronal cell bodies implying a critical loss of the neuronal mass. The 50% neuronal reduction correlated with a variety of symptoms / signs of SD patients. This study indicates that quantitative neuronal abnormalities can be demonstrated in patients with AN histopathology.

Disclosure: Nothing to disclose.

OP062 DIFFERENTIATION OF DENTAL PULP-DERIVED MESENCHYMAL STEM CELLS INTO HEPATOCYTES AND THEIR REPOPULATION IN NUDE RAT LIVER

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Introduction: Dental pulp-derived mesenchymal stem cells (DP-MSCs) as a source for regenerative medicine are now the subject of much clinical attention. There are high expectations due to their safety, low tumorigenic risk, and low ethical concerns. Tooth-derived MSCs are known to have a great potential in their proliferation and differentiation capacities, even when compared with bone-marrow-derived MSCs.

Aims and Methods: We aimed to examine the hepatic properties and gene expression patterns of DP-MSC-induced hepatocytes and to investigate the affinity of these cells to liver by using a nude rat model. Dental pulp cells obtained from extracted teeth were cultured under the presence of Activin A, FGF, and then insulin and HGF. Production of liver specific proteins including albumin were extracted teeth were cultured under the presence of Activin A, FGF, and then insulin and HGF. Production of liver specific proteins including albumin were investigated. 3 dimensional cultures were perfused with medium containing 5mM NH4Cl and urea concentration in the eluate was assayed. RT-PCR analysis for the genes that are responsible for the experiments was performed. 38 cells labelled cells (1.51x 10^6) were infused via hepatic artery of nude rats and autoradioluminographic images were taken (Dr. Shirai N, Nenmo Science, Co., Ltd, Tsukuba Institute).

Results: Cells differentiated into polygonal hepatocyte-like cells. Production of human albumin fibrinogen, alanine aminotransferase, and hepaplastin in the culture medium were confirmed. The result of conversion of NH4Cl to urea (Table 1). Mean and SD values from these cells to liver by using a nude rat model. Dental pulp cells obtained from extracted teeth were cultured under the presence of Activin A, FGF, and then insulin and HGF. Production of liver specific proteins including albumin were investigated. 3 dimensional cultures were perfused with medium containing 5mM NH4Cl and urea concentration in the eluate was assayed. RT-PCR analysis for the genes that are responsible for the experiments was performed. 38 cells labelled cells (1.51x 10^6) were infused via hepatic artery of nude rats and autoradioluminographic images were taken (Dr. Shirai N, Nenmo Science, Co., Ltd, Tsukuba Institute).

Table 1.

| Urea (mM) | min | 5 | 10 | 15 | 20 | 30 | Mean | 0.68 | 2.28 | 3.72 | 4.96 | 7.60 | SD 0.08 | 0.13 | 0.13 | 0.15 | 0.20 |

Conclusion: Dental pulp MSC-induced hepatocytes had characteristic functions of mature hepatocytes including the production of liver specific proteins and the presence of urea cycle. Because the cells repopulated in livers of nude rat even 168 hrs after the infusion, this methodological approach with high concordance rate (80%), identified an overall 50% decrease of MP and SP neuronal cell bodies implying a critical loss of the neuronal mass. The 50% neuronal reduction correlated with a variety of symptoms / signs of SD patients. This study indicates that quantitative neuronal abnormalities can be demonstrated in patients with AN histopathology.

Disclosure: Nothing to disclose.

OP064 CHARACTERISATION OF A NOVEL JUVENILE ONSET DIABETES (JOD) CELL USING HUMAN PLURIPOTENT STEM CELLS

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Introduction: Diabetes represents one of the major burdens in the 21st century with approx. 350 million people affected worldwide. Monogenic diabetes such as juvenile onset insulin-dependent diabetes (JOD) or maturity onset diabetes of the young (MODY) accounts for approximately 1-2% of diabetes cases and results from mutations that primarily reduce β-cell function. The identification of the genetic basis of these diabetes forms has translated into novel avenues of personalized medicine in the diabetes field, but only few of these genes have been identified to date.

Aims and Methods: Based on published data, we hypothesize that a proportion of the genetic contribution to common diabetes (T1D and T2D) may be caused by rare monogenic variants/ mutations missed by the current GWAS strategies targeting common variant. The current project reports on such a novel gene relevant as regulator of human pancreatic islet formation but also as a novel juvenile onset diabetes (JOD) gene. For this purpose a stage-specific genome wide profiling complemented with Chip-seq data in differentiating human embryonic stem cells was used.

Results: In our approach we could show that our gene binds and activates Nkx2.2, Nkx6.1 and Pdx1, all belonging to the core suite of isletogenesis transcription factors. Interestingly, this gene co-occupies the enhancer and promoter regions of the latter genes together with Foxa2, Pdx1 and Gata6. Finally, we enter T1D human embryonic stem cells with previously identified mutations in JOD patients. Directed differentiation studies of these cells showed an altered binding pattern of Nkx2.2, Nkx6.1 and Pdx1 finally leading to reduced amounts of monohormonal b-cells. This reduced target gene binding results from a limited zinc affinity due to the mutation that would be necessary as co-factor for gene binding.

Conclusion: The platform provided allows personalised drug-testing and further sheds light on the mechanism how our JOD gene regulates pancreatic development and leads to diabetes in case of certain mutations in humans.

Disclosure: Nothing to disclose.
**OP065**

**LONG-LIVED SECRETORY CELLS RESIDING IN THE MOUSE PROXIMAL COLON SERVE AS TRUE STEM CELLS UNDER DNA DAMAGE-INDUCED MUCOSAL INJURY**


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**Introduction:** While most intestinal epithelial cells (IECs) are rapidly renewed, small intestinal IECs residing at the 4+ position quiesce and thereby reside as long-lived IECs. Those long-lived small intestinal IECs are committed to a secretory lineage function as reserve stem cells upon massive loss of the genuine intestinal stem cell (ISC) pool. However, the existence of a long-lived IEC counterpart in the colon remains uncertain.

**Aims and Methods:** We recently reported a newly developed lineage tracing system for secretory IECs by using the Atoh1-CreER::tdTomato mouse. This approach, which combines lineage tracing of Atoh1 IECs and BrdU-based lineage tracing of Atoh1 IECs, we employed the Atoh1-CreER::tdTomato mice (BrdU Cell Rep, 2018). Using these mice, we performed a pulse-chase experiment combining tdTomato-based lineage tracing of Atoh1 IECs and BrdU-based lineage tracing of Atoh1 IECs was conducted to label the aptitude of the limited number of Atoh1 IECs in each region of the colon. Also, region-specific gene expression was examined by subjecting tdTomatomice cells collected from the proximal or distal colon. To investigate the IEC-intrinsic mechanism required for the maintenance of long-lived Atoh1 IECs, we employed the organoid 3D-culture system. Cell cycle status of organoid IECs derived from different parts of the colon was analyzed by flow cytometry or immunoblotting.

**Results:** A distinct population of Atoh1 IECs in the proximal colon exclusively resided as true stem cells, not by BrdU labeling for over 20 days. These label-retaining Atoh1 IECs were generally post-mitotic, as shown by the BrdU labeling experiment consisting of a 1-month labeling period and a subsequent 3-month chasing period. Microarray analysis of Atoh1 IECs in the proximal colon revealed that they exhibited enhanced expression of genes required to maintain quiescence. Consistently, organoids established from the proximal colon showed increased induction of cell cycle arrest and subsequent reduction of proliferation activity, compared to their distal colon counterpart, by promoting Atoh1 IEC differentiation. In addition, secretion-based lineage tracing of Atoh1 IECs, we employed the organoid 3D-culture system. Cell cycle status of organoid IECs derived from different parts of the colon was analyzed by flow cytometry or immunoblotting. In vitro tolerance analysis of 5-FU-induced DNA damage was examined by real-time cell viability monitoring. Finally, we established an IEC-specific 5-FU-induced mucosal injury model to investigate the reserve stem cell capacity of long-lived secretory IECs in vivo.

**Results:** A distinct population of Atoh1 IECs in the proximal colon exclusively resided as long-lived IECs, not by BrdU labeling for over 20 days. These label-retaining Atoh1 IECs were generally post-mitotic, as shown by the BrdU labeling experiment consisting of a 1-month labeling period and a subsequent 3-month chasing period. Microarray analysis of Atoh1 IECs in the proximal colon revealed that they exhibited enhanced expression of genes required to maintain quiescence. Consistently, organoids established from the proximal colon showed increased induction of cell cycle arrest and subsequent reduction of proliferation activity, compared to their distal colon counterpart, by promoting Atoh1 IEC differentiation. In addition, secretion-based lineage tracing of Atoh1 IECs, we employed the organoid 3D-culture system. Cell cycle status of organoid IECs derived from different parts of the colon was analyzed by flow cytometry or immunoblotting. In vitro tolerance analysis of 5-FU-induced DNA damage was examined by real-time cell viability monitoring. Finally, we established an IEC-specific 5-FU-induced mucosal injury model to investigate the reserve stem cell capacity of long-lived secretory IECs in vivo.

**Discussion:** Nothing to disclose

**References**


MONDAY, OCTOBER 22, 2018 14:00–15:30

**OP066**

**BAVENO VI CRITERIA FOR SCREENING VARIABLES IS ASSOCIATED WITH THE RISK OF HCC AFTER DAA THERAPY IN PATIENTS WITH HCV INFECTION AND ADVANCED FIBROSIS**

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**Introduction:** The interferon-free antiviral therapies (Direct Antiviral Agent, DAA) for hepatitis C virus (HCV) infection have allowed treatment of a larger number of patients, including those with cirrhosis, advanced age and comorbidities. It is known that the annual incidence of hepatocellular carcinoma (HCC) in HCV infected patients increases with the degree of fibrosis and is between 2 and 8%. Meta-analysis on interferon antiviral therapy showed a risk reduction of HCC incidence of more than 70%, irrespective of fibrosis stage, in patients who achieved an SVR. Data on DAA therapy are more controversial. Despite previous studies reported a high incidence of recurrent HCC in patients treated with DAA and in whom HCC was previously treated, this data was not confirmed by subsequent large multicentric studies. Some concerns on higher incidence of de novo HCC after DAA treatment have also been reported.

**Aims and Methods:** The aim of this study was to evaluate which variable are eventually associated to HCC occurrence or recurrence in patients with HCV infection and advanced fibrosis. The study included 297 consecutive HCV patients (M 192/F 105; mean age 60.9±12.1; 54.3% with genotype 1 and 23.8 with genotype 3) with high fibrosis stage detected by transient elastography (81 F3 and 216 F4 sec. Metavaric, 16 of whom had a past history of HCC. The following variables were assessed at baseline: liver stiffness, platelets count, Baveno VI criteria for screening varices (stiffness > 20 Kpa and platelet counts < 150,000/mm³), alphafetoprotein, Child Pugh score, MELD score, presence or absence of esophageal varices, presence or absence of diabetes. All patients received an optimal DAA treatment from April 2015 to May 2017. All treated patients were randomly followed up with a median of 20 months (7-33 months). Chi square analysis for categories variables was used.

**Results:** SVR-12 was achieved in 290 patients (97.6%). 23/297 (7.7 %) patients developed HCC de novo or recurrence during the period of follow-up. Among the variable assessed at univariate analysis, liver stiffness > 20 Kpa and platelet counts < 150,000/mm³ known as Baveno VI criteria for screening varices, may be a useful tool to differentiate patients at greater risk of developing hepatocellular carcinoma after DAA treatment. This risk seems to be further increased by the presence of diabetes. Further studies with a larger population of patients will be needed to confirm this observation.

**Disclosure:** Nothing to disclose

**References**


**OP067**

**ASSOCIATION BETWEEN SARCOPENIA AND NONALCOHOLIC FATTY LIVER DISEASE AND ADVANCED FIBROSIS IN THE UNITED STATES**

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**Introduction:** Nonalcoholic fatty liver disease (NAFLD) may be associated with sarcopenia, which share risk factors including chronic inflammation, insulin resistance, vitamin D deficiency.

**Aims and Methods:** This study aimed to determine whether sarcopenia is independently associated with NAFLD and advanced fibrosis in a nationally representative sample of US adults. Cross-sectional data from 11,323 participants in the third National Health and Nutrition Examination Survey were analyzed. NAFLD was diagnosed by ultrasonographic hepatic steatosis without evidence of other liver diseases. The presence of advanced fibrosis was determined by the NAFLD fibrosis score. Sarcopenia was defined as skeletal muscle index that was measured by bioelectrical impedance analysis.

**Results:** NAFLD was more common in subjects with sarcopenia than in those without (46.7% vs. 27.5%), which was consistent in analyses stratified by gender, obesity status, and ethnicity. A univariate analysis showed that sarcopenia was associated with NAFLD (odds ratio [OR], 2.31; 95% confidence interval [CI], 2.01–2.64), which remained significant after adjustment for age, gender, ethnicity, metabolic risk factors, and vitamin D deficiency (OR 1.24; 95% CI 1.03–1.48). This finding persisted even after adjustment for c-reactive protein as a marker of chronic inflammation. Furthermore, NAFLD-associated advanced fibrosis was more common in subjects with sarcopenia than in those without (7.8% vs. 1.6%), which was also consistent in analyses stratified by gender, obesity status, and ethnicity. Sarcopenia was associated with NAFLD-associated advanced fibrosis independent of metabolic risk factors, vitamin D deficiency, and chronic inflammation (OR, 1.79; 95% CI, 1.18–2.72). An additional sensitivity analysis was conducted including insulin resistance in the model with similar results.

**Conclusion:** In this nationally representative sample of American adults, sarcopenia was independently associated with increased risk of NAFLD and NAFLD-associated advanced fibrosis independent of well-defined risk factors. Interventions to strengthen muscle mass may present an opportunity to reduce the burden of NAFLD and advanced fibrosis.

**Disclosure:** Nothing to disclose
**OP068** GENETIC SUSCEPTIBILITY TO INCREASED INTESTINAL PERMEABILITY IS ASSOCIATED WITH STEATOHEPATITIS, LIVER FIBROSIS AND TYPE 2 DIABETES MELLITUS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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**Introduction:** Increased intestinal permeability (IP) has now been considered as a key factor in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM). Given the pivotal role of Gut-Liver Axis in NAFLD pathogenesis, genes involved in the modulation of IP are perfect candidates in exploring SNPs that might significantly impact on fatty liver disease severity.

The aim of our study was to assess whether a single nucleotide polymorphisms (SNP) (rs2542151 G>T) of Protein Tyrosine Phosphatase Non-Receptor Type 2 (PTPN2), known to be involved in regulation of IP, is associated with severity of NAFLD (non-alcoholic steatohepatitis -NASH- and/or liver fibrosis) and type 2 diabetes mellitus.

**Aims and Methods:** We recruited a prospective consecutive cohort of NAFLD cases and healthy controls among Caucasian patients from 2 Italian tertiary care centers. PTPN2 genotype was assessed in both patients and controls. Anthropometrics, clinical data and laboratory data were collected for each patient. In the entire cohort the presence of fibrosis was non-invasively assessed by Fib-4 score. A subgroup of patients underwent liver biopsy. Unconditional multiple logistic regression models were used to investigate the association between selected SNP (rs2542151 G>T), comorbidities and histological severity of liver disease.

**Results:** We enrolled 566 cases (males 64.6%, mean age 45.3± 13.8 years) and 377 controls (males 41.3± 3.1 years). PTPN2 genotype distribution was not significantly different between NAFLD patients and controls. Liver biopsy was available for 345 patients; 198/345 (57.4%) had NASH. In the whole study population, considering a genetic dominant model, the analysis showed that patients with the rs2542151 G>T polymorphism had an increased risk of NASH (OR 1.19 95% CI 1.01-1.41 p = 0.01) independently from age and sex. At a subgroup analysis of patients who underwent liver biopsy, rs2542151 G>T of PTPN2 was associated with the presence of severe steatosis (OR 2.19 95% CI 1.35-3.55 p < 0.01), NASH (OR 1.81 95% CI 1.13-2.90 p = 0.05) and severe fibrosis (OR 2.55 95% CI 1.50-4.33 p < 0.01) independently from age and sex.

**Conclusion:** Our study showed that rs2542151 G>T of PTPN2 is associated with the severity of steatosis, fibrosis and NASH histologically assessed. Furthermore, rs2542151 G>T of PTPN2 is associated with the presence of T2DM in patients affected by NAFLD. These results still suggest that in NAFLD patients an individual genetic susceptibility could play a key pathogenic role on IP impairment and consequent liver disease, to lead to a higher histological severity of fatty liver disease and the presence T2DM.

**Disclosure:** Nothing to disclose

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**OP070** LIVER AND CARDIOVASCULAR MORTALITY AFTER TREATMENT WITH DAAS: DATA FROM THE RESIST-HCV COHORT


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**Introduction:** Large scale, real-life data on the long-term course of liver disease after HCV clearance obtained with DAAs are still scanty, and the separate effects on hepatic and non- hepatic causes of death still unclear.

**Aims and Methods:** Between March 2015 and December 2016, 5,166 patients (mean age 55.7±11.5 years; 3,687 (71.3%) c-Jun and Opn expression co-localized in both, human and murine hepatocytes as well as NPLCs and we therefore wondered whether the increased fibrosis observed in c-Jun+/* mice could be rescued by additional deletion of c-Jun in NPLCs (Jun−/−). Indeed, NASH in c- Jun−/− mice was characterized by reduced liver damage, impaired Opn expression, impaired ductular reaction and subsequently less fibrosis. A comparable phenotype was observed in Opn+/− mice, indicating that the phenotype observed in Jun−/− mice was indeed very likely Opn-dependent.

**Conclusion:** These results suggest that c-Jun exerts cell-type specific functions during NASH pathogenesis: c-Jun expression in hepatocytes promotes hepatocyte survival and protects against the NASH-related DR and fibrosis. In contrast, c-Jun expression in NPLCs rather promotes the DR and subsequent fibrosis by regulating Opn expression.

**Disclosure:** Nothing to disclose
Disclosure: Nothing to disclose.

OP071 BLOOD-BORNE HEV TRANSMISSION: TRANSFUSION-TRANSMITTED HEPATITIS E VIRUS INFECTIONS AND EXPERIENCE WITH ROUTINE HEV SCREENING AT A TERTIARY CENTRE
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Introduction: Hepatitis E virus (HEV) infection has become a relevant topic with increasing attention and is a major threat for immunosuppressed patients. Routine HEV testing of blood products has recently been implemented in Great Britain and the Netherlands. The relevance of blood-borne hepatitis E virus (HEV) infections for these patients has been discussed controversially within the last months and still requires further investigations.

Aims and Methods: We report (A) our experience of routine HEV testing of blood products at our center and (B) cases of immunosuppressed patients developing transfusion associated chronic HEV infection.

From 10/2016 onwards all blood donors at the University Hospital Hamburg-Eppendorf were routinely screened for HEV RNA (pools of 24 donations) by PCR using the Roche cobas 6800 (LLOD single: 19 IU/ml; 24 pool: 456 IU/ml). HEV RNA positive blood products were not transfused. All immunosuppressed patients with HEV infection (2011-2017) were retrospectively studied. All blood products given to chronically HEV-infected patients were retrospectively analyzed.

Results: (A) 30/29891 donors (0.1%) were HEV-RNA-positive (median viral load 960 IU/ml), whereas only 3 of them (10%) presented with elevated serum transaminases at time of donation (ALT: 83 U/l, 192 U/l and 101 U/l). Retrospective analysis of all HEV-positive donors revealed that 4 donors with asymptomatic infection had been HEV-viremic for up to 3 months. (B) 37 immunosuppressed patients with HEV infection were identified whereas 11 of these (30%) developed chronic HEV infection. In 4/11 (36%) we were able to confirm HEV-infection by HEV RNA testing in blood donations. 2 of these (50%) acquired chronic HEV infection by plasmapheresis/rituximab as treatment for heart transplant rejection.

Conclusion: Overall incidence of HEV RNA in asymptomatic blood donors in our center was higher than previously reported although most donors had low viral load. However, blood products are a relevant source of HEV-infection in particular for immunosuppressed individuals as 36% of chronic HEV infections were transfusion associated. Therefore routine screening of blood products should be implemented in standard care.

Disclosure: Nothing to disclose.

MONDAY, OCTOBER 22, 2018 14:00–15:30
Gasric carcinogenesis – Room L7

OP072 HELICOBACTER PYLORI, GASTRIC CARCINOGENESIS AND THE ASSOCIATION WITH ER-STRESS AND AUTOPHAGY
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Introduction: Helicobacter pylori (HP) is one of the most successful pathogens in the world, infecting nearly half of the world’s population. Importantly, HP is the biggest risk factor in the development of gastric pathology including gastric atrophy, intestinal metaplasia (IM) and dysplasia, all of which are considered precursor lesions to gastric cancer. Autophagy is a cellular degradation mechanism, the physiological role of which is to recycle cytoplasmic components. A specialized form of autophagy, xenophagy, contributes to clearance of intracellular pathogens. Recently it has been shown that HP may modulate autophagy through activation of the endoplasmic reticulum stress (ER stress) pathway. Our previous studies have shown that a single nucleotide polymorphism (SNP) in the autophagy gene ATG16L1 (rs2241880) modulates intestinal ER stress. The aim of this study was to investigate the role of this SNP in HP-mediated autophagy, ER stress and intestinal metaplasia.

Aims and Methods: DNA (n = 262) was isolated from EDTA blood of a cohort of IM patients (PROREGAL Cohort), and the ATG16L1 SNP (rs2241880) status was determined by PCR-RFLP. ER stress and autophagy experiments were performed with gastric cancer cell line SK-GT-2 and immortalized gastric cell line GES-1. ER stress was induced by tunicamycin. ER stress (GRP78) and autophagy (LC3B) were detected by western blot analysis. HP (ATCC 43504) was cultured on Columbia sheep blood agar and heat-killed before cell stimulation. Antral biopsies were taken from 47 patients with IM of which 23 were actively infected with HP (determined by histology), these same patients were biopsied 1 year after eradication. The other 24 biopsies were from patients IM who have never been infected with HP (determined by serology). Immunofluorescence and confocal microscopy was performed on these biopsies using GRP78 as a marker for ER stress. Positivity was scored using the Allredscore taking the average of 4 high powered fields. Statistical significance was determined by Students t-test.

Results: The minor allele frequency (MAF) of rs2241880 (i.e. the A allele, associated with lower intestinal ER stress levels) was calculated as 0.53 in the IM cohort, which was significantly higher than the reference population (Rotterdam study, MAF 0.45, p = 0.0003). After stimulation with HP, ER stress levels in gastric cell lines were reduced, whereas autophagy was induced, as determined by LC3B1 to LC3B1 conversion. These differences were not observed when cells were stimulated with non-pathogenic E. coli bacteria. Biopsies from patients actively infected with HP showed a reduced amount of GRP78 positivity as compared to uninfected patients (p = 0.0171) and the same patients one year after eradication (p = 0.0006).

Conclusion: These results show that HP upregulates the autophagy pathway and thereby reduces ER-stress in vitro and in vivo. Furthermore we show that a genetic variant of the ATG16L1 gene which causes reduced levels of ER stress is more prevalent in patients who have developed precancerous gastric lesions, suggesting that promotion of autophagy and thereby reduction of ER stress contributes to HP-induced changes of the gastric epithelium.

Disclosure: Nothing to disclose.

OP073 HELICOBACTER PYLORI INFLUENCES THE METAGENOMIC PROFILE OF HUMAN GASTRIC MUCOSA
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Introduction: The discovery of H. pylori surpassed the long-held conception of the stomach being a sterile organ that does not contain specific microbiota. Further research has shown that H. pylori is not the only inhabitant of the stomach, and other microorganisms can also colonize it. However, the influence of H. pylori on other members of the gastric microbiota remains poorly understood. Research on the bacterial biodiversity within the stomach in H. pylori-positive versus H. pylori-negative gastric mucosa is still controversial.

Aims and Methods: The aim of the study was to characterize the microbial composition of the gastric mucosa in H. pylori-positive and H. pylori-negative subjects by high-throughput 16S rRNA sequencing. Ten gastric mucosal biopsy samples were obtained for metagenomic analysis. According to the rapid urease test combined with cytology results, 6 H. pylori-positive and 4 H. pylori-negative samples were detected. Total RNA from each sample was extracted, which then was used to synthesize cDNA. This step was needed to detect only the living microorganisms of the stomach. DNA libraries of V3-V4 variable region of the 16S rRNA gene were sequenced on the Illumina MiSeq platform. Trimmed reads were analyzed by the QIIME software to characterize the composition of the microbiota.

Results: There is a significant difference in bacterial composition between H. pylori-positive and H. pylori-negative samples. In case of H. pylori-positive patients, a significant dominance of the Helicobacter genus was found, whereas 2 out of 6 samples represented up to 99% of the total microbiota. In the absence of H. pylori infection the predominance of the Streptococcus genus was observed, as well as the presence of the Rothia, Gemellaceae, Fusobacterium and Neisseria genera, which are usually recognized as the normal gastric microbiota. It is interesting to note that H. pylori occurs in small quantities even in cases when no evidence of H. pylori infection is detected according to the rapid urease test and cytology. It is worth noticing that in 4 samples quite a large number of the Nesterenkonia and Helanmona bacterial genera was found, which are usually isolated from the environment, e.g. soil or marine samples, and have not previously been detected in the human digestive tract. Thereby, their role among the other gastric microbiota representatives needs further study.

Shannon diversity index was calculated to analyze the biodiversity in all studied samples. The biodiversity decreased in all H. pylori-positive samples and was in average three times lower than in H. pylori-negative samples. In case of H. pylori infection the predominance of the Streptococcus genus was observed, as well as the presence of the Rothia, Gemellaceae, Fusobacterium and Neisseria genera, which are usually recognized as the normal gastric microbiota. It is interesting to note that H. pylori occurs in small quantities even in cases when no evidence of H. pylori infection is detected according to the rapid urease test and cytology. It is worth noticing that in 4 samples quite a large number of the Nesterenkonia and Helanmona bacterial genera was found, which are usually isolated from the environment, e.g. soil or marine samples, and have not previously been detected in the human digestive tract. Thereby, their role among the other gastric microbiota representatives needs further study.

Conclusion: Microbial composition differs significantly in H. pylori-positive and H. pylori-negative samples; H. pylori tends to prevail in the stomach of H. pylori-positive patients. Bacterial biodiversity is shown to be decreasing in the presence of H. pylori infection. This allows assuming that H. pylori has some sort of inhibitory effect on other inhabitants of the gastric microbiota.

Disclosure: All authors have declared no conflicts of interest.
OP074 CLINICOPATHOLOGICAL FEATURES OF EPSTEIN-BARR VIRUS-ASSOCIATED GASTRIC CARCINOMA WITH SUBMUCOSAL INVASION
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Introduction: The frequencies of lymph node metastasis (LNM) in pT1a and T1b gastric cancer (GC) are 3% and 20%, respectively, namely the majority of them have no LNM. The Cancer Genome Atlas Research Network proposed the concept of molecular phenotype classifying GC into 4 phenotypes including Epstein-Barr virus-CIMP (EBV). The EBV group accounts for 8.8% and is considered to have low prevalence of LNM. This study aimed to evaluate clinicopathological features of submucosal invasive (ptmT1b) GC without lymphovascular invasion to choose lower risk group for LNM from ptT1b GC, for expanding indications of endoscopic submucosal dissection (ESD).

Aims and Methods: 411 pT1b GCs without lymphovascular invasion that underwent gastrectomy between 2009 and 2012 at the Cancer Institute Hospital, were enrolled and retrospectively analyzed. Tissue microarray was made and EBV-encoded RNA in situ hybridization was performed for evaluation of EBV status. Patients’ age, sex, tumor location, macroscopic type, predominant histologic type, tumor diameter, depth of submucosal invasion, the presence of ulceration and the presence of LNM were compared between EBV group and non-EBV group.

Results: The EBV group accounted for 11.4% (47/411). Compared to the non-EBV group, the EBV group was more frequent in men (80.8% vs. 64.8%, p = 0.032), located more frequent in upper third region (44.6% vs 18.1%, p < 0.0001), showed deeper submucosal invasion depth (mean 1200 μm vs 600 μm, p = 0.004), and lower frequency of ulceration (21.2% vs 42.8%, p = 0.004). The predominant histologic type of “carcinoma with lymphoid stroma” was more frequent in EBV group than in non-EBV group (46.6% vs 2.2%, p < 0.0001). No LNM was found in EBV group (0% vs 7.7%, p = 0.059). Compared with lymphoma without lymph vascular invasion showed low prevalence of regional LNM regardless of tumor diameter and the extent of submucosal invasion. This group will be a good candidate to be included curative resection criteria of ESD.

Disclosure: Nothing to disclose

OP075 FGFR2 SIGNALING CROSSSTALKS WITH HIPPO PATHWAY TO DRIVE GASTRIC CARCINOCENESIS
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Introduction: FGFR2 (fibroblast growth factor receptor 2) has been reported to be associated with cellular growth and carcinogenesis. However, the mechanism underlying its functional role in gastric cancer (GC) remains elusive. Although it is known to be a potent downstream target of Wnt signaling, the function of FGFR2 in the context of cellular proliferation has not been comprehensively revealed. Thus, the aim of this study was to elucidate the function of FGFR2 in gastric cancer cell lines, and to investigate the potential clinical and prognostic implications.

Aims and Methods: A total of 280 subjects with gastric cancer who underwent EGD in Toyoshima Endoscopy Clinic were enrolled in this study. Genotyping by TaqMan assay and subsequently correlated with COX-2 expression level.

Results: miR-155 and miR-223 expression was strongly dependent on H. pylori infection in gastric mucosa and in short-term view shows a trend towards higher expression level as a result of H. pylori eradication treatment. Daily low-dose aspirin as well as NSAIDs intake did influence the expression both in healthy subjects and in patients. However, regular PPI intake was associated with a substantial reduction of miR-155 expression predominantly in patients with gastric cancer independently of the density of neutrophils and mononuclear cell infiltrates. Furthermore, miR-155 expression was inversely associated with COX-2 levels in subjects without H. pylori infection. Further studies are needed to elucidate the potential clinical and prognostic benefit of PPI-related miR-155 modification.

Disclosure: Nothing to disclose

OP076 MODIFICATION OF INFLAMMATORY MICRONAS IN GASTRIC MUCOSA BY ASPIN, NSAIDS AND PROTON-PUMP INHIBITORS
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Introduction: Gastric carcinogenesis is a multistep H. pylori-related process. Deregluation of microRNA (miRNA) expression is one of the crucial contributing events in the progression from chronic inflammation to preneoplastic conditions and gastric cancer. Several miRNAs have been suggested as potential biomarkers for preneoplastic conditions. However, nothing is known regarding the modulating effects of non-steroidal anti-inflammatory drugs (NSAIDs) or proton pump inhibitors (PPI) on the miRNA expression.

Aims and Methods: The aim of this study was to investigate the effect of aspirin, NSAIDs and PPI on the expression of mucosal inflammatory miRNAs (miR-155 and miR-223) in H. pylori-infected and non-infected subjects. The study was performed in 2 cohorts: 1) an interventional study in 20 healthy subjects with and without H. pylori infection (each n = 10), and 2) in prospective case-control observational study (n = 188). In interventional study, low-dose aspirin (100mg) was given for 7 days and upper GI-endoscopy including histological sample collection was accessed on the days 0, 1, 3, 7, 9 H. pylori-eradicated subjects repeated the protocol following eradication treatment. Patients from the second cohort underwent upper GI endoscopy including histological evaluation, H. pylori testing (incl. cultivation), biopsy collection and were systemically followed for 2 months. To determine the modulating effects of NSAIDs and PPI on the expression of miR-155 and miR-223 levels were assessed in total RNA extracted from the biopsies using TaqMan Assay and subsequently correlated with COX-2 expression level.

Results: miR-155 and miR-223 expression was strongly dependent on H. pylori infection in gastric mucosa and in short-term view shows a trend towards higher expression level as a result of H. pylori eradication treatment. Daily low-dose aspirin as well as NSAIDs intake did influence the expression both in healthy subjects and in patients. However, regular PPI intake was associated with a substantial reduction of miR-155 expression predominantly in patients with gastric cancer independently of the density of neutrophils and mononuclear cell infiltrates. Furthermore, miR-155 expression was inversely associated with COX-2 levels in subjects without H. pylori infection. Further studies are needed to elucidate the potential clinical and prognostic benefit of PPI-related miR-155 modification.

Disclosure: Nothing to disclose

OP077 PSCA SNP-HELICOBACTER PYLORI INTERACTION ASSOCIATES TO GASTRITIS PROGRESSION IN THE GASTRIC CANCER SEQUENCE AND PSCA EXPRESSION
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Introduction: In addition to H. pylori virulence, host genetic backgrounds and other environmental factors also exhibit complex interactions in gastric cancer development. Prostate stem cell antigen (PSCA) single nucleotide polymorphism (SNP) and its decreased expression are associated with gastric cancer1. Genetic variation may develop through a multiple step process known as the gastritis-gastric cancer sequence that is triggered by H. pylori infection. Severe gastritis has been proven to be a precursor condition2.

Aims and Methods: Here, we investigated PSCA SNP rs2294008 and PSCA expression of background gastric mucosa in the gastritis-gastric cancer sequence and revealed host-bacterial interactions in the disease pathogenesis. A total of 280 subjects with H. pylori infection and 28 H. pylori-negative controls who underwent EGD in Toyoshina Endoscopy Clinic were enrolled in this study. Genotyping results of 309 H. pylori-negative controls and 2,329 gastric cancer patients analyzed in our previous study3 were used in this study. DNA was purified from peripheral blood leukocytes. mRNA was purified from remaining biopsy tissues from the gastric mucosa of the incisura angularis. Quantitative real-time PCR was conducted. The expression of the actin, beta gene was used for normalization. To grade the neutrophil activity according to the updated Sydney system, we used 2 biopsy specimens from the greater curvature of the corpus and the antrum. We topographically classified the gastritis into 4 categories
MONDAY, OCTOBER 22, 2018
14:00–15:30
Translational research in liver, biliary and pancreas – Room L8

**OP078 THE ROLE OF METABOLICOMICS IN THE DISEASE PROGRESSION AND DEVELOPMENT OF BILARY DYSPLASIA AND CHOLANGIOMA IN PRIMARY SCLEROSING CHOLANGITIS (PSC)**

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**Introduction:** PSC is a chronic inflammatory liver disease leading to strictures in intra- and extrahepatic ducts and finally to cholestasis and secondary biliary cirrhosis. The etiopathogenesis of PSC is unknown [1]. PSC is a premalignant condition associated with high risk for cholangiocarcinoma (CCA) [2,3]. Currently there are no sensitive surrogate markers to predict the risk. High-throughput metabolomics analysis could offer a potential source to identify biomarkers for risk prediction and personalized disease prevention.

**Aims and Methods:** We aimed to discover metabolomics profiles of serum and biliary samples in 1) controls and PSC patients to find new noninvasive markers for screening and diagnosing PSC, 2) PSC patients with non-advanced disease compared to those with advanced disease to assess the disease progression, 3) PSC patients with and without biliary dysplasia or CCA to find more sensitive and specific markers to detect biliary dysplasia and CCA.

The patients (N = 184) were recruited from the PSC registry of Clinic of Gastroenterology; serum and bile samples are collected and stored at -80°C. Samples are extracted using acetonitrile, and analysed using WATERS Acquity UPLC coupled to XEVO-TQ-S QQQ MS for targeted and quantitative metabolomics analysis [4].

**Results:** Model-based analyses (Generalized Estimating Equations) pinpointed 60 metabolites with significant p-values in bile and/or serum after correction for type-I error. In both bile and serum samples, 2-Aminoobutyric acid, Acetic acid, Asymmetric dimethylarginine, Citrulline, Dodecanoylcarnitine, Guanosine, Homocysteine, Inosinic acid, L-Glutamic acid, L-Glutamine, L-Palmitoylcarnitine, L-Tyrosine, Sorbitol, Stearoylcarnitine, Symmetric dimethylarginine, and Tetradecanoylecarnitine showed consistent differences between healthy controls and PSC patients. Of the above except Citrulline, Inosinic acid, L-Glutamine, and Stearoylcarnitine also allowed differentiating between healthy controls and all affected patients (non-advanced PSC, advanced PSC and dysplasia).

In bile samples alone, Adenine, Chenoecysdohyocid acid, Creatine, Creatinine, Cyclic GMP, Glycicyclic acid, Hippuric acid, Hydroxykynurenine, O-Phosphothanolamine, S-Adenosyl-L-Homocysteine, and Tyrocidine acid Tetradecanoylecarnitine showed consistent differences between healthy controls and PSC patients. With the exception of Chenoecysdohyocid acid, and Hippuric acid, all the above also allowed differentiating between healthy controls and all affected persons. Importantly, Cytidine, L-Kynurenine, L-Tyrosine, and Propionylcarnitine, also differentiated between PSC and dysplasia patients. In serum samples alone, 5-Hydroxyindoleacetic acid, Adenosine monophosphate, Carnosine, D-Ribose-5-phosphate, Decanoylcarnitine, Dimethylglycine, Folic acid, Gamma-Glutamylcysteine, L-Asparagine, L-Kynurenine, L-Tryptophan, NAD, Neopterin, Nicotinamide, Nicotinic acid, Normetanephrine, Spermidine, and Xanthosine showed consistent differences between healthy controls and PSC patients. With the exception of L-Tryptophan, and Spermidine, all the above also allowed differentiating between healthy controls and all affected persons.

**Conclusion:** This study detected a consistent group of metabolites characterizing PSC and dysplasia patients in both serum and bile samples. In addition, fluid-specific candidate biomarkers were pinpointed. Of these, alterations in bile L-tyrosine, Cytidine, L-Kynurenine and Propionylcarnitine characterized dysplasia in particular.

**Disclosure:** Nothing to disclose

**References**

**OP079 CYSTIC FIBROSIS RELATED PANCREATIC DUCT DAMAGE IN THE CYSTIC FIBROSIS NEWBORN FERRET AND PIG MODEL**

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**Introduction:** Several animal models are available to study the cystic fibrosis (CF) related pancreatic damage although they have clear limitations. Recently cystic fibrosis transmembrane regulator (CFTR) knockout ferret and pig models have been generated.

**Aims and Methods:** We aimed to characterize the fluid and bicarbonate secretion of CF and wild type (WT) ferret and pig pancreatic ducts. Pancreatic ducts were isolated from newborn CF and WT ferret and pig pancreas. In the ferret model the expression of CFTR was detected by immunohistochemistry and resting pH, buffer capacity and Cl–/HCO3– exchange activity were evaluated by microfluorometry. Fluid secretion of ducts from CF and WT ferrets and pigs were examined by videomicroscopy.

**Results:** Our results indicate that the bicarbonate secretion is significantly decreased in CF ferret ducts compared to WT. Videomicroscopy revealed a significant increase in fluid secretion to HCO3– and to 5m forskolin and 100 μM IBMX stimulation in both WT pig and WT ferret ducts. In CF ferret and pig ducts increases of the fluid secretion were not detected during the stimulation period.

**Conclusion:** Concerning our data, absence of the CFTR can lead to decreased or completely abolished pancreatic ductal fluid secretion. Our interesting results highlights the importance of studying pancreatic ductal secretion of these new CF animal models more closely.

**Disclosure:** Nothing to disclose

**References**

**OP080 MUSCLE MIR-34A IS ACTIVATED DURING NADL PROGRESSION, PROMOTING INSULIN RESISTANCE AND MITOCHONDRIAL DYNAMICS DISFUNCTION**

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**OP082** THE EFFICACY OF PENTOXIFYLLINE ON ACUTE PANCREATITIS

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**Introduction:** Acute pancreatitis is an inflammatory condition that occurs in the pancreatic parenchyma and systemically affects other organs. The first phase of the disease, usually during the first week, is caused from the patient’s systemic inflammatory response elicited by acinar cell injury. During this phase, the severity of acute pancreatitis is directly related to extrapancreatic organ failure, and several intercellular signaling proteins such as tumor necrosis factor-a (TNF-a) are involved. Although there is currently no specific treatment for such condition, recent evidence in animal models showing that the administration of pentoxifylline, a competitive nonselective phosphodiesterase inhibitor, is able to reduce inflammation through TNF-a inhibition. However, its benefit in acute pancreatitis in humans remains unclear.

**Aims and Methods:** We aimed to study clinical outcomes of pentoxifylline in APACHE II score in acute pancreatitis patients at 72 hours after treatment and to study effects of pentoxifylline on inflammatory markers level (i.e., CRP, ESR, procalcitonin, and Interleukin-6).

**Results:** Pentoxifylline did not decrease severity of disease determined by a reduction in APACHE II score and a percent reduction of APACHE II compared with control group (0 vs. 2; p = 0.267 and 0% reduction vs. 3% reduction; p = 0.019). Interestingly, the level of the systemic inflammatory responds syndrome (SIRS) after 72 hours of treatment was significantly lower than those without pentoxifylline. (7.7% vs. 29.2%; p = 0.048).

**Conclusion:** Pentoxifylline is an anti-TNF-a drug that seems to reduce the inflammatory process of early phase of acute pancreatitis, particularly in patients presenting within 24 hours of onset. The overall severity of the disease and clinical benefit was similar to control group. A future study of pentoxifylline is needed to confirm its efficacy.

**Disclosure:** Nothing to disclose.

**OP081** THE SERUM LEVELS OF SERINE PALMITOYLTRANSFERASE LONG-CHAIN SUBUNIT 3 ARE ASSOCIATED WITH NONALCOHOLIC FATTY LIVER DISEASE-RELATED HEPATOCARCINOGENSE

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**Introduction:** In recent years, the prevalence of nonalcoholic fatty liver disease (NAFLD) has been increasing, and accordingly, the proportion of hepatocellular carcinoma (HCC) patients with a background of NAFLD has also been on the rise. Although it is important to identify patients with HCC among NAFLD patients, a useful biomarker has not yet been established, so its discovery is needed.

**Aims and Methods:** In addition, we compared the serum SPTLC3 levels and the clinical features. In addition, we compared the serum SPTLC3 levels and the clinical features. In addition, we compared the serum SPTLC3 levels and the clinical features. In addition, we compared the serum SPTLC3 levels and the clinical features. In addition, we compared the serum SPTLC3 levels and the clinical features.

**Results:** 47 muscle miRNAs were found to increase from simple steatosis to non-alcoholic steatohepatitis (NASH), including miR-34a (p < 0.05). Concomitantly, expression of SIRT1, a known target of miR-34a, and activation of AMPK, a metabolic SIRT1-mediator, were decreased (p < 0.05). Mitochondrial dynamics dysfunction was evidenced by decreased Mfn2, a mitochondrial fusion protein and increased Drp1, a mitochondrial fission protein (p < 0.05). Activation of the miR-34a/SIRT1/AMPK pathway is essential to impair mitochondrial and mitochondrial dysfunctions in the skeletal muscle of all three NAFLD animal models, as well as in C2C12 cells incubated with PA (p < 0.05). In note, in an alternative in vivo model, we alleviated PA-induced SIRT1/AMPK and mitochondrial deregulation (p < 0.05). Inversely, miR-34a overexpression mimicked PA-induced dysfunction, an effect that was abolished when downstream AMPK was activated (p < 0.05).

**Conclusions:** These results indicate that activation of the miR-34a/SIRT1/AMPK pathway leads to impairments in mitochondrial metabolism in skeletal muscle of NAFLD patients. As the role of miR-34a in global NAFLD pathogenesis keeps expanding, its further exploitation as a putative therapeutic target is warranted. (Gilead Sciences International – Research Scholars Program in Liver Diseases and SFRH/BD/104160/2014, FCT, Portugal).

**Disclosure:** Nothing to disclose.

**OP083** DELETION OF BRG1 PREVENTS LIVER FIBROSIS AFTER CCL4 INJECTION IN MICE

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**Introduction:** Liver fibrosis is known to be a progressive pathological process that results in the accumulation of excess extracellular matrix proteins, ultimately leading to the development of cirrhosis and, at times, hepatocellular carcinoma. BrG1, a core subunit of the SWI/SNF chromatin-remodeling complex, is known to modulate proliferation in the liver and genes regulating extracellular matrix. However, the role of BRG1 in the progression of liver fibrosis is not well understood. This study aimed to investigate the effect of BRG1 on the progression of liver fibrosis.

**Aims and Methods:** A hepatocyte-specific BrG1 knockout mice model was being used by intercross of BrG11/1 and AlbCre single mutant mice on a mixed genetic background. Carbon tetrachloride (CCL4) was injected in order to induce liver fibrosis for 4, 6, and 12 weeks. BrG1 expression was determined by immunohistochemistry. Liver fibrosis was assessed by analysis of liver fibrosis, particularly in patients presenting within 24 hours of onset. The overall severity of the disease and clinical benefit was similar to control group. A future study of pentoxifylline is needed to confirm its efficacy.

**Disclosure:** Nothing to disclose.

**Intervention:** Intramyocellular lipoprotein deposition associates with mitochondrial dysfunction and insulin resistance (IR), constituting a key pathophysiologic event in non-alcoholic fatty liver disease (NAFLD). Our group has previously shown that human muscle IR correlates with NAFLD severity, while microRNAs (miRNAs/miRs), including pro-apoptotic miR-34a, are progressively regulated during disease progression, in both liver tissue and plasma.

**Aims and Methods:** Now, we aimed to investigate the functional role of miRNAs in the skeletal muscle of NAFLD patients modulating local mitochondrial dysfunction and IR and, hence, contributing for development of metabolic syndrome and NAFLD.

Skeletal muscle biopsies were obtained from morbid obese NAFLD patients undergoing bariatric surgery. Muscle RNA was run in TaqMan™ array microRNA cards. qPCR array data was analyzed using the HFePCR package in Bioconductor. C57Bl/6 mice were fed with different NAFLD-inducing diets including a fast food diet for 25 weeks; a choline-deficient, high-fat diet for 14 weeks; and a choline-deficient amino-acid-defined diet for 32 weeks. C2C12 muscle cells were incubated with palmitic acid (PA) in the presence or absence of A-769662, a AMPK specific activator, or upon miR-34a functional modulation.

**Results:** 47 muscle miRNAs were found to increase from simple steatosis to non-alcoholic steatohepatitis (NASH), including miR-34a (p < 0.05). Concomitantly, expression of SIRT1, a known target of miR-34a, and activation of AMPK, a metabolic SIRT1-mediator, were decreased (p < 0.05). Mitochondrial dynamics dysfunction was evidenced by decreased Mfn2, a mitochondrial fusion protein and increased Drp1, a mitochondrial fission protein (p < 0.05). Activation of the miR-34a/SIRT1/AMPK pathway is essential to impair mitochondrial and mitochondrial dysfunctions in the skeletal muscle of all three NAFLD animal models, as well as in C2C12 cells incubated with PA (p < 0.05). In note, in an alternative in vivo model, we alleviated PA-induced SIRT1/AMPK and mitochondrial deregulation (p < 0.05). Inversely, miR-34a overexpression mimicked PA-induced dysfunction, an effect that was abolished when downstream AMPK was activated (p < 0.05).

**Conclusions:** These results indicate that activation of the miR-34a/SIRT1/AMPK pathway leads to impairments in mitochondrial metabolism in skeletal muscle of NAFLD patients. As the role of miR-34a in global NAFLD pathogenesis keeps expanding, its further exploitation as a putative therapeutic target is warranted. (Gilead Sciences International – Research Scholars Program in Liver Diseases and SFRH/BD/104160/2014, FCT, Portugal).

**Disclosure:** Nothing to disclose.
liver-specific knockout mice was decreased compared to wildtype mice. In addition, lesions in Brg1 knockout mice as shown by Sirius red staining and α-SMA staining. Moreover, serum ALT levels were lower in Brg1 liver-specific knockout mice compared to wildtype mice.

Conclusion: We were able to show that hepatocyte-specific Brg1 deletion prevents liver fibrosis after CCl4 injection in mice. We conclude that Brg1 promotes progression of hepatic fibrosis and may, thus, be used as a potential therapeutic target for the treatment of patients with liver fibrosis due to chronic injury.

Disclosure: Nothing to disclose

OP084 - THE EFFICACY OF SCISSOR-TYPE KNIFE IN ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL CANCER: A MULTI-CENTER RETROSPECTIVE STUDY

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Introduction: Scissor-type knife was invented as a device for endoscopic submucosal dissection (ESD) for gastrointestinal neoplasms, which enabled to perform ESD-like biopsy procedure. Therefore, ESD with scissor-type knife (ESD-S) is considered as a technically easier procedure than ESD with non-scissor-type knife (ESD-N). However, there are few reports suggesting efficacy of ESD-S by comparing with ESD-N.

Aims and Methods: This study aimed to compare the technical outcomes of ESD-S with those of ESD-N by propensity score matching analysis. Superficial esophageal cancer treated by ESD between October 2015 and March 2018 at 3 hospitals were retrospectively reviewed. Lesions treated by ESD-S (n = 48) and lesions treated by ESD-N (n = 114) were compared. Multivariate analyses and propensity score matching analysis were used to compare the differences in age, gender, tumor size, tumor location, tumor depth, degree of tumor circumference, operator level and traction method use, including factors which were previously reported to affect the outcomes of ESD. Primary outcome was the procedure time during ESD. Secondary outcomes were the rate of en-block complete resection and the rates of complication (perforation/delayed bleeding) among 2 groups.

Results: Before matching, non-experts had a higher rate of selecting scissor-type knife than experts. Propensity score matching analysis created 34 matched pairs. Adjusted comparisons between 2 groups showed a significant difference in procedure time (median; 42.5 min in ESD-C vs 68.5 min in ESD-D, p = 0.014). In addition, they also showed similar treatment outcomes (en-block resection rate: 100% vs 97.1%; complete resection rate: 88.2% vs 82.4%, p = 0.734; perforation during ESD: 0% vs 5.9%, p = 0.493, delayed bleeding: 0% in both groups).

Conclusion: ESD using scissor-type knife achieved shorter procedure time than ESD using non-scissor-type knife without increase of complication. Therefore, scissor-type knife may become one option as an endo-knife of ESD for superficial ESD.

Disclosure: Nothing to disclose

OP085 - FEASIBILITY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGEAL CANCER IN PATIENTS WITH A HISTORY OF ESOPHAGECTOMY OR GASTRECTOMY: A PILOT STUDY

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Introduction: Patients with a history of esophagectomy for gastrectomy may have a higher risk of suffering from esophageal squamous cell carcinoma (ESCC) due to tumor recurrence or reflux of alimentary juice. Early ESCC can be found by endoscopy examination during the follow up in part of patients. Esophagectomy has been viewed as the gold standard for ESCC, however, a second alimentary tract reconstruction is extremely difficult, which remains esophageal replacement surgery, and some of them accepted radiotherapy. No fatal perioperative adverse events were found. 1 patient had bilateral pleural effusion and treated by improvement of respiratory function and antibiotics, without surgery or drainage. 3 patients suffered from stricture and were treated by endoscopic dilation to relieve stenosis.

Conclusion: ESD is found to be safe and technically feasible in treating early ESCC in patients with a history of esophagectomy and gastrectomy. More follow-up data are needed to be analyzed by further studies to prove its efficacy in these groups of patients in a long run.

Disclosure: Nothing to disclose

OP086 - COMPARISON OF OUTCOMES OF PER-ORAL ENDOSCOPIC MYOTOMY BETWEEN ACHALASIA PATIENTS WITH OR WITHOUT PRIOR LAPAROSCOPIC Heller’s MYOTOMY (LHM)

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Introduction: Recurrence of achalasia symptoms after laparoscopic Heller’s myotomy (LHM) occurs in about 10% of patients due to inadequate myotomy or fibrosis at the site of myotomy. Re-operation can be technically challenging with increased perioperative complications and decreased response. POEM is emerging as a less invasive treatment modality for redo-myotomy in such patients. In this study, we compared the outcomes of POEM in patients with and without prior LHM.

Aims and Methods: Achalasia patients who underwent POEM between April 2014 and June 2017 with at least 2-month post-treatment follow-up were included in the study. Patients were categorized as those with prior LHM and those without prior LHM. Patient demographics, pre-treatment and 2 month post-treatment timet barium esophagram (TBE), high resolution esophageal manometry (HREM) and pH study parameters were compared between the 2 groups. All POEM procedures were performed under general anesthesia and with standard steps. Fisher’s exact test and Mann-Whitney U test was used to test the significance of differences for categorical and continuous variables respectively.

Results: A total of 138 patients (No LHM = 109; prior LHM = 29) were included and 53.8% were females. There was no significant difference in the age, gender, prior treatments for achalasia (apart from LHM), pre-treatment Eckardt’s score, length of stay and complication rates in both groups. The length of POEM procedure (110 [91–130] vs. 97.5 [95.9–110.5 minutes]; p = 0.023) and duration of symptomatic achalasia (5 [4–8] vs. 2 [1–6] years; p = 0.002) were significantly longer in the prior LHM group, 2-month post treatment Eckardt’s scores and
HREM parameters improved significantly in both groups. Post-treatment, patients with prior LHM showed improved vision in all the TBE parameters except for height of barium column at 1 minute, which did not change significantly. On comparing pre-treatment TBE and HREM parameters, patients in the no LHM group had smaller width of barium column at 5 minutes and significantly higher basal LES pressure and lower LES integrated relaxation pressure (LES-IRP) as compared to the prior LHM group. All TBE parameters (except, height at 1 cm) improved more significantly in the no LHM group as compared to prior LHM group. Abnormal pH study with increased DeMeester scores (>14.72) was not significantly different in the 2 groups. **Conclusion:** POEM takes longer procedure time but is safe and effective for palliation of symptoms in patients with recurrent symptoms after prior LHM. Clinical improvement reflected by a decrease in Eckardt’s scores is similar in both groups, although objective improvement in TBE parameters are more impressive in patients without prior LHM.

## OP087 Efficacy and safety of endoscopic resection for small submucosal tumors originating from the muscularis mucosae layer in gastric fundus

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**Introduction:** Gastrointestinal submucosal tumors (SMTs) are most commonly found in the stomach, as often as 1 in every 300 endoscopies. Small tumors may be asymptomatic or only present with nonspecific gastrointestinal symptoms, and are usually detected incidentally during upper gastrointestinal endoscopy. Recently, as the widespread use of digestive endoscopy and advances in endoscopic ultrasonography (EUS), the diagnostic rate of small SMTs, including gastrointestinal stromal tumors (GISTs) with malignant potential, has been increasing. According to guidelines set by the National Comprehensive Cancer Network (NCCN), surgical referral should be considered for non-metastatic SMTs, including the following: size >2 cm lacking high-risk features upon EUS. Despite this, the high-risk potential to increase the safety of ESD and overcome difficulties in resecting SMTs is crucial. Our aim was to evaluate the efficacy, safety and feasibility of resection for small gastric SMTs using the ESE and EFTR technique in a large series of patients with long-term outcomes.

**Aims and Methods:** In this study, we evaluated the efficacy, safety, and long-term outcomes of ER for small SMTs of the gastric fundus in a large series of patients which were lacked before. 537 consecutive patients with SMTs no more than 2 cm of the gastric fundus originating from the muscularis propria (MP) layer and treated with endoscopic submucosal excavation (ESE) or endoscopic full-thickness resection (EFTR) were included in this retrospective study at Zhongshan Hospital of Fudan University from January 2013 to September 2016. Clinopathological, endoscopic and follow-up data were collected and analyzed.

**Results:** The en bloc resection was achieved in 100% of patients and complete resection was achieved for 530 (98.7%) lesions. Although total rate of complications was 9.3%, serious adverse events only occurred in 3 (0.6%) patients including major pneumoperitoneum, major hydrothorax and bleeding. Unlike larger tumor size and longer procedure time, endoscopic experience had positive impact on decreasing complications. Based on statistical analysis, tumors with greater size, near cardiac and treated by EFTR were the significant contributors to longer operative times. A median follow-up of 32 months was available and all patients were free from local recurrence or distant metastasis during the study period.

**Conclusion:** Although technical difficulties present in gastric fundus, ER is quite effective and safe for resection of small gastric SMTs with high complete resection rate and rare serious adverse events.

**Disclosure:** Nothing to disclose

## OP088 Endoscopic resection via antral submucosal tunneling for safe en bloc removal of tumors in the duodenal bulb

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**Introduction:** Generally, endoscopic submucosal dissection (ESD) of the duodenal tumor remains less prevalent due to anatomical characteristics of the duodenal bulb, technical difficulties of the procedure, and a high risk of complications including delayed bleeding and perforations which may require invasive surgical intervention [1][2][3].

**Aims and Methods:** Herein, we describe a novel endoscopic technique, endoscopic resection via antral submucosal tunneling (ERAST), for the en bloc removal of tumors in the duodenal bulb. The specific steps of the ERAST are as following.

1. A mucosal incision is made using a Hybrid knife (1-type, ERBE, Germany) approximately 5 cm proximal to the pylorus.
2. A submucosal tunnel extending to the duodenal tumor via the pylorus is then created. To completely expose the tumor, submucosal tunneling following entry into the duodenal bulb is continued until approximately 10 mm distal to the pylorus. Soft coagulation (80 W on effect 4, ERBE, Germany) is recommended for hemostasis in the bulb to prevent potential perforation of the thin duodenal muscularis propria.

**Results:** As shown in Table 1, 4 tumors, independent of their location in the duodenal bulb, were successfully resected by ERAST and 100% en bloc resection was achieved. No major bleeding or perforation occurred during ERAST and no postoperative complications such as delayed bleeding, perforation or hyperpyrexia was observed. Esophagogastroduodenoscopy carried out 2 months after the ERAST revealed that the indicated wound had healed completely without recurrence or biliary reflux and no patients reported any discomfort. Leveraging the use of submucosal tunneling to facilitate endoscopic resection, the endoscopic view enabled by ERAST facilitates recognition of anatomic layers of the thin duodenal wall and hence, demarcation of a clear and safe dissection line above the pylorus. A submucosal tunnel extending to the duodenal tumor via the pylorus is then created. To completely expose the tumor, submucosal tunneling following entry into the duodenal bulb is continued until approximately 10 mm distal to the pylorus. Soft coagulation (80 W on effect 4, ERBE, Germany) is recommended for hemostasis in the bulb to prevent potential perforation of the thin duodenal muscularis propria. Next, a mucosal incision is made from the inner side of the submucosal tunnel towards the duodenal lumen. The circumferential mucosa of the tumor is then incised in a step-by-step manner to remove the tumor en bloc. An endoclip tied with floss is used to extract the tumor out from the duodenum. Finally, the mucosal defect in the bulb and the mucosal incision in the antrum are closed using endoclips (Micro-Tech, Nanjing, China) combined with endoloop (MAJ-254, Olympus). ERAST takes advantage of submucosal tunneling to facilitate tumor resection and has the potential to increase the safety of ESD and overcome difficulties in resecting tumors that are anatomically challenging to access.

In this preliminary study, we evaluated the feasibility and safety of ERAST for the treatment of lesions in the duodenal bulb.

**Conclusion:** In conclusion, our findings suggest that ERAST is feasible and safe for the removal of lesions in the duodenal bulb, particularly for those in challenging anatomical locations. However, further prospective studies with a larger number of cases are warranted to investigate the long-term recurrence rates and potential adverse effects.

**Disclosure:** Nothing to disclose
**OP089 THE POCKET-CREATION METHOD FACILITATES ENDOSCOPIC SUBMUCOSAL DISSECTION OF LARGE SESSILE TUMORS**

**T. Yamashina**

**Introduction:** Large sessile and subpedunculated tumors are frequently associated with severe submucosal fibrosis and retraction of the muscularis (1,2). Therefore, endoscopic en bloc resection by endoscopic submucosal dissection (ESD) is challenging. Pocket-creation sign during endoscopy may be diagnostic since the fibrosis is often benign without tumor invasion and many of these tumors are limited to the mucosa. The pocket-creation method (PCM) provides adequate submucosal traction enabling ESD, even with submucosal fibrosis (3). We previously reported that the PCM facilitates ESD of laterally spreading colorectal tumors, non-granular type, frequently complicated by submucosal fibrosis (4).

**Aims and Methods:** The aim of this study is to assess the utility of PCM to overcome the difficulties caused by even severe fibrosis associated with large sessile and subpedunculated tumors by comparing ESD using the PCM with conventional methods (CM).

A total of 887 colorectal lesions were resected by ESD between April 2010 and June 2016. Of the 109 lesions, 18 were smaller than 20 mm in diameter and one non-neoplastic lesion was excluded. This is a retrospective review of the remaining 90 colorectal large sessile and subpedunculated tumors. Of the 109 lesions, 18 were smaller than 20 mm in diameter and one non-neoplastic lesion was excluded. This is a retrospective review of the remaining 90 colorectal large sessile and subpedunculated tumors in 89 patients. The lesions are divided into PCM (n = 40) and CM groups (n = 50). The primary outcome measure was en-bloc resection rate. Secondary outcome measures included (1) R0 resection (en bloc resection with histologically negative resection margins); (2) complications; (3) dissection time (min); (4) dissection speed (mm²/min).

**Results:** PCM and CM achieved high en bloc resection rates. (PCM, 100% [40/40]; CM, 94% [47/49]; p = 0.05). ESD of 2 lesions in the CM group were stopped during the procedure, 1 after immediate perforation was recognized, and 1 with a deep invasive tumor converted to Endoscopic Mucosal Resection. 1 lesion in the CM group was resected in a piecemeal fashion. Tumor diameters (mm) were similar (median (range), PCM: 30.5 (20-57) vs. CM: 30.5 (20-90), p = 0.77) There were no differences in R0 resection rates (88%, 35.4% vs. 78%, 38.4% vs. 1.0, p = 0.05) or incidence of adverse events (perforation and late delayed bleeding, 5%, 2.0% vs. 1.0, p = 0.50, 0.69). When the PCM was used, the rate of pathologically negative vertical margins (p = 0.04) was significantly greater, dissection time (p = 0.04) shorter and dissection speed (p = 0.02) faster than when CM was used.

**Conclusion:** ESD using PCM increases the rate of negative vertical margins with rapid dissection for the treatment of large colorectal sessile and subpedunculated tumors.

**Disclosure:** Nothing to disclose

**References:**


**OP900 EOSINOPHILIC OESOPHAGITIS WITH INFLAMMATORY BOWEL DISEASE: EPIDEMIOLOGY AND OUTCOMES FROM A LARGE POPULATION-BASED ANALYSIS**

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**Introduction:** Eosinophilic oesophagitis (EoE) is an immune-mediated condition that shares some immunological pathways with inflammatory bowel diseases (IBD). Few case reports have suggested an overlap between EoE and IBD, although some studies have suggested that this overlap is rare. The epidemiology and implications of this relationship are unknown.

**Aims and Methods:** The primary objectives of this study were to estimate the prevalence of EoE in IBD and to identify potential adverse outcomes of co-diagnosis. Given the rarity of EoE in IBD, we relied on a very large population-based cohort to maximize the sensitivity and precision of our analyses. All enrollees in the Truven Health MarketScan® Research Database (2007–2016), the largest health claims database in the United States, were included in this study. Patients with EoE, Crohn’s disease (CD), and ulcerative colitis (UC) were identified based on recurrent diagnoses using the International Classification of Diseases 9 and 10 codes. Descriptive analyses were used to estimate the prevalence and characterize the demographics of IBD patients with or without EoE. Cox proportional hazards models were used to compare the longitudinal risk of major adverse outcomes (corticosteroid use, initiation or change in biologic therapy, hospitalization, and abdominal surgery) between IBD patients with and without EoE. Regression models controlled for age, sex, and geographic region.

**Results:** There were 153,232,283 individuals with a median follow-up time of 18 years (interquartile range 0.8 to 3.8). The overall prevalence of EoE was 68.5 per 100,000 individuals. The prevalence rates of EoE were significantly higher in patients with CD (508.0 per 100,000; p < 0.01) and UC (1325.0 per 100,000; p < 0.01) than in the general population. CD and UC patients with EoE were predominantly male (CD: 61.8% vs. 38.2%, p < 0.01; UC: 56.6% vs. 43.4%, p < 0.01) and younger (CD: 33.9 vs. 46.1 years, p < 0.01; UC: 34.1 vs. 48.9 years, p < 0.01) than IBD patients without EoE. For CD patients, EoE was associated with an increased risk of corticosteroid use (adjusted hazard ratio [aHR] 1.16; 95% CI 1.07 to 1.25; p < 0.01) and the initiation or change in biologic therapy (aHR 1.21; 95% CI 1.05 to 1.39; p < 0.01), but not hospitalization or abdominal surgery. For UC patients, EoE was similarly associated with an increased risk of corticosteroid use (aHR 1.26; 95% CI 1.13 to 1.40; p < 0.01) and the initiation or change in biologic therapy (aHR 1.50; 95% CI 1.03 to 2.20; p = 0.04), but not hospitalization or abdominal surgery.

**Conclusion:** In this first population-based study of EoE in IBD, EoE was found significantly more common in younger and male patients. EoE was associated with increased risk of corticosteroid use and biologic therapy, but not hospitalization or abdominal surgery. Given the observed relationship between EoE and IBD, further investigation into the epidemiology and pathophysiology of both diseases may provide insight into shared mechanisms of pathogenesis.

**Disclosure:** Nothing to disclose

**References:**


Introduction: Mesenchymal cell therapy is promising for the treatment of perianal CD fistulas refractory to conventional therapy. Autologous adipose-derived stem cells (ADSVF) are a group composed by 16 Sicilian centres which continuously enter in a web based software all clinical data of IBD patients treated with biologics. In the absence of head-to-head trials, there is an unmet need to compare different biologics for the treatment of perianal disease with a PDAI score that passed from 7.3 at baseline at 3.8 at week 48 (40% of remission, 20% of complete response, 20% of partial response) which was achieved in 13 (48%) cases and endoscopic efficacy in 12 (40%) patients. A study evaluating efficacy and safety in the majority of the patients at short term and allow avoiding surgery in almost half the patients at long term. 

Disclosure: Nothing to disclose

Reference: From October 2015 and March 2017, 10 patients were treated by this innovative local treatment (among 10 cc of microfat and about 30 millions of ADSVF viable cells subsequently injected into the soft tissue around the fistula). No serious adverse events have been described. The most frequent side effect was local pain on lipoaspiration site. No case of incisional infection post treatment was described. About 70% of response was found at week 12 (50% of partial response and 20% of remission) and 80% of response at week 48 (40% of remission, 20% of complete response, 20% of partial response). These results were confirmed to significant improvement of quality of life score (p = 0.038).

Conclusion: This first study evaluating co-local administration of ADSVF in association with fat graft appears to be a simple, safe and efficient surgical regenerative therapy for perianal CD fistula refractory to conventional therapy.

OP0903 A PROPENSITY SCORE-MATCHED COMPARISON OF INFLIXIMAB AND ADALIMUMAB IN NON-NAÏVE PATIENTS WITH CROHN’S DISEASE: REAL-LIFE DATA FROM THE SICILIAN NETWORK FOR INFLAMMATORY BOWEL DISEASE (SICILIAN NETWORK FOR INFLAMMATORY BOWEL DISEASE (S-NIBD))


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Introduction: In the absence of head-to-head trials, there is an unmet need to better understand the effectiveness of different biologics in inflammatory bowel disease (IBD). The Sicilian Network for Inflammatory Bowel Disease (S-NIBD) is a group composed by 16 Sicilian centres which continuously enter in a web based software all clinical data of IBD patients treated with biologics.
Aims and Methods: Data of all incident Crohn’s disease (CD) patients treated with 5-Aminosalicylic acids (5-ASA) during 2013 to January 2014 were extracted from the cohort of SN-IBD. Patients were divided in biologic-naive and non-naïve, and the 2 groups were analyzed singularly. We used a 1-to-2 propensity score matching (2:1) for accounting for the main baseline characteristics in naïve patients, and a 1-to-1 propensity score matching (1:1) for non-naïve patients. Clinical outcomes were evaluated at 12 weeks and 1 year.

Results: 632 patients (735 total treatments) were included. After propensity score matching, 214: 1:IFX: 47 patients were matched for 214:1 non-naïve patients (total treatments: 94; ADA: 47; IFX: 47) were analyzed. Among naïve patients, a clinical benefit was achieved in 175/214 (81.8%) patients treated with ADA and in 84/107 (77.6%) patients treated with IFX (adjusted OR: 1.23, 95% CI 0.95–1.61; p = 0.027). After 12 weeks, 80% of patients treated with ADA and 90% of patients treated with IFX (adjusted OR: 1.10, 95% CI 0.61–1.96, p = 0.766). The rate of adverse events was significantly higher in patient treated with IFX (incidence rate ratio 1.87, 95% CI 1.02–3.43, p = 0.040). Conditional logistic regression model showed that previous surgery (adjusted OR: 0.19, 95% CI 0.04–0.78, p = 0.021), upper GI localization (adjusted OR: 0.20, 95% CI 0.05–0.84, p = 0.028), and fistulizing behavior (adjusted OR: 0.29, 95% CI 0.10–0.87, p = 0.027) were independent risk factors for a reduced rate of clinical benefit at 1 year. Among non-naïve patients, a clinical benefit was achieved in 29/47 (61.7%) patients treated with ADA and in 32/47 (68.1%) patients treated with IFX (adjusted OR: 0.72, 95% CI 0.21–2.44, p = 0.600) at 12 weeks and after 1 year, clinical benefit was achieved in 23/47 (48.9%) patients treated with ADA and in 19/47 (40.4%) patients treated with IFX (adjusted OR: 1.23, 95% CI 0.54–2.86, p = 0.620). The rate of adverse events was significantly higher in patient treated with IFX (incidence rate ratio 2.57, p = 0.009). No prognostic factor of clinical benefit was found among non-naïve patients.

Conclusion: In the first study comparing the clinical effectiveness of ADA and IFX in moderate to severe CD patients via propensity score, there was no significant difference between the 2 drugs, neither in naïve nor in non-naïve patients.

Disclosure: Ambrogio Orlando served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals and received lecture grants from AbbVie, MSD, Sandoz, and Takeda Pharmaceuticals. Sara Renna served as an advisory board member for AbbVie and MSD Pharmaceuticals, and received lecture grants from AbbVie, MSD, and Takeda Pharmaceuticals. Caterina Maria Cappello served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals, and received lecture grants from AbbVie, MSD, Chiesi, and Takeda Pharmaceuticals.

OP0904 TREATMENT PATTERNS AMONG PATIENTS WITH MODERATE-TO-SEVERE ULCERATIVE COLITIS IN WESTERN EUROPE

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Introduction: The goal of treatment in ulcerative colitis (UC) is to induce clinical response and maintain steroid-free disease remission in the long term. The aim of the present study is to examine how moderately-to-severe UC is currently managed in real-world clinical practice across select Western European countries.

Aims and Methods: Data from the 2017 Adelphi Inflammatory Bowel Disease Specific Programmes (IBD-DSP) were used. The IBD-DSP is a database of patient chart information abstracted by selected gastroenterologists across the European Union Five [EUS]: i.e., France, Germany, Italy, Spain, and the United Kingdom [UK]. Eligible gastroenterologists who agreed to participate were asked to complete patient record forms for the next 7 consecutive eligible adult patients with UC. Only charts from patients with moderate-to-severe UC were included in the analysis (defined as those with documented administration of either an immunomodulator [IM] or a biologic). Treatment usage by line of therapy (defined as the sequential order of treatments after diagnosis) and the percentage of dose escalation was reported using descriptive statistics (mainly percentages).

Results: A total of N = 1191 patient charts were included (France: N = 331, Germany: N = 271, Italy: N = 207, Spain: N = 230, UK: N = 152; 56.5% male; median age at diagnosis (55 years). Patients had been diagnosed for a mean of 4.7 years (SD = 5.9). For those with complete treatment history (N = 1060), 47.1% used 5-ASA/s and/or steroids as their first-line therapy. The remaining 52.9% used either an IM or biologic as first-line therapy (IM without biologic = 27.4%; infliximab [IFX] = 13.3%; adalimumab [ADA] = 9.8%; golimumab [GOL] = 1.3%; vedolizumab [VDZ] = 0.8%). Use of IM therapy (without a biologic) was higher in subsequent lines: second-line = 41.3%, third-line = 38.3%. Similarly, the use of a biologic also increased in second-line (IFX = 19.0%, ADA = 10.4%, GOL = 3.6%, VDZ = 2.4%) and then again in third-line (IFX = 19.9%, ADA = 14.6%, GOL = 4.0%, VDZ = 6.6%). The percentage of patients treated with biologic therapy who were also using a concomitant IM increased over time from first-line to third-line: IFX = 19.9% to 32.0%, ADA = 12.5% to 25.9%, GOL = 7.1% to 20.6%, VDZ = 11.1% to 20.0%. Treatment preferences for patients currently using a biologic therapy, dose escalation during maintenance therapy (i.e., a higher than indicated dose or greater than indicated dosing frequency) was observed as follows: IFX = 39.1%, ADA = 36.1%, VDZ = 30.9%, GOL = 20.8%.

Conclusion: Among patients with UC in the EU5 who go on to use an IM or biologic treatment, many patients use these treatments as their first therapy after diagnosis. Combination therapy with both IM and biologic therapy is also common and increases over the course of the disease. For patients who use biologic therapy, between 27.4% of patients use a higher than indicated dose and/or frequency. These findings suggest a number of patients experience sub-optimal levels of disease control.

Disclosure: A Armuzzi has received research support from MSD, lecture fees from AbbVie, AstraZeneca, Chiesi, Ferring, Hospira, MSD, Mundipharma, Nikkiso, Otsuka, Pfizer Inc, Takeda, TiGenix, Zambon, and consultancy fees from AbbVie, Allergan, Biogen Idc, Celltrion, Eli Lilly, Ferring, Hospira, Jansen, MSD, Mundipharma, Pfizer Inc, Samsung Bioeps, Sofar, Takeda; M DiBonaventura is an employee of Adelphi Real World; D Bargo, L Sales, J Cappelleri, G Gigante are employees and shareholders of Pfizer Inc; J Lucas, B Bluff and B Hoskin are employees of Adelphi Real World.
Abstract No: OP096

Table 1: Final list of Appropriate Quality Indicators based on all 4 statistical methods

<table>
<thead>
<tr>
<th>Pre-endoscopy</th>
<th>Appropriate QI</th>
<th>Median Score</th>
<th>Performance Threshold Median % (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-procedural (Resection)</td>
<td>Patients considered for BET, should be discussed in a Oesophago-Gastric MDT</td>
<td>9</td>
<td>100 (90, 100)</td>
</tr>
<tr>
<td>Pre-endoscopy</td>
<td>It is recommended that endoscopist undertaking BET should have undergone formal hands on training at a high-volume centre</td>
<td>9</td>
<td>100 (90, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Resection)</td>
<td>Centres should carry out sufficient numbers of BET cases per year to meet efficacy and safety standards</td>
<td>9</td>
<td>N/A</td>
</tr>
<tr>
<td>Intra-procedural (Resection)</td>
<td>Adherence to the Prague and Paris classification is recommended</td>
<td>9</td>
<td>95 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Resection)</td>
<td>It is recommended that all patients undergoing BET and follow-up should have assessment with High-definition white light (WL) endoscopy with chromoendoscopy</td>
<td>9</td>
<td>93 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Resection)</td>
<td>Where appropriate ALL visible lesions should be entirely resected with EMR or ESD</td>
<td>9</td>
<td>93 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Resection)</td>
<td>For patients having BET, the use of EUS is not routinely recommended</td>
<td>8.5</td>
<td>90 (70, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Resection)</td>
<td>Lesions with SM invasion should only be considered for curative BET if low risk of metastasis</td>
<td>8.5</td>
<td>90 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Ablation)</td>
<td>Low and High grade dysplasia without visible lesions should be considered for endoscopic ablation</td>
<td>9</td>
<td>95 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Ablation)</td>
<td>Following endoscopic resection, patients should undergo ablative therapy, every 2-4 months in order to achieve CR-IM</td>
<td>9</td>
<td>90 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Ablation)</td>
<td>For patients undergoing RFA with a focal device, the recommended dose is 12 J / cm² × 3 (with cleaning)</td>
<td>8</td>
<td>N/A</td>
</tr>
<tr>
<td>Intra-procedural (Ablation)</td>
<td>Centres undertaking BET should achieve CR-D ≥ 90 % and CR-IM ≥ 80 % within 18 months after the first treatment</td>
<td>8</td>
<td>N/A</td>
</tr>
<tr>
<td>Intra-procedural (Ablation)</td>
<td>Patients with residual dysplasia after 18 months, should be re-discussed at a Oesophago-Gastric MDT</td>
<td>9</td>
<td>90 (80, 100)</td>
</tr>
<tr>
<td>Intra-procedural (Ablation)</td>
<td>Post-BET symptomatic stricture rate should not exceed 10-15 %</td>
<td>8</td>
<td>N/A</td>
</tr>
<tr>
<td>Post Endoscopy</td>
<td>Following successful BET, patients should undergo follow up endoscopy at appropriate intervals stratified according to risk of recurrence</td>
<td>9</td>
<td>90 (80, 100)</td>
</tr>
<tr>
<td>Post Endoscopy</td>
<td>At follow-up endoscopy, biopsies should be taken from the Squamo-columnar junction and within the extent of the original BE length, for the first 2 years; thereafter biopsies should be taken from the Squamo-columnar junction and any visible lesion</td>
<td>8</td>
<td>90 (80, 100)</td>
</tr>
<tr>
<td>Post Endoscopy</td>
<td>All centres should regularly audit their outcomes and adverse events</td>
<td>9</td>
<td>N/A</td>
</tr>
</tbody>
</table>

References

OP097 BARRETT’S OESOPHAGUS: ENDOSCOPIC TREATMENT OR SURVEILLANCE? A COMPARATIVE COST-EFFECTIVENESS ANALYSIS


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Introduction: Barrett’s oesophagus (BO) is a known precursor lesion to oesophageal adenocarcinoma (OAC). All clinical guidelines recommend surveillance and/or treatment of BO patients depending on the severity of the precursor lesion. However, the optimal management strategy for non-dysplastic BO (NDBO) and low-grade dysplasia (LGD) patients remains controversial. Prior modeling studies have reported conflicting results on the management of these patients.

Aims and Methods: We aimed to identify the optimal management strategy for BO patients through a comparative modeling analysis. We used 3 independently developed population-based models from the NCI Cancer Intervention and Surveillance Modeling Network (CISNET). A cohort of 60-year-old US men with 100% smoking and followed until death without surveillance or treatment (natural history). Then, we implemented 78 unique BO management strategies. The strategies varied in (a) LGD management: with or without confirmation of LGD by a repeat endoscopy at 2 months, and surveillance with different intervals or endoscopic treatment; and (b) NDBO management: no surveillance or surveillance with different intervals. In all strategies, patients with high-grade dysplasia received endoscopic treatment. An incremental cost-effectiveness analysis, assuming a willingness-to-pay threshold of $100,000 per quality-adjusted life-year (QALY), determined the optimal strategy using the average results of the 3 models. To assess the robustness of our findings, we also analyzed the separate results of each model and simulated a cohort of US women with BO.

Results: The model’s average OAC incidence in the natural history was 110 (93-120) and the average cost was $5.57 million ($4.5-6.7 million) per 1000 BO patients. Surveillance and/or endoscopic treatment of BO patients prevented 23-37% of OAC cases, but they increased costs to $6.3-17.0 million. Considering cost-effectiveness, all strategies with only surveillance for LGD patients were dominated by those with LGD treatment. Repeated endoscopy to confirm LGD was more cost-effective than strategies without confirmatory endoscopy. The optimal strategy was treatment after confirmation by repeat endoscopy for LGD patients and surveillance every 3 years for NDBO patients.

Conclusion: Our analyses show that endoscopic treatment of patients with LGD is cost-effective, even if only these patients undergo repeat endoscopy to confirm LGD before treatment. The optimal strategy for NDBO patients is surveillance using 3-year intervals in men and 5-year in women.

BO: Barrett’s oesophagus, LGD: low-grade dysplasia, m: month, mln: million

Analysis

<table>
<thead>
<tr>
<th></th>
<th>NDBO5</th>
<th>LGD</th>
<th>OAC prevented2</th>
<th>Net cost ($2)</th>
<th>QALY gained2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (average)</td>
<td>3y</td>
<td>2m, Tx1</td>
<td>69%</td>
<td>4.1 mln</td>
<td>351</td>
</tr>
<tr>
<td>Women (average)</td>
<td>5y</td>
<td>2m, Tx2</td>
<td>62%</td>
<td>3.2 mln</td>
<td>217</td>
</tr>
<tr>
<td>Erasmus/University of Washington model4</td>
<td>2y</td>
<td>2m, Tx1</td>
<td>71%</td>
<td>6.4 mln</td>
<td>431</td>
</tr>
<tr>
<td>Massachusetts General Hospital model4</td>
<td>3y</td>
<td>2m, Tx3</td>
<td>63%</td>
<td>3.2 mln</td>
<td>371</td>
</tr>
<tr>
<td>Fred Hutchinson Cancer Research Centre model4</td>
<td>5y</td>
<td>2m, Tx3</td>
<td>73%</td>
<td>3.1 mln</td>
<td>262</td>
</tr>
</tbody>
</table>

[Table 1. Optimal management strategy for BO patients]

Disclosure: Nothing to disclose
Aims and Methods: Multicenter study in 9 European centers on patients with biopsy proven neoplastic BE. Following endoscopy (EMR) and a maximum of 5 H-APC sessions was allowed; exclusion ablation for neoplastic BE (LGIN/ HGIN) could be performed at the discretion of the endoscopists for neoplastic BE (LGIN or HGIN) without visible lesions. Primary therapeutic success was defined as one follow-up endoscopy showing normal endoscopic neo-Z-line with negative biopsies.

Results: 130 of 164 included patients (112 male, 18 female, mean age 63.8 years) have completed therapy with 3 month follow-up, 19 were excluded from the therapeutic concept for a variety of reasons. Final diagnoses were mucosal cancer (n = 79), high-grade (HGIN, n = 23), low-grade dysplasia (LGIN n = 26) and normal BE (n = 2). Therapy: Combined resection and ablation (n = 117), exclusion ablation (n = 13). Mean number of H-APC sessions: 2.69 (range 1-5). Short-term treatment outcome: Endoscopic treatment success (normal Z line) was seen in 99 cases, but in 6 cases histopathology showed intestinal metaplasia (minimal residual BE disease) or (n =1) residual cancer. 31 further cases each had either indeterminate endoscopy (minimal residual BE possible) but either negative biopsies (n = 27) or minor residual normal BE on biopsies. Based on histopathologic proof, short-term eradication rates were 89.2% (116/130). Treatment for minor residual BE is currently ongoing in some patients. Immediate complications: bleeding n = 5, post-procedure fever n = 9 and 1 perforation treated conservatively by clipping. Later strictures requiring dilation: n = 5 (5/130 = 3.8 %). In the 12 months follow-up (n = 101 at present), the endpoint of a macroscopically normal Z-Line with negative biopsies was maintained in 88/101 cases (87.1%), with 2 cases included who had indeterminate endoscopy (suggesting minor residual BE) but negative biopsies. Of the 13 cases with positive biopsies (macroscopically visible BE in 2 of them), all had non dysplastic BE. The H-APC for BE ablation appears to be feasible and safe with a short- and mid-term efficacy of close to 90% in this interim analysis; final results of this large prospective study have to be awaited. The comparative value of H-APC to RFA will be assessed in a prospective randomized trial.

Disclosure: Study was supported by Erbe Company, Germany

OPI01 FEASIBILITY, SAFETY, TOLERABILITY AND DOSE-RELATED EFFICACY OF A NOVEL SWIPE CRYOBALLOON ABLATION (90°-SCBA) DEVICE IN DYSPLASTIC BARRETT’S ESOPHAGUS
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Introduction: Cryotherapy has been used for years to eradicate flat dysplastic Barrett’s esophagus (BE), since it may be better tolerated and result in lower strictures rates when compared to heat-based ablation techniques. Cryoballon ablation (CBA) is a new technique comprising a through-the-scope catheter with a conformable balloon that is inflated and cooled using nitrous oxide. Thus far, focal CBA has been promising, but only suitable for treatment of limited BE. The novel swipe CBA (90°-SCBA) covers 90° of the esophageal circumference over 3cm in a single step. The controller software allows for adjustment of the dose (the rate at which the diffuser traverses the 3cm long axis of the balloon catheter while emitting oxygen). 90°-SCBA has been feasible and safe in animal and pre-endoscopy/gastroenterology studies.

Aims and Methods: The aim of this study is to assess feasibility, safety and dose-related efficacy of 90°-SCBA in patients with dysplastic BE. Patients with flat BE (circumferential extent ≤3cm) and low or high-grade dysplasia (LGD/HGD) or residual cancer after endoscopic resection (ER), were enrolled in 5 Dutch BE expert centers. Half of the esophageal circumference was treated, starting with 0.8mm/sec (dose 1). The dose was then escaladed with 1.0mm/sec (6 patients per dose) until the effective dose (ED) was found. ED was defined as the lowest dose resulting in a median BE regression >90% in the absence of dose-related serious adverse events (DR-SEA). ED was subsequently confirmed in a confirmation cohort. DR-SAES included severe pain (VAS > 6) for >7 days or stenosis requiring dilation. Pain (VAS 0-10), dysphagia (0-4) and other adverse events were evaluated at days 0, 1, 7 & 14. Primary outcomes were technical success, 90°-SCBA success and efficacy (BE regression at 8 weeks follow-up (FU) endoscopy assessed by 2 independent endoscopists by systematic comparison of baseline and FU videos).

Disclosure: No conflicts of interest.
Results: In total, 25 patients were included (74% male, median BE C0.5). Baseline pathology was ID (76%), HGD (12%) and adenosinarctinoma (12%). Five patients were treated with ER before inclusion. The 90-SCBA procedure was technically successful in 23 patients (92%). Device malfunctions occurred in 2 other patients (8%) and were resolved with device replacement. No DR-SAEs occurred (Table). BE regression at FU was 78% (IQR 69-86) with 0.7mm/sec (dose 1, N = 6) and 85% (75-95) with 0.7mm/sec (dose 1, N = 6) and 85% (75-95) with 0.7mm/sec (dose 1, N = 6). Age, median (IQR) 67 (52-80) 67 (53-70) 67 (62-71).

Previous EMR, n(%) 1 (17) 3 (43) 1 (8). Median dysphagia score was 0 at all FU timepoints. Conclusion: Our multicenter pilot study suggests that semi-circumferential treatment with 90-SCBA is feasible, safe and well tolerated for eradication of flat dysplastic BE. Results in a median BE regression of 85% in the 19 patients treated at a dose of 0.7mm/sec (ED) and is a promising new modality for endoscopic eradication.

Disclosure: This study was sponsored by C2 Therapeutics, Inc.

MONDAY, OCTOBER 22, 2018 15:45–17:15
OP103 LUMINAL PROTEASE ACTIVITY IS INCREASED IN PATIENTS WITH POUCH INFLAMMATION
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Introduction: Restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA) is the surgical therapy of choice for patients with refractory or complicat- ed ulcerative colitis (UC). Approximately 60% of these patients develop pouch inflammation (pouchitis).

The hypothesis is that pouchitis may occur due to compromise of the epithelial barrier function and exposure of the intestinal immune system to microbial antigens. Increased luminal proteolytic activity was associated with exacerbation of colitis in animal models as well as in patients with inflammatory bowel diseases.

Aims and Methods: We aimed to study whether luminal proteolytic activity is increased in UC patients with pouchitis and what are the functional implications on epithelial barrier function.

FCal supernatants were exposed to fecal supernatants. Epithelial integrity and permeability were determined by measuring trans-electrical epithelial resistance (TEER) and permeability of a 4 kDa FITC-dextran across the monolayers. Immunofluorescence and Western blot were performed on Caco-2 cells to assess for tight junction proteins integrity (ZO-1, occludin) after exposure to fecal supernatants.

Results: Fecal supernatants were obtained from 25 patients: 6 NP, 10 AP and 9 HC participants. Proteolytic activity was determined using FITC-casein florescence assay. Caco-2 cell monolayers were exposed to fecal supernatants. Epithelial integrity and permeability were determined by measuring trans-electrical epithelial resistance (TEER) and permeability of a 4 kDa FITC-dextran across the monolayers. Immunofluorescence and Western blot were performed on Caco-2 cells to assess for tight junction proteins integrity (ZO-1, occludin) after exposure to fecal supernatants.

Disclosure: Nisar Maharshak reports consulting fees from Janssen, Neopharm, BiomX and Mybiotics. Speaking fee from Abbvie and Takeda
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TO AN IMMUNOSUPPRESSIVE PHENOTYPE

J. Geginat10, M. Vecchi2,11, M. Rescigno1, M. Paroni12, F. Caprioli2,3

Locally injected mesenchymal stem cells (Alofisel Contact E-Mail Address: Takeda) are now an approved therapy in European Union for treatment of vector containing shRNA for COX-2 (hMSCshCOX-2) to knockdown secretion by different experimental colitis models. Pathogenicity of IL-17-secreting intestinal clones is directly implicated in the epithelial barrier disruption through the modulation of tight junction proteins. Conclusion: Intestinal Th17 cell dysfunction is associated to IFNγ production, which in turn affects intestinal permeability through the disruption of epithelial tight junctions.

Disclosure: Nothing to disclose

OP106 THE INTERLEUKIN-6 RECEPTOR AS A DRUG TARGET IN INFLAMMATORY BOWEL DISEASE; A MENDELIAN RANDOMIZATION STUDY

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Introduction: Excessive production of interleukin-6 is associated with active inflammatory bowel disease (IBD). Blockade of the interleukin-6 receptor (IL6R) with a monoclonal antibody (tocilizumab) is licensed for treatment of rheumatoid arthritis. Clinical trials of IL6R inhibitors in IBD have been small in numbers, with varying efficacy. The IL6R SNP rs2228145 associates with a similar pattern of effects to tocilizumab therapy (higher soluble IL6R, lower c-reactive protein and fibrinogen), making it an attractive genetic instrument for drug target validation.

Aims and Methods: We performed a two sample Mendelian randomization study of IL6R SNPs with impaired IL6R signaling (lower soluble IL6R, lower c-reactive protein and fibrinogen) using genome-wide association study (GWAS) summary statistics.

Results: In a fixed-effects meta-analysis of 26788 cases with Crohn’s disease (CD), 23045 with ulcerative colitis (UC) and 61630 controls, genetically elevated IL6R was associated with decreased odds of Crohn’s disease (CD) odds ratio (OR) 0.87, 95% CI 0.82–0.92, p = 0.000001463 and ulcerative colitis (UC) (OR 0.92, 95% CI 0.89–0.99, p = 0.0378) per 2-fold increment.

Conclusion: On the basis of genetic evidence in human beings, defective IL6R signaling is a strong candidate to protect against the development of both CD and UC; it is an attractive an drug target suitable for further exploration. Genetic studies in populations could be used more widely to help validate and prioritize novel drug targets or to repurpose existing agents for new therapeutic and preventive uses.

Disclosure: Nothing to disclose

References

Disclosure: Nothing to disclose
OP107 CD103⁺ DENDRITIC CELLS ARE SPECIFICALLY DECREASED IN THE INFAMED COLON FROM PATIENTS WITH ULCERATIVE COLLITIS BUT NOT IN CROHN'S DISEASE


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Introduction: Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammatory disease of the human gastrointestinal (GI) tract. Dendritic cells (DC), the most potent antigen presenting cells, are essential to maintain the mechanisms of GI-homeostasis towards nutrients and commensal in health, while initiating immune responses towards pro-inflammatory invading pathogens. However, despite the relevance of DC in modulating GI-immune responses, there is not much information about DC composition in the human GI-tract both in health and IBD.

Aims and Methods: Our aim was to characterize human GI-DC subsets, phenotype and function both in health and in IBD patients. To that end, human intestinal biopsies were obtained from healthy controls and IBD patients (including UC and CD, both active and quiescent). Tissue was disaggregated and the lamina propria mononuclear cells (LPMC) characterized by flow cytometry.

Results: Human intestinal DC were identified within singlet viable leukocytes as CD14⁻CD4⁺HLA-DR⁺CD1c⁺. Type 1 conventional DC were defined as CD11c⁺I-κBα⁻CD123⁻, while type 2 conventional DC were identified as SIRPα⁺, while further divided into subsets based on the expression of CD103. Total DC numbers were indeed further divided into subsets based on the expression of CD103 and SIRPα. Type 1 (minority) and type 2 (majority) DC further decreased in the duodenum. Type 1 (minority) and type 2 (majority) (either distal or proximal) compared with the ileum. DC numbers were indeed further divided into subsets based on the expression of CD103. Total DC numbers were indeed further divided into subsets based on the expression of CD103 and SIRPα. Type 1 CD103⁺ DC had higher levels of HLA-DR, CD40, CCRL, CD137, ICOSL and PD-L1. CD103⁺ DC were also more phagocytic and were acquired in multiple integran genes in inflammatory bowel disease. Nut. Genet. 2017; 49(7); 979–986.

Conclusion: Our data indicate that ADR-driven signals inhibit pathogenic responses in the gut of CD patients.

Disclosure: Nothing to disclose

OP109 TOLERogenic IMMUNE-MODIFYING NANOPARTICLES CONTAINING GLIADIN RESTORE TOLERANCE & ABRAGE TOLEROGENIC DISEASE IN MURINE MODELS OF COELIAC DISEASE

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Introduction: In coeliac disease (CD), tolerance to gluten (gliadin) proteins from cereals is lost. Tolerogenic immune modifying nanoparticles (TIP) are effective at restoration of antigen-specific immune tolerance in various autoimmune conditions. The identification of gliadins as dietary antigens and drivers of immune-mediated pathology in CD suggests that TIP containing gliadin (TIP-GLIA) may serve as a cure.

Aims and Methods: Here, we tested immunomodulatory effects of TIP-GLIA vs. control TIP in 3 different mouse models of CD, 1) a delayed-type hypersensitivity, 2) a HLA-DQ2 transgenic, and 3) a gliadin memory T cell enteropathy model. Nanoparticles were administered intravenously.

Results: Treatment with TIP-GLIA reduced gliadin-specific T cell proliferation, inflammatory cytokine secretion, circulating gliadin-specific IgG IgG2, and T cell proliferation. Protective effects were also observed on CD11b⁺/CD11c⁺ DC following mucosal conditioning. The specific reduction of CD103⁺ DC in the inflamed mucosa from UC patients, but not CD, suggests the presence of different pathogenic mechanisms occurring in IBD.

Conclusion: Nothing to disclose

Disclosure: Nothing to disclose

References


MONDAY, OCTOBER 22, 2018

A43
an agreement between the University of Helsinki and Cour Pharmaceuticals Development Company, T.L.F. and S.M. received funding to conduct experiments.

OP110 ABERRANT INTRA-EPITHELIAL LYMPHOCYTES CAUSE VILLOUS ATROPHY IN REFRACtORY CELIAC DISEASE TYPE II BY GRANZYME B-INDUCED APOPTOSIS OF ENTEROCYTES MEDIATED VIA CD103(eGF)7-E-CADHERIN-INTERACTIONS

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Introduction: Refractory celiac disease type II (RCDII) is an indolent intestinal tumor of aberrant intraepithelial T-lymphocytes (IEL). The severe enteropathy found in RCDII is caused by aberrant IEL that exert cytotoxicity against the enterocytes. In this study, we investigated the cell death mechanisms that are responsible for villous atrophy in RCDII and their potential diagnostic and therapeutic implications.

Aims and Methods: mRNA and protein expression were determined using RT-MLPA analysis, immunofluorescence and flow cytometry, respectively. Enterocyte killing and degranulation by aberrant IEL were measured in the presence of a transwell, specific inhibitors or therapeutic agents, using flow cytometry. Secretion of granzyme B was detected by ELISA.

Results: mRNA and protein expression of granzyme B were significantly upregulated in the cytoplasm of aberrant IEL of patients with RCDII compared to levels of granzyme B expression in patients with celiac disease on a gluten-free diet (GFD). The level of granzyme B expression in RCDII patients correlated with the severity of villous atrophy and with clinical response to therapy. RCDII cell lines also demonstrated increased levels of granzyme B expression. Furthermore, in RCDII patients and RCDII cell lines degranulation and secretion of granzyme B were observed in the presence of epithelial cells. Incubation of RCDII cell lines with epithelial cell line Caco2 showed that aberrant IEL induced apoptosis of Caco2. Treatment with a granzyme B inhibitor demonstrated that killing of enterocytes was granzyme B dependent and that degranulation by IEL was imperative. In addition, we found that the aberrant IEL induced cell death through triggering of the intrinsic apoptosis pathway via mitochondrial membrane depolarization and caspase-3 and -9 activation. For degranulation of granzyme B and killing of the enterocytes, binding of the aberrant IEL to the epithelial cell was necessary. CD103(eGF) expression was significantly increased in RCDII patients compared to CD patients on GFD. Functional studies revealed that CD103(eGF)7-E-cadherin interaction was essential for release of granzyme B and loss of enterocytes. Treatment with therapeutic agent etrolizumab, an anti-P7 mAb, inhibited degranulation of granzyme B and killing of the epithelial cells by RCDII cell lines.

Conclusion: Killing of enterocytes in RCDII is dependent on upregulated expression of granzyme B and interaction with the aberrant IEL through CD103(eGF)7-E-cadherin binding. These data contribute to a better understanding of the pathogenesis of villous atrophy in RCDII and therefore can be important for diagnostic purposes and during follow-up of RCDII patients. Moreover, our preclinical findings support the potential use of etrolizumab as a novel therapeutic agent for the treatment of RCDII patients.

Disclosure: Nothing to disclose.
OP112 COELIAC DISEASE DIAGNOSIS IN INDIVIDUALS ON A GLUTEN-FREE DIET

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Introduction: Coeliac disease (CD) is a gluten-dependent enteropathy that develops in genetically susceptible individuals. Current treatment is a gluten-free diet (GFD), which leads to the recovery of the normal morphology and function of the intestine, with the subsequent disappearance of clinical symptoms and specific antibodies. Therefore, CD diagnosis needs to be established under gluten containing diet, a problem due to the increasing number of individuals following a GFD.

Aims and Methods: Based on the study of Han et al. (1), we studied the utility of detecting activated γδ and CD8 T cells expressing gut-homing receptors after a 3-day gluten challenge aimed to diagnose CD in individuals on a GFD. We studied 18 patients previously diagnosed with CD and 20 controls, mainly composed by healthy volunteers that followed a gluten containing diet, a problem due to the increasing number of individuals following a GFD for at least 1 month. All subjects were exposed to 12-15 g of gluten every day for 3 consecutive days. Peripheral blood was collected before (day 0) and 6 days after the gluten challenge aimed to diagnose CD in individuals on a GFD.

Results: The 3-day gluten challenge was completed by all participants. In all of them, the studied T cell populations were undetectable or barely present at day 0, but on day 6, γδ and CD8 T cells coexpressing CD103, CD7 and CD8 were observed in every CD patient, but only in 1 control. No differences were observed between patients with high and low/low-HLA risk genetics.

Conclusion: A short gluten challenge elicits the activation of CD103+CD8γδT cells that can be detected by flow cytometry in peripheral blood, even in those patients with a more difficult diagnosis, opening new possibilities for CD diagnosis in individuals on a GFD.

Disclosure: Nothing to disclose

References

OP113 CLASSIFICATION OF REFRACTORY CELIAC DISEASE WITH FLUORESCENCE-ACTIVATED CELL SORTING OF INTESTINAL LYMPHOCYTES: DATA FROM A TERTIARY REFERRAL CENTER

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Introduction: Refractory celiac disease (RCD) is classically categorized into two different entities: RCD type I is an autoimmune disease that responds to immunosuppression while in RCD type II a monoclonal transformation of IEL is found. This is usually detected by means of TCR clonality analysis. Patients with RCD type II have a poor prognosis and a high risk of development of enteropathy-associated T-cell lymphoma (EATL), so that it has been proposed to consider RCD type II as a low-grade intraepithelial lymphoma (pre-EATL). Recently, flow cytometric analysis of isolated intestinal lymphocytes has been introduced as new diagnostic modality for the detection of so-called aberrant intestinal lymphocytes (ILs).

Aims and Methods: The purpose of this study was to (i) detect aberrant ILs in a cohort of non-celiac, celiac and RCD patients by means of flow cytometry, (ii) to verify whether there is an association between cellular characteristics of RCD patients and presence of aberrant ILs, (iii) to evaluate the diagnostic accuracy of aberrant ILs for RCD pre-EATL in our cohort.

Immunostaining (CD3, CD4, CD8, CD7, CD103, TCRγδ, lineage markers) and flow cytometric analysis of isolated IELs from duodenal biopsies of patients with RCD, uncomplicated CD and controls were performed. Aberrant ILs were defined by means of different gating strategies including cytCD3+/surfCD3−/CD7−/CD103− (Table 1). Patients with evidence of aberrant ILs also showed significantly more criteria for severe malabsorption (as assessed by a cumulative malabsorption score). A cut-off of 11% ILs for the most reliable strategy allowed to identify a subgroup of low risk RCD patients (n = 21) and a small group of high-risk RCDs (n = 5) that were classified as pre-EATL (2 of them with a later EATL diagnosis). Nevertheless, sensitivity gaps were uncovered: 1 patient with ulcerative jejunoileitis who later developed an EATL was not identified as pre-EATL. Furthermore, 2 overt EATL cases were false negative (i.e., overall sensitivity 67%, NPV 89%). Alternative, simpler gating strategies for aberrant ILs showed similar accuracy to the main strategy.

Conclusion: In clinical practice, flow cytometry of aberrant ILs may be a simple predictor of high-risk RCD. However, its use as the only diagnostic strategy for classifying patients in RCD I (low risk) and RCD II pre-EATL may also lead to misclassification. A multimodal diagnostic approach for the diagnosis of RCD (including TCR clonality and malabsorption score) maximizes diagnostic accuracy.

Disclosure: Nothing to disclose

References
It is necessary to externally validate the score and conclusion:

49.3%

High-risk group (≥21 points): 21.2%

Medium-risk group (17-24 points): 4.4%

Low-risk group (<17 points): 95.8%

Hospitalization for less than 30 days (100% versus 68.4%, p = 0.0002). The prevalence of Diabetes Mellitus (71.7% versus 31.6%) and hepatocellular carcinoma (33.6% versus 31.6%) were not relevant as factors predisposing to MDRO infection (p = 0.6526 and p = 0.9214, respectively).

Conclusion: Indiscriminate use of antibiotics and PPIs increases the risk of MDRO infections, suggesting that the prescription of these drugs should be restricted to formal indication. Also hospitalization for more than 48 hours or hospital discharge for less than 30 days have been shown to influence the onset of MDROs. This suggests that hospitalizations in LC patients should be limited to the minimum number of days and risk factors should be identified to prevent the emergence of these microorganisms.

Disclosure: Nothing to disclose.

References


Disclosure: Nothing to disclose.

OP115 RISK FACTORS FOR THE EMERGENCE OF MULTIDRUG-RESISTANT ORGANISMS IN LIVER CIRRHOSIS

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Introduction: Infections in patients with liver cirrhosis (LC) are common and one of the major causes of hospitalization. Multidrug-resistant organisms (MDROs) are a current reality that can alter the paradigm of treatment and prevention of infection in these patients.

Aims and Methods: The aim of this study is to identify the risk factors for the occurrence of MDROs in patients with LC. Prospective study from October 2017 to March 2018 in consecutively hospitalized patients with uncomplicated LC with infection. Blood, urine and ascitic fluid cultures were analyzed.

Results: 52 episodes of infection (43 males, mean age 63 ± 14.6 years, 30 Child-Pugh B or C, 15 episodes no microorganisms were identified) were analyzed in the last 90 days (including norfloxacin prophylaxis) (94.4% versus 47.4%, p = 0.0033) and hospitalization for more than 48 hours or discharge for less than 30 days (100% versus 68.4%, p = 0.0082). The presence of Diabetes Mellitus (71.7% versus 31.6%) and hepatocellular carcinoma (33.6% versus 31.6%) were not relevant as factors predisposing to MDRO infection (p = 0.6526 and p = 0.9214, respectively).

Conclusion: Indiscriminate use of antibiotics and PPIs increases the risk of MDRO infections, suggesting that the prescription of these drugs should be restricted to formal indication. Also hospitalization for more than 48 hours or hospital discharge for less than 30 days have been shown to influence the onset of MDROs. This suggests that hospitalizations in LC patients should be limited to the minimum number of days and risk factors should be identified to prevent the emergence of these microorganisms.

Disclosure: Nothing to disclose.

OP117 RANDOMIZED PLACEBO-CONTROLLED STUDY OF ORPHENADRINE IN TREATMENT OF MUSCLE CRAMPS IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Muscle cramps are common in patients with liver cirrhosis and adversely influence quality of life with no available highly effective treatment.

Aims and Methods: The aim of this study was to assess the efficacy and safety of orphenadrine in treatment of muscle cramps in cirrhotic patients. Methods: 122 patients with liver cirrhosis were enrolled in this study who suffering from frequent muscle cramps (≥ 3 per week), randomized to receive either orphenadrine 100 mg twice daily or placebo for 1 month twice daily as a control.
33 patients in the orphenadrine group and 36 patients in the placebo group were on diuretic treatment. Orphenadrine was administered orally in a single dose of 15 mg every 4 hours. The overall compliance with the medication was found to be high, with over 80% of patients taking the medication as prescribed.

Results: The results of the study showed a significant difference in the incidence of muscle cramps between the orphenadrine and placebo groups. The incidence of muscle cramps in the orphenadrine group was 14% vs. 28% (p < 0.001). The side effects were few such as dry mouth, drowsiness, and nausea, with no significant difference between their occurrences in the 2 groups.

Conclusion: Orphenadrine is safe and effective in treatment of muscle cramps in patients with liver cirrhosis.

Disclosure: Nothing to disclose.

Reference

OP118 EFFECTIVENESS OF ACTIVE OUTPATIENT FOLLOW-UP PROGRAM ON LONG-TERM SURVIVAL OF PATIENTS WITH ALCOHOLIC LIVER DISEASE

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Introduction: Alcoholic liver disease (ALD) is the most prevalent cause of advanced liver disease and liver-related mortality in Europe and Russia. Abstinence is the first line and the basic therapeutic procedure for any form and stage of ALD. Combined comprehensive supportive and behavioral (repeated short brief intervention sessions) treatments provided by clinicians may increase abstinence rate followed by liver function stabilization and improves patient’s outcome.

Aims and Methods: The main aim of this study was to estimate the effectiveness of the active outpatient follow-up (AOF) program in achieving and maintaining abstinence, liver function compensation and improving the long-term outcome of patients with ALD.

In this historical control study 29 patients with ALD were enrolled in the group of AOF that included active supervision by hepatologist: physical and motivation assessment, motivational interviewing, liver panel lab tests with the rate once at 3 months. The duration of the AOF was 12 months with 1 follow-up visit after 12 month. The historical control group included 36 patients with ALD and history of 2-year follow-up in the hepatology department, who received comprehensive therapy and education to avoid alcohol.

Results: There were significant differences in adherence to abstinence between AOF and control groups at 6 (88% vs 43%, p < 0.001), 9 (84% vs 44%, p < 0.001), 12 (81% vs 44%, p < 0.001) and 24 (80% vs 40%, p = 0.007) months of follow-up, respectively. The 24-month alcohol relapse occurred in 2 (8%) patients in the AOF group compared with 13 (36%) patients in the control group (p = 0.005). Unvariable analysis showed that only AOF was significantly associated with abstinence and maintaining of abstinence. Multivariable regression analysis of alcohol relapse during the 24 month showed that AOF is independent factor for being abstenor (OR: 0.80 [95% CI 0.14-0.479]; p = 0.006).

Conclusion: The program of active outpatient follow-up provided by hepatologist can increase likelihood of achieving and maintaining abstinence, prolonged compensation of liver function and improve the long-term survival of patients with ALD.

Disclosure: Nothing to disclose.

MONDAY, OCTOBER 22, 2018
15:45-17:15
Diagnosis and risk factors of pancreatic diseases – Room L8

OP120 DEFINING PANCREATITIS AS A RISK FACTOR FOR pancreatic cancer: THE ROLE, INCIDENCE, AND TIMELINE OF DEVELOPMENT

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Introduction: Pancreatic cancer has a high mortality rate and is the third leading cause of cancer related deaths in the United States. Risk factors for developing pancreatic cancer include age > 55, male sex, obesity, tobacco, and diagnosis of diabetes. Additionally, acute and/or chronic pancreatitis has been implicated as an important risk factor for pancreatic cancer; however, the incidence and temporal relationship of pancreatitis prior to the diagnosis of pancreatic cancer is unclear.

Aims and Methods: We aim to establish the role and incidence of pancreatitis temporally with the development of pancreatic cancer. A population-based study, with a web-based platform called Explorys was used to collect de-identified patient data. Over 50 million patients, spanning nationally in over 20 health-care systems’ electronic medical records is in this cloud-based, HIPPA-enabled platform. Data was obtained using ICD-9 code criteria with search terms “acute pancreatitis,” “chronic pancreatitis,” and “malignant tumor of the pancreas.” A temporal relationship between pancreatitis diagnoses, followed by pancreatic cancer diagnosis was investigated. Intervals of 3, 6, 12, 24, and 36 months were observed. Demographic data, including age, gender, and race was also recorded and analyzed.

Results: A total 50,080 patients were found to have a diagnosis of pancreatic cancer. 7,420 (14.8%) of these patients were found to have diagnoses of pancreatitis prior to their cancer diagnoses. Of those, 91.6% were between the ages of 45-89. Interestingly, there was a higher incidence of pancreatic cancer in the African-American population vs. the Caucasian population (21.2% vs 14.8%, p < 0.05) group with prior pancreatitis diagnosis. Further analysis of pancreatic cancer diagnosis revealed that 6,030 of the 7,420 patients were diagnosed within 3 months of their acute and/or chronic pancreatitis (81.3%) diagnosis. Finally,
OPI12  THE WAY FROM ABDOMINAL PAIN TO PEDIATRIC PANCREATITIS – THE PINEAPPLE STUDY


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Introduction: The documented incidence of pediatric pancreatitis (PP) is low, but it shows a rising pattern from Eastern to Western Europe and the USA. The cause of this phenomenon is not clear, but based on a single center study the amylase and lipase measurements correlate with the incidence of the disease.

Aims and Methods: The aim of the PINEAPPLE study is to investigate the current diagnostic practice for PP and to estimate the occurrence of pancreatitis among children suffering from abdominal pain. Furthermore we would like to develop an IBM guideline to establish a scoring system in order to evaluate the necessity of diagnostic steps for PP in children with abdominal pain. PINEAPPLE is a registered (ISRCTN53618458), observational, multinational clinical trial and the pre-study protocol is published (http://www.dnm.nlm.nih.gov/pubmed/26641250).

Results: PINEAPPLE-R: 9.7% (2775/28707) of the children appeared at ER unit with abdominal pain. In case of abdominal pain sPEM was performed in 14% whereas 32% of the patients had transabdominal ultrasonography. In our cohort the number of sPEM decreases from the USA (21.6%) to Eastern Europe (13% in Hungary and 0.6% in Romania) and it correlates (r = 0.97) with the incidence of PP (0.775). PINEAPPLE-P: 8 pancreatitis from 496 patients with abdominal pain were diagnosed. Positive family history and upper abdominal pain were characteristic for PP but fever and forced posture were not typical.

Conclusion: The PINEAPPLE-R shows that the incidence of PP is 0.3% among children with abdominal pain based on the current diagnostic practice. Better awareness of PP results 1.6% incidence of PP as a reason of abdominal pain. These data strongly suggest that acute pancreatitis is underdiagnosed in children.

Disclosure: Nothing to disclose.

OPI123  IS DIABETES BEING IGNORED IN PATIENTS WITH PANCREATIC CANCER?

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Introduction: Many risk factors have been implicated in pancreatic cancer, including age > 55, male gender, obesity, tobacco use, pancreatitis and diabetes mellitus (DM). It has been reported in literature that as high as 80% of patients with pancreatic cancer have glucose intolerance or frank diabetes.

Aims and Methods: We aim to evaluate if physicians are diagnosing, reporting, and managing diabetes in patients with pancreatic cancer. A population-based study, using an IBM platform called Explorys, was used to collect de-identified patient data. Over 50 million patients, spanning nationally in over 40 healthcare systems’ electronic medical records (EMR) is in this cloud-based, HIPPA-enabled platform. Data was obtained using ICD-9 code criteria with search terms “diabetes mellitus” and “malignant tumor of the pancreas.” Further, patients were also included if they were on anti-diabetic medications, including metformin, sulfonylureas, and insulin. These search terms were observed to ensure diagnosis of DM after pancreatic cancer as a first occurrence. Subsequently, HbA1c levels were observed in correlation to rates of mortality within this cohort.

Results: A total of 50,080 patients in the Explorys database with diagnosis of pancreatic cancer. Of those, 20,160 (40.3%) had concomitant diagnosis of DM in their EMR. African-Americans had a higher rate of DM development when compared to Caucasians (50.2% vs. 39.9%, p < 0.001). Majority of the diabetic patients were aged 60-89, with predominance between 70-79. As levels of HbA1c increased, rates of mortality did as well. Patients with HbA1c levels between 4-6.4% were found to have a lower mortality rate than those with HbA1c levels in the range between 6.5-8% (44.8% vs. 46.6%, p=0.0293) and 9-12% (44.8% vs. 47.6%, p=0.00672).

Conclusion: It has been reported in literature that as high as 80% of patients with pancreatic cancer have concomitant diagnoses of DM. We found drastically different percentages; these variations may be due to several factors. Firstly, it is very possible clinicians are underdiagnosing diabetes, especially in patients with pancreatic cancer. It is possible because of the high mortality of these patients, their other diagnoses, including DM, are being overlooked. Secondly, if DM is being diagnosed, physicians are not adequately reporting it in a patient’s EMR. Moreover, patients with DM with HbA1c levels greater than 6.5% have a higher rate of mortality as compared to patients with HbA1c levels below 6.5%. Clinicians need to be aware of the high incidence of DM in patients with pancreatic cancer, so proper diagnosis and management can be implemented to possibly decrease mortality. Increased awareness should be also be in elderly patients between 60-69, as well as the African-American population where prevalence was highest.

Disclosure: Nothing to disclose.

[Demographics and Risk Factors of Pancreatic Cancer with concomitant Diabetes]

Disclosure: Nothing to disclose.
OP124 PANCO: AN OPEN-LABEL, SINGLE-ARM PILOT STUDY OF ONCOSIL® IN PATIENTS WITH UNRESECTABLE Locally ADVANCED Pancreatic Adenocarcinoma IN COMBINATION WITH FOLFIRINOX OR GEMCITABINE+NA-PACLITAXEL CHEMOTHERAPIES

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Introduction: Locally advanced pancreatic cancer (LAPC) is associated with a poor prognosis. Current standard treatment is limited to chemotherapy or chemo-radiotherapy. Novel treatment approaches are crucial in attempting to combat this unmet medical need. Phosphorus-32 (P-32) Microparticles is a brachytherapy device that implants a predetermined dose of the beta radiation emitting isotope (P-32) directly into pancreatic tumours via endoscopic ultrasound (EUS) guidance. The presented data are early results from an ongoing international, multi-institutional, single-arm pilot study. The study objective is to determine the safety and efficacy of P-32 Microparticles in a patient population undergoing standard chemotherapy for unresectable LAPC.

Aims and Methods: Eligible patients were allocated to receive either gemcitabine+na-paclitaxel or FOLFIRINOX by physician choice. P-32 implantation took place during the 4th or 5th week following the initiation of chemotherapy. P-32 was implanted directly into the pancreatic tumour via EUS guidance, using a fine needle aspiration (FNA) needle. Each patient’s dose was calculated from the tumour volume where the absorbed dose of P-32 to the tumour was calculated to equal 100 Gy. Diffusion pattern of the P-32-suspension following implantation was assessed by EUS and by Bremsstrahlung SPECT/CT imaging. Chemotherapy was continued after the implantation. Safety data was collected weekly and toxicity was graded using the Common Terminology Criteria for Adverse Events (CTCAE). Cetuximab read CT scans were conducted every 8 weeks to assess response defined as complete response (CR), partial response (PR), and stable disease (SD) rate, according to RECIST 1.1 criteria. FDG-PET scans were performed at baseline and at week 12.

Results: Data is reported on the first 20 implanted patients (12 males and 8 females, median age 65 years [range 54-84]) up to week 16 of follow-up. At 16 weeks, the objective response rate was 20% – PR in 4/20 patients. The local disease control rate (CR, PR and SD) was 85% – either PR or SD in 17/20 patients. Median change in tumour volume from baseline to week 16 was 33% (range +56% to -80%). Total lesion glycolysis (TLG) as measured via FDG-PET scan showed a median reduction of 54% (range +45% to -100%) from baseline to week 12.

The EUS-guided implantation was carried out successfully in all patients and with no serious complications. By week 16, 318 adverse events (AEs) were reported. 33 Grade 3 AEs (10%) and 6 (2%) Grade 4 toxicities were reported. The most common AEs of Grade 3 and 4 severity were neutropenia (7), anaemia (2), constipation (2), vomiting (2) and fatigue (2). None of the G3 and G4 AEs were attributable to the device or the implantation procedure.

Conclusion: Early data indicates that the use of EUS-guided implantation of P-32 is highly feasible, well tolerated and has an acceptable safety profile in combination with standard first-line chemotherapy for LAPC. Preliminary data shows evidence of tumour regression and local disease control. These results, however, warrant further evaluation. The clinical trial is ongoing and additional safety and efficacy data will be presented.

References: ClinicalTrials.gov Identifier: NCT03030378

Disclosure: Acknowledgement: Nabo-paclitaxel was supported by Specialised Therapeutics Australia Pty Ltd. PanCO is a commercially sponsored clinical trial. OncoSil Medical is the trial Sponsor. D Crough, D Williams, V Kwan, N Nguyen, N Phillips, E Godfrey and P Ross are participating trial investigators. T Mahler and A Kraszewski are employees of OncoSil Medical. This abstract has been accepted as a poster presentation at the ESMO World Congress on Gastrointestinal Cancer 2018. This meeting will take place in Barcelona on 20 - 23 June 2018.

TUESDAY, OCTOBER 23, 2018 08:30–10:00
Diagnosis and management of malignant distal biliary obstruction – Room F2

OP126 ANTIFLUX METAL STENT VERSUS CONVENTIONAL COVERED METAL STENT FOR NONRESECTABLE DISTAL MALIGNANT BILIARY OBSTRUCTION: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: An antiflux metal stent (ARMS) for nonresectable malignant biliary obstruction may prevent recurrent biliary obstruction (RBO) caused by common bile duct (CBD) or distal common bile duct (DCBD) stricture. The superiority of the ARMS over conventional covered self-expandable metal stents (SEMSs) has not fully examined.

Aims and Methods: We conducted a multicenter randomized controlled trial to examine whether RBO of an ARMS with a funnel-shaped valve was longer than that of a covered SEMS in patients without a history of SEMS placement. Secondary outcomes included causes of RBO, adverse events, and patient survival.

Results: We enrolled 104 patients (52 patients per arm) from September 2014 to June 2016 at 11 tertiary care centers in Japan. The median TRBO did not differ significantly between the ARMS and covered SEMS groups (251 days vs 351 days, respectively; p = 0.11). RBO due to biliary sludge or food impaction was observed in 13% and 9.8% patients who received an ARMS and covered SEMS, respectively (p = 0.038). The ARMS appeared to be associated with a higher rate of stent migration compared with the covered SEMS (31% vs 12%, respectively; p = 0.038). No significant between-group difference was observed for adverse events or patient survival.

Conclusion: The current ARMS is neither associated with longer TRBO compared with the covered SEMS. Further modifications including addition of an anti-migration system are required to justify the use of the current ARMS as a first-line palliative treatment modality for distal malignant biliary obstruction.

Disclosure: The authors declare no conflicts of interest.

OP127 EUS-GUIDED BILARY DRAINAGE VERSUS ERCP FOR THE PRIMARY PALLIATION OF MALIGNANT BILIARY OBSTRUCTION: A MULTICENTER RANDOMIZED CLINICAL TRIAL

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Introduction: Although ERCP for the palliation of malignant biliary obstruction is the standard care, post-procedure pancreatitis and stent dysfunctions are not uncommon. While endoscopic ultrasound (EUS)-guided biliary drainage (EUS-BD) is garnering interest as a viable option when ERCP is impossible, its role as a primary palliation of malignant distal biliary obstruction is yet to be proven.

Aims and Methods: The aim of the study was to determine whether EUS-BD is comparable to conventional transpapillary stenting with ERCP in the primary palliation of malignant distal biliary obstruction. We performed a randomized allocation to EUS-BD or ERCP in 125 patients with unresectable malignant distal biliary obstruction at four tertiary academic referral centers in South Korea.

Results: Technical success rates were 93.8% (60/64) for EUS-BD and 90.2% (55/61) for ERCP (difference 3.6%, 95% 1-sided confidence interval lower limit 0.44%, p = 0.003 for noninferiority margin of 10%). Clinical success rates were 90.0% (54/60) in EUS-BD and 94.5% (52/55) in ERCP (p = 0.49). Lower rates of overall adverse events (6.3% vs 19.7%, p = 0.03) without post-procedure pancreatitis (0.0% vs 14.8%), reinfection (15.6% vs 42.6%), and higher rate of stent patency (85.1% vs 48.9%) were observed with EUS-BD at the study end. EUS-BD was associated with more preserved QoL than transpapillary stenting after 12 weeks of the procedure.
Conclusion: This study demonstrated comparable technical and clinical success rates for ERCP in relief malignant distal biliary obstruction. Coupled with longer duration of bile duct patency, lower rates of adverse events and re-intervention, EUS-BD should be considered as a viable primary treatment option in patients with distal biliary obstruction from unresectable malignancy.

Disclosure: Nothing to disclose.

TUESDAY, OCTOBER 23, 2018 08:30–10:00
Oesophageal disorders: Mechanisms and management – Room G

OP128 HYPERCONTRACTILE (JACKHAMMER) ESOPHAGUS: DEMONSTRATES EXCESSIVE EXCITATORY AND ABNORMAL INHIBITORY DYSFUNCTION ON PROVOCATIVE TESTING DURING HIGH RESOLUTION MANOMETRY (HRM)

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Introduction: Excessive excitation of the esophageal smooth muscle is thought to induce esophageal hypercontractility. Abnormal inhibition can lead to prematurity esophageal contractions, with or without abnormal lower esophageal sphincter (LES) relaxation. Esophageal provocative testing (multiple rapid swallows, MRS) during HRM evaluates esophageal excitation and deglutitive inhibition, and could provide insights into the pathophysiology of hypercontractile esophageal disorders.

Aims and Methods: We aimed to evaluate interrelationships between excessive excitation and abnormal inhibition in esophageal hypercontractile disorders, using MRS. Esophageal HRM fulfilling Chicago Classification 3.0 criteria for hypercontractile esophagus (HE) with and without esophageagastic junction (EGJ) obstruction were reviewed from 5 centers (4 in Europe, 1 in US). Incomplete studies, and prior foregut surgery were exclusions. Upper endoscopy and barium studies excluded structural processes (rings, hiatus hernia, stricture). Single swallows (SS) and MRS were analyzed using HRM software tools assessing integrated relaxation pressure (IRP, >15 mmHg·cm·s) excitation, distal latency (DL) and distal contractile integral (DCI); MRS:SS DCI ratio >1 defined contraction reserve. Comparison groups were achalasia type 3 (positive control for EGJ obstruction) and healthy volunteers (negative control).

Results: Study groups consisted of 40 patients with HE (62.6 ± 2.0, 63% F), 30 with HE and EGJ obstruction (65.6 ± 2.7, 55% F), 72 with achalasia type 3 (66.2 ± 2.0, 30% F) and 18 normal controls (27.4 ± 6.7, 56% F). Higher mean DCI values were noted in HE and HE with EGJ obstruction groups (p = ns between SS and MRS, and between groups), these DCI values were significantly higher than comparison groups (p < 0.0001 for each comparison). MRS:SS DCI ratio was lower in HE with obstruction compared to achalasia type 3 (p = 0.03) and normal controls (p < 0.001), and trended toward significance in HE vs. achalasia type 3 (p = 0.16). Proportions with contraction reserve were lower in HE subgroups (p = 0.03 across groups). Incomplete inhibition was similar between EGJ obstruction categories (HE: with obstruction, achalasia type 3, p = ns), and lower in HE without obstruction (p = 0.04 vs. achalasia type 3, p = 0.06 vs all obstructive categories). On symptom analysis, perceptual symptoms (heaviness, chest pain) were common in HE subgroups (p = 0.09 across groups), while transit symptoms (dysphagia) were more frequent in the setting of EGJ obstruction.

Conclusion: The esophageal smooth muscle demonstrates excessive excitation at HE subgroups, manifest as high DCI and diminished contraction reserve on MRS. In contrast, abnormal inhibition is predominant in achalasia type 3, and participates in the pathophysiology of HE with obstruction. Our findings indicate that the balance of excitation and inhibition defines the clinical and therapeutic manifestations of HE, HE with obstruction and achalasia.

Disclosure: Nothing to disclose.

References


LARYNGOPHARYNGEAL REFLUX AND COUGH REFLUX SENSITIVITY
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Introduction: Cough reflex sensitivity to inhaled irritants is influenced by the functional state of cough-triggering afferent nerve terminals in the larynx and large airways. Laryngopharyngeal reflux (LPR) causes irritation of the larynx and possibly large airways. However, the relationship between the cough reflex sensitivity to inhaled irritants and LPR is incompletely understood.

Aims and Methods: We hypothesized that cough reflex sensitivity in patients with LPR is positively correlated with LPR. Our hypothesis predicts that patients with more frequent LPR have lower cough reflex threshold. Consecutive patients referred for LPR were evaluated and those with positive reflux symptom index (RSI > 13) and/or reflux finding score (RFS > 7) were evaluated. LPR was evaluated by 24-hour dual pharyngeal and distal esophageal 24-hour pH/impedance monitoring. Appropriate distance between pharyngeal and distal esophageal pH sensors was chosen based on manometrically determined LES and UES. LPR event was inferred from the pharyngeal reflux following reflux detection in the distal esophagus. For each LPR event we determined the maximum drop of pH at the pH levels < 6, < 5.5, > 5.0, < 4.5 and < 4.0 to perform the analysis independently of the assumption how the pH of LPR is required to affect the LPR episodes with pH drop.

Correlations between cough reflex sensitivity expressed as C5 and the numbers of LPR episodes, irrespective of the acidity of the LPR event. Cough reflex sensitivity was determined by single breath capsaicin inhalation challenge of doubling concentrations of capsaicin (0.01–0.1 mg/ml). Seven subjects who demonstrated the lowest concentration of capsaicin that evoked at least 2 coughs (C2) or 5 coughs (C5). Statistical analysis C2 and C5 values were log transformed and Pearson coefficients were calculated for correlation with reflux parameters.

Results: 27 consecutive patients were evaluated. The number of LPR events that reached pH 6.0, 5.5, 5.0, 4.5 and 4.0 was 14[8-21], 42[7], [0-2], [0-1], [0-0]. Correlations between cough reflex sensitivity expressed as C5 and the numbers of LPR episodes with pH drop to < 6.0, 5.5, 5.0, 4.5 and 4.0 as expressed as the R value were 0.07, 0.04, 0.01, 0.02, 0.23, respectively (p > 0.1 not significant in all cases). Correlations between cough reflex sensitivity expressed as C2 and the number of LPR episodes, irrespective of the acidity of the LPR event.

Conclusion: The number of LPR episodes does not correlate with the cough reflex sensitivity in patients with laryngopharyngeal reflux, irrespective of the acidity of LPR event. This suggests that a direct simple relationship between the intensity of laryngeal irritation and cough is improbable.

Support: Biomedical Center Martin [ITMS 26220220187]

Disclosure: Nothing to disclose.

A LARYNGOPHARYNGEAL REFLUX AND COUGH REFLUX SENSITIVITY

OP310 ANTI-REFLUX ENDOSCOPIC SURGERY: ENDOSCOPIC CARDIOPLASTY USING ENDOSCOPIC MUCOSAL RESECTION MAY EFFECTIVELY TREAT REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE
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Introduction: Anti-Reflex Endoscopic Surgery (ARES) is a new efficacious treatment of option for gastroesophageal reflux disease (GERD). We propose to define “esophageal remodeling” as the functional restoration of the esophagogastric junction (EGJ) that involves increased lower esophageal sphincter (LES) pressure. ARES is a esophageal fundoplication technique using endoscopic mucosal resection (EMR) to treat such refractory GERD patients. This study investigated the clinical outcomes of ARES for refractory GERD patients.

Aims and Methods: ARES was performed in 106 patients with drug-refractory GERD from December 2015 to July 2017. We analyzed data from a prospectively collected database of ARES subjects, which included preprocedure and 6-month postprocedure of GERD-Q symptom scores, and results from esophageal high resolution manometry (HRM) and 24-hour pH monitoring. Symptom control rates were compared according to clinical and surgical factors to identify predictive factors of successful surgical outcomes.

Results: ARES was performed for 106 patients (55% male; mean age 46.8 years) with PPI-refractory GERD. Mean PPI medication periods were 5.7 (1-30) years and ARES procedure time was 32.6 (15.8-33) minutes. The GERD-Q score and 24hr pH monitoring were significantly improved after ARES. Mean post-treatment GERD-Q score was 7.54 ± 2.6, compared to 10.87 ± 2.7 pre-treatment (p < 0.001). In impedance planimetry, the mean distensibility was 16.1 ± 8.3 prior to treatment and 19.7 ± 10.2 significantly complications after ARES were occurred. But 6 patients underwent post-treatment stricture, and were treated using balloon dilution and steroid injection. 3 patients suffered from minor post-ARES bleeding, successfully treated with argon plasma coagulation.

Conclusion: ARES is a very effective and safe treatment option for PPI-refractory GERD patients. ARES can be a good alternative treatment for refractory GERD.

Support: Nothing to disclose.

Efficacy of RPC4046, an Anti-Interleukin-13 Monoclonal Antibody, in Patients with Active Eosinophilic Esophagitis: Analysis of the Steroid-Refractory Subgroup from the Heroes Study
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Introduction: The HEROES study was a 16-week double-blind, placebo-controlled phase 2 multicenter trial that evaluated the efficacy and safety of RPC4046 in adult patients with active eosinophilic esophagitis (EoE). The study included steroid-refractory EoE patients based on post corticosteroid use and investigator judgment. Both pre-specified and post-hoc analyses were undertaken to assess the effect of RPC4046 treatment on this important subgroup.

Aims and Methods: In this study, 99 adult patients with active EoE were stratified by steroid-refractory status (yes/no) and randomized 1:1:1 to receive RPC4046 360 mg, 180 mg, or placebo weekly for 16 weeks. The primary endpoint was change from baseline in mean eosinophil esophageal count at week 16. Secondary endpoints included mean change from baseline to week 16 in EoE Endoscopic Reference Score (EREFS), improvements in dysphagia determined by the Daily Symptom Diary (DSD), Eosinophilic Esophagitis Activity Index (EoEAI) score, and EoE histology scoring system (EoEHSS) based on grade and stage.

Results: Of the steroid-refractory patients, 17 were randomized to RPC4046 360 mg, 14 to RPC4046 180 mg, and 16 to placebo. The differences in change in mean eosinophil eosophageal counts from baseline to week 16 between RPC4046 360 mg and placebo as well as RPC4046 180 mg and placebo were statistically significant. The difference in mean change in EREFS between each RPC4046 group and the placebo group was statistically significant for total score over all esophageal locations. The mean change in DSD composite score in the RPC4046 360 mg group compared to the placebo group approached statistical significance. Statistically significant improvement from baseline to week 16 in the RPC4046 treatment groups also were observed on histology as determined by EoEHSS and on symptom severity as determined by EoEAI. The most frequently reported adverse events in the study were headache, upper respiratory tract infection, arthralgia, nasopharyngitis, and diarrhea.

Conclusion: RPC4046 treatment improved mean and peak eosinophil count and histopathologic parameters, improved endoscopic features, and improved symptoms in steroid-refractory EoE patients. Although this pre-specified analysis was undertaken in a subgroup of patients in the HEROES trial, these data provide support that treatment with RPC4046 results in marked improvement in multiple EoE-related disease measures in steroid-refractory EoE patients. In the overall study population, oxolarizim was generally safe and well-tolerated.

EPI13 FIRST-LINE THERAPEUTIC OPTIONS AND EFFECTIVENESS RATES IN EUROPEN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: INITIAL RESULTS FROM THE EOE CONNECT REGISTRY

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory esophageal disorder characterized by symptoms of esophageal dysfunction and dense eosinophil-predominant infiltration. EoE constitutes a distinct non-IgE mediated food allergy, avoiding specific food antigen is the only therapy that targets the cause of the disease. Limitations from dietary therapy hampering its implementation in clinical practice promoted the use of anti-inflammatory drugs, mainly swallowed topical steroids and proton-pump inhibitor therapy, hampering its implementation in clinical practice.

Results: A total of 407 consecutive patients with LGB were identified 106 of whom (26%) were transfused. We included 115 transfusion episodes in 74 patients (18.2%) with a total of 206 RBC units transfused. Median age was 82.6 years; 59 (79.4%) of patients were over 70, and 54.1% were men. 75 transfusion episodes (65.2%) were appropriate. Over-transfusion occurred in 34 episodes (29.6%). A "1-in-1 transfusion" was performed in only 25 (21.7%) transfusion episodes. The number of over-transfused RBC units was 69 (33.5%).

Conclusion: RBCT in LGB is inadequate in a third of the cases due to over-transfusion, caused by an inappropriate assessment of the relevant Hb threshold in stable patients, and one of Hb thresholds in intensive care patients. The decision-determining factors. Frequency tables were generated for each treatment option. Comparative studies among available options are lacking. The EoE CONNECT registry resulted from the UEG Link Award program is a suitable way to document and understand how the treatment of EoE patients to reduce variability in clinical management.

Disclosure: Nothing to disclose.

TUESDAY, OCTOBER 23, 2018

Help! I've got a bleeder! – Room K

OP134 APPROPRIATE USE OF RED BLOOD TRANSFUSION IN ACUTE LOWER GASTROINTESTINAL BLEEDING

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Introduction: Unnecessary blood cell transfusion (RBCT) increases the risk of side effects and the cost of the treatment of gastrointestinal bleeding, without providing benefits.

Aims and Methods: We aimed to assess the appropriateness of RBCT in acute lower gastrointestinal bleeding (LGB).

Results: A total of 407 consecutive patients with LGB were identified 106 of whom (26%) were transfused. We included 115 transfusion episodes in 74 patients (18.2%) with a total of 206 RBC units transfused. Median age was 82.6 years; 59 (79.4%) of patients were over 70, and 54.1% were men. 75 transfusion episodes (65.2%) were appropriate. Over-transfusion occurred in 34 episodes (29.6%). A "1-in-1 transfusion" was performed in only 25 (21.7%) transfusion episodes. The number of over-transfused RBC units was 69 (33.5%).

Conclusion: RBCT in LGB is inadequate in a third of the cases due to over-transfusion, caused by an inappropriate assessment of the relevant Hb threshold in stable patients, and one of Hb thresholds in intensive care patients. More measures should be implemented to increase the appropriateness of RBCT.
A53

OP136 CAN PROPHYLACTIC ARSENAL PLASMA COAGULATION REDUCE DELAYED POST-PAPILLECTOMY BLEEDING? A PROSPECTIVE RANDOMIZED MULTICENTER TRIAL


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Introduction: Endoscopic post-papillectomy bleeding usually occurs in 3 to 20% of cases or higher prevalence. Moreover, delayed post-papillectomy bleeding within 1 week is also problematic. However, there is no definite guideline or consensus for prevention or reduction of delayed post-papillectomy bleeding. Additive role of prophylactic argon plasma coagulation (APC) after papillectomy was not defined.

Aims and Methods: The aim of this study was to evaluate the efficacy of prophylactic APC to minimize delayed post-papillectomy bleeding and reduce the recurrence or persistence of residual tumors. A prospective randomized study was performed at 6 tertiary referral centers. Patients with ampulla of Vater adenoma were enrolled and followed from January 2016 to March 2018, and were randomized to either the prophylactic APC or non-APC group. Endoscopic papillectomy was performed using a conventional snaring papillectomy method without submucosal injection. Then, the prophylactic APC group underwent APC on the resection margin. Immediate post-papillectomy bleeding and followed up with duodenoscopy at 1, 6, and 12 months. The main outcome measurements were delayed (> 24 h) post-papillectomy bleeding rate and tumor persistent rate between 2 groups.

Results: In total, 48 patients underwent endoscopic papillectomy. Delayed bleeding rates in the prophylactic APC and non-APC groups were 33.5% (8/24) and 16.7% (4/24), respectively (p = 0.336). Tumor persistence at 1 month did not differ between the 2 groups (8.3% vs. 4.2%, p = 0.401). However, both groups did not have tumor recurrence at 6 months (0/24 and 0/24). The mean tumor length and width were 11 and 12 mm in the prophylactic APC group, and 13.6 and 12.7 mm in the non-APC group. En bloc resection rates in the prophylactic APC and non-APC groups were 83.3% (20/24) and 95.8% (23/24), respectively. Positive resection margin rates in the prophylactic APC and non-APC groups were 66.7% (16/24) and 33.3% (8/24), respectively (p = 0.076). Post-procedure pancreatitis rates were 20.7% (5/24) in the prophylactic APC and 37.5% (9/24) in the non-APC groups, respectively (p = 0.255). The severity of pancreatitis did not differ between the 2 groups. There were no procedure-related mortalities or serious complications.

OP135 RISK OF POST-POLYPECTOMY BLEEDING WITH UNINTERRUPTED CLOPIDOGREL THERAPY: AN INDUSTRY-INDEPENDENT, DOUBLE-BLIND, RANDOMIZED TRIAL

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Introduction: Current guidelines recommend clopidogrel to be interrupted for at least 5 to 7 days before polypectomy. We investigate whether uninterrupted clopidogrel therapy will increase the risk of post-polypectomy bleeding.

Aims and Methods: In this double-blind randomized trial, we screened for patients receiving clopidogrel due to cardiovascular disease who required polypectomy. Patients were instructed to stop taking their prescriptions of clopidogrel 7 days before colonoscopy and were randomized to 7 days of clopidogrel (75mg daily) or uninterrupted clopidogrel group. Primary endpoint was delayed post-polypectomy bleeding defined as rectal bleeding starting after the colonoscope has been retracted from the anus to 30 days after the procedure, with hypotension, a decrease in hemoglobin of > 2 g/dL from baseline, requirement of transfusion, prolonged hospitalization, hospitalization, and or hemostatic intervention. Secondary endpoints were immediate post-polypectomy bleeding and serious cardiothrombotic events. Immediate post-polypectomy bleeding was defined as bleeding at the time of polypectomy that persisted despite continuous irrigation with diluted epinephrine solution for 5 minutes. Serious cardiothrombotic events were defined as non-fatal myocardial infarction, non-fatal stroke, or death from a vascular cause within 6 months of colonoscopy.

Results: A total of 387 patients received colonoscopy of whom 216 required polypectomy. 106 patients in interrupted clopidogrel group. 110 patients in interrupted clopidogrel group. The cumulative incidence of delayed post-polypectomy bleeding was 3.8% (95% CI 1.1% - 9.7%) in the uninterrupted clopidogrel group and 3.6% (95% CI 1.4% – 9.4%) in the interrupted clopidogrel group (log-rank test p = 0.945). Immediate post-polypectomy bleeding (8.5% versus 5.5%, p = 0.380) and cardiothrombotic events (1.5% versus 2%, p = 0.713) were noted.

Conclusion: Contrary to current guidelines, our study does not show any clinically meaningful increase of post-polypectomy bleeding with uninterrupted clopidogrel therapy in patients undergoing polypectomy. This study was supported by the Research Grant Council of Hong Kong [Grant number: 460912].

Table 1: Characteristics of patients and transfusional episodes.

Disclosure: Nothing to disclose

References
Conclusion: The prophylactic APC may be not effective in reducing delayed post-
portal venous bleeding in patients with portal hypertension (PHT). Further studies
are needed to confirm these findings.

Disclosure: Nothing to disclose

OPI37 EUS-GUIDED MULTI-MODALITY TREATMENT OF PERIPANCREATIC PSEUDO-ANEURYSMS
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Introduction: Pseudoaneurysms may occur in both acute and chronic pancreatitis. Gastronianesthetic bleeding is the most common presentation after rupture. Pseudoaneurysms can be of different size and can have different wall thickness. Managing peripancreatic pseudoaneurysms is complex and challenging. Failure in radiological intervention is followed by surgery. We present a series of 6 cases of pseudoaneurysms from different anatomical locations.

Aims and Methods: All 6 patients were male. 4 patients presented with gastrointestinal bleeding. Delayed diagnosis was made in 2 cases. Initial management consisted of endoscopic therapy. The pseudoaneurysms were characterized by blood flow, size, and wall thickness. The treatment options were coil, thrombin, and glue injection.

Results: There were no major complications. All 6 patients had complete or near complete occlusion of pseudoaneurysm which was evaluated by abdominal ultrasound and endoscopic ultrasound. Multiple sessions were required 4 patients while 2 were treated with single session.

Conclusion: EUS guided treatment of pseudoaneurysms appears as effective, feasible and safe technique with many advantages. It is a minimally invasive procedure with minimal complications.

Disclosure: Nothing to disclose

OPI38 HEMOSTATIC ENDOSCOPIC TREATMENT OF GASTRODUODENAL VARICES BY CHEMICAL GLUE MIXED WITH GLUCOSE SERUM: EXPERIENCE OF HASSAN II UNIVERSITY HOSPITAL CENTER
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Introduction: Gastrointestinal haemorrhage by rupture of gastroduodenal varices has an incidence of 3 to 30% and represents approximately 10% of all upper gastrointestinal haemorrhages associated with portal hypertension (PHT). The aim of this work is to evaluate the therapeutic efficiency and complications of dilute chemical glue injection in glucose serum as an endoscopic haemostasis technique.

Aims and Methods: This is a retrospective study of 24 patients compiled between January 2012 and April 2018. All patients were admitted with upper gastrointestinal bleeding. They all had benefited from a gastrointestinal fibroscopy that had objectified bleeding caused by rupture of gastroduodenal varices. Methacryloxyethylsilicone-associated n-butyl-2-cyanoacrylate (Gibran 2) was prepared with glucose serum. The endoscopic treatment performed under sedation, consists of the injection of chemical glue at the level of gastroduodenal varices.

Results: The average age of our patients was 51 years [23 years -76 years]. A female predominance was noted, with a sex ratio F/M: 2.4. Glucose injection into gastric varice was performed in 21 patients (91.7%) of whom 12 had GOV2 (55%), 8 had GOV1 (36%), 2 had GOV1 (9%). Ectopic duodenal variceous veins were found in 2 patients (8.3%). The injection was performed at 1 or 2 sites of the ruptured varice. The initial haemostasis was obtained in 100% of cases. Recurrence was noted in 2 patients. No immediate or delayed complication was noted.

Conclusion: Our results confirm that endoscopic hemostatic treatment of hemorrhages from ruptured gastroduodenal varices by chemical glue diluted in glucose serum is effective and less expensive compared to dilution in Lipiodol which is not always available in our context.

Disclosure: Nothing to disclose

OPI39 EUS-GUIDED THROMBOLYSIS OF PORTAL VENOUS SYSTEM
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Introduction: Portal venous system (PVS) is one of the most inaccessible systems of the body. Acute thrombosis of portal venous system, resulting in mesenteric ischemia has a high morbidity and mortality. Endoscopic ultrasound (EUS) guided access to the PVS is possible. We report EUS guided thrombolysis of acute portal venous system thrombosis in 6 cases.

Aims and Methods: Between December 2015 and march 2018, all symptomatic patients presenting with acute thrombosis of portal venous system with/without mesenteric ischemia were included in the study. Informed consent was taken. Diagnosis was achieved by clinical evaluation (abdominal pain, vomiting, abdominal distension) and CT abdomen (thrombus in PVS with/without abnormal thickening of ischemic bowel wall). Only patients without indication for surgery, i.e. bowel infarction, bowel perforation, were included. All patients had variable extent of acute thrombus along with dilated portal venous system and clinical features of impending mesenteric ischemia. All patients received intravenous fluids, antibiotics and low molecular weight heparin (LMWH). Patients without clinical improvement to anticoagulation therapy at 48 hours were taken for EUS guided thrombolysis.

Results: The portal venous system was possible by EUS-guided puncture and injection of streptokinase was given as continuous catheter thrombolysis with 30000 unit/hour in three cases. Bolus injections of 50000 units were given in portal vein, splenic vein and superior mesenteric vein in 3 cases. For bolus injection, the splenic vein was punctured from body of stomach, the portal vein was punctured from duodenal bulb and the superior mesenteric vein (SMV) was punctured from descending duodenum. For continuous catheter thrombolysis SMV was punctured through the pancreas with a 22 gauge EUS- FNA needle. A .018 inch guide wire was placed into a tributary of SMV. A tapered tip cannula was advanced over the wire and cannula was positioned in the tributary of SMV. The scope was removed while leaving the cannula in place, the cannula was tunneled through the nose and a syringe pump was fitted for infusion of thrombolytic agent. The thrombolysis was continued for 72 hours to 10 days depending on symptom improvement. Regular follow-up was done to monitor for GI bleed. The thrombolysis catheter was removed in all cases under endoscopic guidance to monitor for a possible bleed from catheter site.

Results: Procedure related: Technical success as defined by successful catheter placement in PVS was achieved in all patients (100%). During hospital course, 1 patient had catheter site bleed while catheter was in situ, for which hemostasis was achieved by inflating an enteroscope assisting device of balloon, fitted over the scope. 1 patient had mild oozes on catheter removal which was controlled by inflating an enteroscope assisting device of balloon fitted over the scope. 1 patient developed splenic infarct on day 7. Despite infarction, thrombolysis could be continued till the resolution of ileus on day 10.

Patient related: All patients tolerated the procedure well. All patients had resolution in pain and ileus. There was no mortality.

There was complete resolution of thrombus in 4 cases with partial resolution in 2 cases.

Conclusion: EUS-guided thrombolysis should be considered in life-threatening acute PVS thrombosis. Multicentre trials in larger number of cases are required and comparison with interventional radiology methods needs to be planned. We require dedicated accessories to ensure continuous delivery.

Disclosure: Nothing to disclose

A54 United European Gastroenterology Journal 6/8(S)
TUESDAY, OCTOBER 23, 2018

08:30–10:00

TSTM: Mechanisms of intestinal inflammation – Room 1.61/1.62

OPI40 FOOD-DERIVED BIOACTIVE PePTIDE: LUNASIN EXERTS AN IMMUNOMODULATORY ROLE IN THE HEALTHY HUMAN INTESTINAL MUCOSA

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Introduction: The gastrointestinal mucosa represents the main interface between dietary components and the organism. Lunasin is a 43-amino acid peptide naturally present in soybean protein with a variety of biological functions demonstrated by in vitro assays, cell cultures and animal models. Nevertheless, its physiological relevance in human primary intestinal cells has been scarcely investigated.

Aims and Methods: Our aim, therefore, was to evaluate the ex vivo biological activity of peptide lunasin in the healthy human intestinal mucosa. peptide was obtained by chemical synthesis. Colonic biopsies from healthy controls were conditioned with peptide lunasin (5, 50, and 200 μM), both in the presence and absence of pro-inflammatory lipopolysaccharide (LPS). The cytokine milieu (IL-1β, TNF-α, MCP-1, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, and IL-33) was subsequently assessed on the culture supernatants following overnight culture. The stability and/or modification of peptide determined cultures was evaluated by liquid chromatography coupled to tandem mass spectrometry (HPLC-MS/MS).

Results: Peptide lunasin exerted immunomodulatory effects on the human intestinal mucosa determined by changes on the global cytokine milieu. While lungasin 5 μM was not bioactive, it regulated the cytokine profile at 50 μM expanding the production of IL-10 and IL-33 by intestinal mucosa. Moreover, at higher doses (lunasin 200 μM), this peptide lowered the production of IFN-γ, IL-6 and MCP-1, as well as enhanced an innate immune response characterized by upregulation of interleukin-1β and TNF-α cytokines. Nevertheless, this peptide did not modulate the global cytokine profile when intestinal mucosa was exposed to LPS. The response of colonic biopsies towards the conditioning with peptide lunasin was monitored by HPLC-MS/MS, confirming its presence during culture.

Conclusion: Bioactive food peptides may exert physiological effects related to digestive health given their direct and continuous contact with immune mucosa. Peptide lunasin modulated in resting conditions the immune cytokine profile of the healthy intestinal mucosa. This peptide might represent, therefore, a novel agent as functional compound for the prevention of immune and inflammatory-mediated intestinal disorders.

Disclosure: Nothing to disclose

OPI41 PREVENTIVE EFFECT OF SPONTANEOUS PHYSICAL ACTIVITY ON GUT-ADIPOSE TISSUE CROSS-TALK IN MICE MODEL MIMICKING CROHN'S DISEASE SUSCEPTIBILITY

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Introduction: Crohn’s disease (CD) is a chronic inflammatory characterized from an aberrant immune response favoring gut microbiota in genetically predisposed individuals and/or under the influence of environmental factors like a high-fat diet. In this context, CD is characterized by an abnormal ileal colonisation by adherent-invasive E. coli (AIEC) and an expansion of mesenteric adipose tissue (AT). Currently, immunosuppressive or biological treatments used in CD are not curative and have many side effects. In this context, physical activity (PA) could be an attractive alternative therapy through its anti-inflammatory properties, its ability to effectively decrease TA and favorably modulate the gut microbiota composition.

Aims and Methods: The aim of this study is to analyze the preventive effect of spontaneous PA on gut-adipose tissue cross-talk in CEABAC10 mice exposed by AIEC bacteria after training. 36 male CEABAC10 mice were divided in spontaneous PA (WHEEL; n = 24) and the control group (CONT; n = 12) during 12 weeks. The distance and the speed performed in WHEEL group were weekly recorded. After this period, both groups were exposed to AIEC LF 82 for 6 days and were killed 4 days later. Animals were fed with high fat/high sugar diet (HF/ HS) and study duration was a per feeding was performed on CONT group. Body composition was analyzed by EchoMRI and the weighing of tissue was realized post-mortem. Glycemic control was evaluated through fasting glycemia, insulinemia and an oral glucose tolerance test. The level of AT cytokines secreted (IL-6 and KC) was measured by ELISA. The expression of tight junction proteins (ZO-1 and occludin) was determined by western-blot and used as a marker of intestinal permeability. Gut microbiota was analyzed using 16S rRNA gene sequencing on an Illumina MiSeq Platform. Fecal short-chain fatty acids (SCFA) concentrations were determined using gas liquid chromatography.

Results: Over the 12 weeks, WHEEL group ran an average of 3.6 ± 0.4 km per day at an average speed of 8.5 ± 0.7 m/min. The total mean mass in WHEEL group was lower compared to CONT from week 7 to the end of protocol (p < 0.005). Total fat mass at 12 weeks was inferior in WHEEL group compared to CONT group (p < 0.05). Before bacterial exposition, glycemic control (fasting glycemia, insulinemia and plasma glucose OGTT response) were not affected by spontaneous PA, however, the distance run and the speed were associated with lower fasting glucose and an increase of glucose tolerance (p < 0.005). Mesenteric AT was lower in WHEEL group, and a negative correlation was found between mesenteric AT and distance ran (r = 0.6, p < 0.05). Tight junction protein content increased in the WHEEL group. Beneficial and anti-inflammatory genera (Bifidobacterium and Lactobacillus) in CONT group decreased while the AP favors slimming-related genera (Oscoolispora) and SCFA producers (Ruminococcus). Concomitantly, proportionate and butyrate were higher in the WHEEL group (p < 0.05).

Conclusion: Spontaneous PA favors a modification of the gut microbiota composition of CEABAC10 mice in response to HF/HS diet and bacterial exposition. This modification could be related to the decrease of total fat mass and more accurately to the mesenteric AT reduction. These effects were greater when the average distance performed and the mean speed were higher. These preliminary results obtained in a rodent model could be expanded to patients with CD in therapeutic clinical protocols. Physical activity could then be considered in patients with CD in order to substantially improve their quality of life.

Disclosure: Nothing to disclose

OPI42 SMALL INTESTINAL EPITHELIAL ENDOPLASMIC RETICULUM STRESS DRIVES A MICROBIOTA-INDEPENDENT IGA RESPONSE THAT PREVENTS FROM EXTENSIVE SMALL INTESTINAL INFLAMMATION

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Introduction: Genome-wide association studies identified many risk genes for inflammatory bowel disease (IBD).1 Amongst these, many genes encode proteins that are involved in proteostasis, including endoplasmic reticulum (ER) stress. Understanding how such defects in proteostasis induce anti-inflammatory protective responses could lead to novel therapy.2 An important mechanism of protection in the intestine is the production of Immunoglobulin A (IgA) by plasma cells.2 Interestingly, plasma cell accumulation around the intestinal crypts, so-called basal plasmacytosis, is a phenomenon often observed in inflammatory bowel disease.

We set out to investigate whether ER stress induces protective IgA responses. Aims and Methods: To model the role of ER in the intestine, mice were developed in which X-box binding protein-1 is deleted specifically in the intestinal epithelium (Xbp1-/-). IgA deficient (IgA−/−), B cell deficient microT mice, and TCRb deficient (TCR−/−) mice were crossed to Xbp1-/- mice to generate double KO (Xbp1−/−;MT mice, and TCR−/−Xbp1−/−;B cell deficient animals generated by injection of females at a gestational day 13.5 with anti-IgM antibodies which abrogates PP ontogeny. Germ free (GF) Xbp1−/−;MT mice were generated as previously described.

Intestinal lamina propria (LP), Peyer’s patch (PP) and peritoneal immune cell populations were studied using flowcytometry and immunohistochemistry.

Disclosure: Nothing to disclose
We here show that innate-like, peritoneal B1 cell-derived IgA well.

References

Nothing to disclose

Disclosure:

innovated involvement in pro-inflammatory pathways. A novel and beneficial “eustress” response that is functionally opposed to its well-

propose that this homeostatic function of epithelial ER stress is conceptually a host-derived response. We further show that such a response serves a critical role in protecting the mucosa and requires secretion of IgA into the lumen. We propose that this homeostatic function of epithelial ER stress is conceptually a novel and beneficial “eustress” response that is functionally opposed to its well-described involvement in pro-inflammatory pathways.

Disclosure: Nothing to disclose

References


OPI44 HPMSCS COTRANPLANTED WITH CHITOSAN-IGF-1C HYDROGEL AMELIORATE TNBS-INDUCED COLITIS BY SECRETING PGE2

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Introduction: Mesenchymal stem cells (MSCs) transplantation is a promising strategy for inflammatory bowel disease (IBD). However, low cell retention and engraftment after transplantation diminish the clinical application of MSCs in IBD. In our previous report, a synthesized bioactive hydrogel by immobilizing the C domain peptide of insulin-like growth factor-1(IGF-1C) on chitosan formed a hydrogel matrix which can refresh stem cells by mimicking niche. Hence we aim to investigate whether co-transplanting this hydrogel with human placenta-derived mesenchymal stem cells (hP-MSCs) into the damaged colon could ameliorate trinitrobenzene sulfonic acid (TNBS)-induced colitis and illustrates its mechanism.

Aims and Methods: Utilizing the lentivirus transfected into hP-MSC which stably express fireflyluciferase (Fluc) and green fluorescent protein (GFP) thereby can be measured proliferation effect of CS-IGF-1C hydrogel for hP-MSCs and tracked by bioluminescence imaging (BLI) and histology, respectively. Colitis was induced with TNBS via enema, mesenteric injection of PBS, chitosan hydrogel, or chitosan-IGF-1C hydrogel with hP-MSCs or PBS without hP-MSCs were performed. After living imaging by BLI for measuring the survival of hP-MSCs and reactive oxygen species (ROS), intestinal tissues were collected for pathological analyses. Interleukin-1 (IL-1) and interleukin-6 (IL-6) were tested by real time PCR. Western blot and immunofluorescence analyses are conducted for detecting the phenotype of macrophages after transplantation. Enzyme linked immunosorbent assay (ELISA) was performed for testing PGE2 from the supernatant of hP-MSCs.

Results: Comparing with free hydrogel or chitosan hydrogel only, the CS-IGF-1C hydrogel significantly increased stem cell proliferation demonstrated by BLI. Moreover, in vivo studies indicated that CS-IGF-1C hydrogel promoted hP-MSCs survival confirmed by BLI and co-transplantation of CS-IGF-1C hydrogel with hP-MSCs alleviated intestinal inflammation, achieved histological improvement compared with free hydrogel or chitosan hydrogel only. Additionally, CS-IGF-1C hydrogel could promote hP-MSC releasing PGE2, polarizing M2 macrophages accompanying expression of Interleukin-10 (IL-10) furthermore reducing the level of M1 macrophages in vitro and in vivo.

Conclusion: Topical application of CS-IGF-1C hydrogel implanted hP-MSCs significantly ameliorates mouse colitis via promoting these donor cells releasing PGE2, which polarizes M2 macrophages accompanying IL-10 expression. To our knowledge, this is the first report on co-transplantation with CS-IGF-1C hydrogel and MSCs on IBD as well as the local-injection as administration which improve the therapeutic effectiveness of MSCs on TNBS-induced colitis significantly. These data could benefit the expansion of application of MSCs transplantation in inflammatory bowel disease.

Disclosure: Nothing to disclose

References

OP145 POLYUNSATURATED FATTY ACIDS INDUCE FERROPTOSIS IN MUCOSAL EPITHELIAL CELLS (IEC) AND ORGANOIDS FROM COLITIC MICE. L. Mayr1, F. Grabherr1, T. Gehmacher1, J. Schwärzler1, L. Niedereiter1, R.R. Gerner1, C. Feistritzer2, Q. Ran3, A.R. Moschen1,4, A. Kaser5, H. Tilg1, T.E. Adolph1

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Introduction: Cron’s disease (CD) is a chronic remittent inflammatory condition of the gastrointestinal tract that arises from a deranged interplay of the immune system, microbiota and unknown environmental factors in genetically susceptible hosts. GWAS studies recently revealed a genetic association of glutathione peroxidase 4 (GPX4) with the development of CD (1). Reduced GPX4 activity leads to a form of iron-dependent regulated cell death that is termed ferroptosis. Recent findings linked ferroptotic cell death with incorporation of polyunsaturated fatty acids into biological membranes, including arachidonic acid (AA) (2). AA is contained within a western style diet and especially animal products. The consumption of these fatty acids paralleled the increased IBD incidence in the last decades. However, the role played by AA in intestinal inflammation is unknown.

Aims and Methods: In this study we aimed to investigate the influence of AA on intestinal epithelial cells, with reduced GPX4 expression evoked by siRNA silencing. For in vitro analysis we crossed Gpx4+/− (mice with Villin-Cre+/− mice to Gpx4+/− mice) with Villin-Cre+/+. Gpx4+/− mice showed dysregulated inflammatory phenotype in Gpx4-deficient murine MODE-K small intestinal epithelial cells (IEC) and organoids from Gpx4+/− mice upon AA treatment. Results: IECs that were Gpx4 silenced, showed increased lipid peroxidation and febriportotic form of cell death was induced by AA. Ferroptosis was paralleled by production of IL-6 and the IL-8 homologue CXCL1. Cytokine production and proximal small intestine as well as increased CXCL-1 expression, while wildtype challenged with AA and ferric maltol showed neutrophilic infiltration in the inflamed and ulcerated mucosa of DSS-treated mice. ST2 staining was more evident during the recovery phase following DSS, mostly localized to IEC and SEMF in close proximity to areas of epithelialization. Both IL33 and ST2 deficiency in mice reduced the severity of colitis after acute DSS, but interestingly dampened epithelial repair throughout the recovery period in WT. IL-33 treat- ment during recovery decreased endoscopic and histologic score, promoting mucosal regeneration, a faster body weight recuperation and disease activity ameliora- tion vs. VEH. ATX and scratch assay, IL-33 significantly increased cell pro- liferation and wound healing vs. untreated Caco-2 cells. Microarray analysis showed IL-33-mediated activation of intracellular proliferative pathways. In par- ticular, IL-33 administration potently upregulated miR-320 vs. untreated cells. These results were confirmed at qPCR in both Caco-2 vs. untreated cells and IECs isolated from IL-33 treated mice vs. VEH. Specific knockdown of MIR320 significantly decreased both epithelial proliferation and wound healing vs. Control at ATX and scratch assay, respectively.

Conclusion: Taken together, IL-33 can play a dichotomous role during gut muco- sal inflammation, stimulates epithelial restitution and repair, and promotes over- all recovery during colitis potentially through a mechanism involving upregulation of miR-320.

Disclosure: Nothing to disclose

References
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TUESDAY, OCTOBER 23, 2018

Small bowel disorders – Room N2

OP147 CHRONIC INTESTINAL FAILURE: WHEN CHILDREN BECOME ADULTS

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Introduction: Major advances in recent years have resulted in improved survival for patients with chronic intestinal failure (CIF). There is very little data on the future of children that became adult with CIF.

Aims and Methods: The aim of our work was to describe this population since the creation of our center.

Results: After an approved HPN centre for adults with a dedicated activity for CIF, we collected retrospectively all data related to patients treated with home parenteral nutrition during infancy (at least 4 years before transition to our centre) and transferred in our centre since 1984. We evaluated demographic data, social evolution and certain complications at adulthood. Results were expressed as median [IQR].

Results: Among a total of 870 HPN patients followed between 1984 and decem- ber 2017, 44 young adults (17/27M) were transferred from 3 paediatric hospi- tals. Age of transition was 19±2 years. The principal etiologies of CIF were short bowel syndrome (n = 18), CIPD (n = 21), mucosal disease (n = 5). At the end of follow up, defined as the last news or death, 7/44 patients had died (2 after intestinal transplantation, 3 after sepsis, 2 due to liver failure), 3/44 were weaned off PN (2 due to growth factors, 1 after intestinal transplantation), 33/44 were alive requiring HPN: (6±1.7 infusions/week; 2.2±1.3 day/s; 29±13 kcal/kg/day). Oral intake was 2000±105 kcal/day but 9/44 presented remaining oral disor- ders. Seventeen/44 had a regular work (35±6 hours/week), 23 lived with their parents; 17 lived in partnerships and had at least one child.

Conclusion: Despite progress in survival and quality of life in HPN, many chil- dren who become adults stay with their parents and do not work. The transition requires probably a better social, educational and psychological preparation if we want to improve the future of these patients.

Disclosure: Nothing to disclose

References
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TUESDAY, OCTOBER 23, 2018
OP148 OUTCOMES OF TREDUGLUTIDE TREATMENT AT 6 MONTHS IN ADULTS WITH SHORT BOWEL SYNDROME AND CHRONIC INTESTINAL FAILURE: A NATIONWIDE FRENCH PROSPECTIVE OBSERVATIONAL COHORT STUDY

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Introduction: Short bowel syndrome with intestinal failure (SBS-IF) is a rare condition that requires parental support (PS). Prolonged trials with teleduglute (TED) in SBS-IF have demonstrated a PS volume reduction ≥20% from baseline (BL) in 63% of treated patients at 6 months (M6). In France, TED has been available since October 2015, and initial results demonstrated an early response and a ≥40% of patients were weaned-off PS. The objectives of the current analysis are to evaluate the real-world setting the outcomes of treatment and to assess the predictive factors of response and of PS wean-off at M6 in adults with SBS-IF.

Aims and Methods: This is a French, multicenter, observational study looking at the clinical status and outcomes of all adult patients with SBS-IF who have initiated TED (N=74). All patients on treatment for ≥6 months between October 2015 and September 2017 are included in this analysis (n=54). Clinical response is defined as ≥20% of PS volume reduction from BL at Week 24 of treatment. Descriptive summary statistics are presented as mean (range) values, and univariate analysis adjusting for nutritional variables (age, sex, body weight) have been conducted to identify predictors of response and of PS wean-off.

Results: 54 patients with SBS-IF were treated with TED (0.03 mg/kg/day) for ≥6 months. 22 (40.7%) were women, age was 52.3 years (range, 22–83). PS duration was 9.8 years (range, 0.5–31), PS days/week was 4.3 (2–7). PS volume was 11,163 mL/week (range, 2000–38,500), and oral energy intake was 6347 kcal/week (range, 0–16,800). 19 patients (35%) had a jejunostomy, 27 (50%) a jejunoduodenostomy, and the remaining 8 patients had colostomies. Clinical response was observed in 37/54 patients (68.5%). The predictive factors of wean-off at M6 were a jeunutopic response (p=0.007), a low PS volume at BL (p=0.001), a high oral energy intake (p=0.018).

Conclusion: This is the largest real-world adult cohort with SBS-IF treated with TED. The results of this analysis confirm the findings from the Phase II study. Our study shows that net volume PS reduction is higher for patients with high baseline PS while all types/causes of SBS may benefit from TED with a similar relative reduction in PS needs. Furthermore, patients with colon in continuity, low baseline PS volume requirements and high oral intake are most likely to fully wean-off PS.

Disclosure: SHIRE

Reference

OP150 PROTEIN-LOSING ENTEROPATHY AFTER FONTAN SURGERY IS ASSOCIATED WITH LIVER DAMAGE AND HIGH LEVELS OF FECAL CALPROCTIN: A CASE-CONTROL STUDY FROM A PROSPECTIVE DATABASE

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Introduction: The Fontan procedure is used in patients with a single functioning ventricle due to a complex congenital heart disease. This results in sustained systemic venous hypertension that in the long term cause liver damage and, in some patients, protein-losing enteropathy (PLE). The association between liver disease and PLE is unknown. Additionally, PLE is thought to be associated with intestinal inflammation. However, data supporting this hypothesis is scarce and fecal calproctin (FC) has not been assessed in this population.

Aims and Methods: We aimed to evaluate if PLE is associated with liver damage through non-invasive methods and to assess if FC is increased in PLE. This is a case-control study from an unicentric prospective-database. Patients were evaluated by blood tests; Fibroscan®; abdominal Doppler-US, MRI or CT (if pectus excavatum); and echocardiography and other cardiological test. PLE was defined as Alpha-1-Antitrypsin clearance > 27 ml/day. Controls were matched by age and Fontan procedure (atriopulmonary/extracardiac). IBD was an exclusion criteria. Univariate analysis using non-parametric tests with adjustment for multiple comparisons was performed.

Results: 14 cases and 15 controls were included. Baseline and cardiological characteristics are detailed in Table 1. Patients with PLE presented worse cardiological function. Non-invasive methods suggested more advanced liver disease in PLE (median: p<0.01) with 20 events of diarrhoea (14 lanreotide vs. 6 placebo; p<0.05) with 20 events of diarrhoea (14 lanreotide vs. 6 placebo; p<0.05). All 7 serious AE occurred during lanreotide treatment (25.4 vs 14.5 Kpa, p=0.03), ascites in US (43% vs 7%, p=0.03), esophageal varices or intrabdominal collateral circulation on CT/MRI (64.3% vs. 33.3%, p=0.03), FIB-4 index (1.4 vs 0.9, p=0.016) and LSPS index (2.2 vs 0.38, p<0.05). No differences were detected in bilirubin, transaminases or cholesterol levels.

PLE patients had higher FC values (median) (80 vs 30 µg/g; p<0.001). No differences were found in NSAID, anticoagulants or antaggregants consumption. Calproctin levels were directly correlated with alpha-1 antitrypsin clearance (rho=0.6, p=0.004) and inversely with the cardiac index (rho=-0.65, p=0.006), total proteins (rho=-0.68, p=0.004) and the body mass index (rho=-0.5, p=0.01).

Conclusion: 1. PLE is associated with more advanced liver disease.
2. Fecal calproctin is increased in PLE and correlates with its severity. Our study suggest that FC could be a useful biomarker in PLE after Fontan surgery.

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Disclosure: Nothing to disclose

Reference

Table 1: Comparison between patients with PLE and patients without PLE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with PLE (n=14)</th>
<th>Patients without PLE (n=15)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>28.1 (13-38)</td>
<td>28.2 (13-39)</td>
<td></td>
</tr>
<tr>
<td>Male Sex</td>
<td>71.4% (10/14)</td>
<td>53.3% (8/15)</td>
<td>0.31</td>
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<tr>
<td>Antidepressant</td>
<td>57.1% (8/14)</td>
<td>73.3% (11/15)</td>
<td>0.45</td>
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<tr>
<td>Fontan surgery: – Atrio pulmonary</td>
<td>42.9% (6/14)</td>
<td>40% (6/15)</td>
<td></td>
</tr>
<tr>
<td>– Extracardiac</td>
<td>57.1% (8/14)</td>
<td>60% (9/15)</td>
<td></td>
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<tr>
<td>Time since Fontan (years)</td>
<td>17.9</td>
<td>18.8</td>
<td></td>
</tr>
<tr>
<td>Body Mass Index (kg/m2)</td>
<td>21.4</td>
<td>24.3</td>
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<tr>
<td>Ejection Fraction MRI</td>
<td>58.5%</td>
<td>53.5%</td>
<td>0.05</td>
</tr>
<tr>
<td>Cardiac Index (Hemodynamic)</td>
<td>2.54 (1.4-5.1)</td>
<td>4.25 (2.4-6.1)</td>
<td>0.016</td>
</tr>
<tr>
<td>Alpha-1-antitrypsin clearance (ml/day)</td>
<td>84 (27-784)</td>
<td>5.8 (3.1-13)</td>
<td>&lt;0.001</td>
</tr>
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</table>

/Baseline characteristics. Median (range)
OP151 ORAL ANTIBIOTICS PREVENT INTESINAL NECROSIS IN ACUTE MESENTERIC ISCHEMIA: A PROSPECTIVE COHORT STUDY

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Introduction: The high mortality of acute mesenteric ischemia (AMI) closely correlates with the occurrence of intestinal necrosis leading to extensive intestinal resection. It is showed that a multi-organ and multidisciplinary man-agemnt of AMI, including a prompt revascularization, decreased the overall mortality as well as the rate of intestinal resection in this setting. These results demonstrated that AMI is potentially reversible and that preventing its progres-sion to irreversible transmural intestinal necrosis (ITIN) should be a primary therapeutic goal. Alongside prompt revascularization, other treatments may help avoid, limit or delay ITIN and its complications. The aim of this study was to assess the efficacy of these therapeutic measures in terms of their effect on the occurrence of ITIN.

Aims and Methods: We conducted a prospective observational cohort study in our intestinal stroke center including all consecutive patients admitted for AMI between January 1st, 2009 and December 31st, 2014. The primary outcome was the occurrence of pathologically proven ITIN in patients who underwent surgery within 90 days from admission. Patients with superficial and non-transmural ischemic necrosis upon pathological assessment and those who recovered from AMI without need for surgery were also considered not to have ITIN. Resected specimens were retrospectively reviewed in order to confirm ITIN by a senior pathologist, expert in gastrointestinal diseases and blinded to the treatments administered before surgery. The origin of AMI, epidemiological and clinical data as well as treatment provided (oral and/or IV antibiotics, antibiotics against intestinal micro-organisms, revascularization and delays) were collected. A Cox regression model with time-dependent variables was performed for statistical analysis.

Results: A total of 67 patients [29 (43%) women; median age 54 (40-63) years] were included. The origins of AMI were arterial, venous, mixed and non-ooclusive in 52%, 37%, 6% and 2% of cases, respectively. Pharmacological treatment immediately provided upon admission included intravenous antibiotics (n = 53; 79%), oral analgesic therapy (n = 37; 55%), anticoagulant therapy (n = 65; 94%), antiplatelet (n = 29; 83% of arterial AMI patients), and revascularization therapy (n = 18; 51% of arterial AMI patients). Median follow-up was 12 months [95% confidence interval (CI) = 9.6-21.7]. 28 (42%) patients underwent intestinal resection and ITIN was noted in 23 (34%) of cases. In multivariate analysis, oral antibiotics was associated with a significant decrease in the risk of ITIN [HR: 0.16 (95%CI = 0.03-0.62); p = 0.01] whereas organ failure was associated with an increased risk [HR: 15.4 (95%CI = 3.2-73.7); p = 0.001]. Overall mortality was 33% and ranged from 2% to 35% in patients without and with ITIN, respectively.

Conclusion: Our results suggest a protective effect of oral administration of antibiotics against the occurrence of irreversible transmural intestinal necrosis in the setting of AMI. A management strategy including at least oral antibiotics in addition to early revascularization might reduce or prevent progression of AMI to intestinal necrosis, avoid surgery and improve survival. Such a strategy should be confirmed with further prospective interventional studies.

Disclosure: MSD Avenir grant

OP152 BOWEL PREPARATION FOR SMALL BOWEL CAPSULE ENDOCOSOPY – THE LATER, THE BETTER!

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Introduction: In small bowel capsule endoscopy (SBCE), the presence of residue in the small bowel lumen limits the observation, hampers the interpretation and may lead to diagnostic mistakes.

Aims and Methods: We aimed to assess differences in the diagnostic yield of SBCE using 3 different preparation protocols, as well as the rate of complete examinations and small bowel transit time (SBTT).

Prospective, randomized, blind study, including 101 patients that consecutively preformed SBCE (PillCam® SB3, Given Imaging). Protocol A: Clear liquids diet the day before the examination with fasting from 8 pm.; Protocol B: Protocol A + 2 pouches of Moviprep® (polyethylene glycol electrolyte solution) in 1 liter of water from 8p.m. of the day before the examination; Protocol C: Protocol A + 2 pouches of Moviprep® in 1 liter of water to be consumed after real-time confirmataion of SBCE arrival at small bowel.

Small bowel preparation was classified by an experienced physician, considering the percentage of the examination in which mucosal observation was adequate: Excellent (>90%), Good (90-75%); Fair (75-50%); Poor (<50%).

Results: 101 patients were randomized to the 3 protocols (A: 37, B: 31 and C: 33 patients). Protocol C had an excellent or good small bowel preparation in a higher percentage of examinations (A: 37.8% vs B: 45.2% vs C: 78.8%, p = 0.002). No significant differences were found between the 3 protocols regarding the transit time (A: 378+/−197 minutes vs B: 334+/−197 minutes vs C: 344+/−148 minutes = 0.904) or complete examinations rates (A: 89.2% vs B: 100.0% vs C: 93.9%, p = 0.171).

Conclusion: In SBCE the administration of Moviprep® after the confirmation of capsule arrival at the small bowel associated with a better small bowel prepara-tion and a higher detection of angiectasia. Therefore, this innovative protocol should be systematically used to improve procedure results.

Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 08:30–10:00

Murine models of intestinal inflammation – Room L7

OP153 LOSS OF PTPN2 IN DENDRITIC CELLS PROMOTES T CELL ACTIVATION AND DIFFERENTIATION INTO TH1 CELLS BUT DOES NOT AFFECT REGULATORY T CELLS

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Introduction: Variants within the gene locus encoding protein tyrosine phosphatase non-receptor type 2 (PTPN2) are associated with the development of inflam-matory disorders, including IBD. The role of PTPN2 in T cells and intestinal epithelial cells has been investigated in depth, but its role in dendritic cells (DCs) remains unclear. Understanding the DC specific role of PTPN2 is of particular interest, since DCs play a crucial role in activation of T cells and orchestrating immune responses in general. Here, we addressed whether loss of PTPN2 in DCs affects the expression of co-stimulatory molecules and subsequently activation and differentiation of T cells.

Aims and Methods: Mice with a LoxP flanked PTPN2 gene were crossed with mice expressing Cre-recombinase under control of the CD11c promoter in order to specifically delete PTPN2 in DCs (PTPN2-CD11cCre mice). Using multico-lour flow cytometry, we analysed immune cells in the spleen, mesenteric lymph nodes, lung, liver, kidney, and skin in PTPN2-CD11cCre mice and their wild-type littermate controls.

Results: PTPN2-CD11cCre mice show symptoms of splenomegaly and skin inflammation, as well as increased infiltrates in the liver and lung in some mice. Severity of the inflammation varies between individuals, resulting in spon-taneous death in some mice. We found increased expression of co-stimulatory molecules CD80 and CD86 on PTPN2-deficient DCs. Of note, there was no difference in the expression of MHCI or CD11c in DCs from PTPN2-deficient mice compared to wild-type littermate controls. Consistent with increased expression of co-stimulatory molecules, we observed increased numbers of CD80+T cell memory; CD4+Th1 cells in both DCs from PTPN2-CD11cCre mice and their littermate controls. Further, increased expression of co-stimulatory molecules was noted in CD80+T cell memory; CD4+Th1 cells in both DCs from PTPN2-CD11cCre mice and their littermate controls.

Conclusion: In conclusion, our results show that PTPN2 has an important anti-inflamma-tory role in DCs. Loss of PTPN2 in DCs promotes T cell activation as well as increased expression of co-stimulatory molecules CD80 and CD86. Further, it affects differentiation into Th1 but not Th2 or Th17 T cells. However, PTPN2 in DCs does not affect gamma delta T cells. Further studies will investigate the interaction of PTPN2-deficient DCs and T cells in terms of antigen presentation and subsequent T cell proliferation and differentiation.

Disclosure: Nothing to disclose

OP154 MURINE MODELS OF INTESTINAL INFLAMMATION – ROOM L7

PTPN2-CD11cCre mice show symptoms of splenomegaly and skin inflammation, as well as increased infiltrates in the liver and lung in some mice. Severity of the inflammation varies between individuals, resulting in spontaneous death in some mice. We found increased expression of co-stimulatory molecules CD80 and CD86 on PTPN2-deficient DCs. Of note, there was no difference in the expression of MHCI or CD11c in DCs from PTPN2-deficient mice compared to wild-type littermate controls. Consistent with increased expression of co-stimulatory molecules, we observed increased numbers of CD80+T cell memory; CD4+Th1 cells in both DCs from PTPN2-CD11cCre mice and their littermate controls. Further, increased expression of co-stimulatory molecules was noted in CD80+T cell memory; CD4+Th1 cells in both DCs from PTPN2-CD11cCre mice and their littermate controls.
OP154 LACK OF SUCNR1 PROTECTS FROM INTESTINAL FIBROSIS

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Disclosure: Nothing to disclose

Introduction: Intestinal fibrosis is a common complication associated with Crohn’s Disease (CD) which cannot be reverted with any drug and forces repeated surgery. It has been reported that succinate, a metabolite accumulated in inflammatory pathologies, plays an important role in the activation of synovial fibroblasts and hepatic stellate cells through its receptor called SUCNR1 or GPR91.

Aims and Methods: We aim to analyse the relevance of SUCNR1 receptor in intestinal fibrosis. Intestinal resections from CD patients and colon carcinoma patients were obtained and the expression of SUCNR1 and α-sma were analysed by immunostaining. Primary intestinal fibroblasts from human resections or from colon of wild-type (WT) or SUCNR1−/− (KO) mice were isolated, maintained in culture and treated with different concentrations (0, 0.1, 0.5, 1, 5 mM) of succinate for 24 hours. Intestinal fibrosis was induced in vivo introducing one intestinal graft from WT or KO mice into the neck of a receptor mice for 7 days. The expression of pro-fibrotic markers was analysed by qPCR. Sirius Red staining was performed and the collagen layer was quantified using ImageJ. Results are expressed by mean ± SD (n=5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test. Correlations were analysed with the Spearman coefficient.

Results: SUCNR1 is expressed in epithelial cells and α-sma+ cells of intestinal resections from CD patients. The SUCNR1 expression positively and significantly correlates with the expression of α-sma (r=0.759, p<0.001, n=24) and collagen α1S (r=0.82, p<0.001, n=24). In primary fibroblasts isolated from CD patients (13.54±4.6) the expression of SUCNR1 was significantly higher than in those obtained from control patients (2.07±0.86). In these cells, succinate induced the expression of profibrotic markers such as COL1A1, α-sma, Tgfb, and TIMP1 in a dose-response manner. This pro-fibrotic effect of succinate was also observed in fibroblasts from WT mice and it was completely reverted in fibroblasts from GPR91−/− mice and treated with different concentrations (0, 0.1, 0.5, 1, 5mM) of succinate in a dose-response manner. This pro-fibrotic effect of succinate was also observed in fibroblasts from WT mice and it was completely reverted in fibroblasts from GPR91−/− mice and treated with different concentrations (0, 0.1, 0.5, 1, 5mM) of succinate for 24 hours. Intestinal fibrosis was induced in vivo introducing one intestinal graft from WT or KO mice into the neck of a receptor mice for 7 days. The expression of pro-fibrotic markers was analysed by qPCR. Sirius Red staining was performed and the collagen layer was quantified using ImageJ. Results are expressed by mean ± SD (n=5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test. Correlations were analysed with the Spearman coefficient.

Conclusion: An increased expression of SUCNR1 receptor is detected in fibroblasts from CD patients the activation of which induces a pro-fibrotic effect. This receptor mediates murine intestinal fibrosis and we propose its blockade as a new pharmacological target in CD treatment.

Disclosure: Nothing to disclose

OP155 RELEASE OF UNCONTROLLED ACTIVE ELASTASE BY INTESTINAL EPITHELIAL CELLS PARTICIPATES TO MUCOSAL INFLAMMATION IN IBD

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Disclosure: Nothing to disclose

Introduction: Imbalance between proteases and their inhibitors appears to be crucial to the development of Inflammatory Bowel Diseases (IBD). We have previously shown that colonic biopsies from IBD patients released higher elastolytic activity compared to biopsies from healthy controls. In addition, expression of ELAFIN, an endogenous elastase inhibitor, was significantly down-regulated in mucosa from IBD patients, compared to healthy controls.

Aims and Methods: The aim of our study was to identify the source of elastase hyperactivity released by IBD biopsies and to examine its impacts on colonic barrier function and inflammatory response. In situ zymography with FITC-elastin was performed on cryosections of colonic biopsies from healthy and IBD patients taken from inflamed and non-inflamed areas. Immunostaining for epithelial elastase was performed on cryosections from human biopsies, human organoids, or from mouse colon. A Ca2+ dependent epithelial cell line expressing and secreting elastase (Tg-ELA) was constructed and the potential of elastase hyperactivity to modulate the release of cytokines and permeability changes was evaluated. Transgenic murine model, which over-expressed the epithelial elastase specifically in epithelial cells in a temporally controlled manner, was developed (pVillin-CREERT2-ELA) and analysed at macroscopic and molecular levels.

Results: In situ zymography evidenced strong elastolytic activity in enterocytes of healthy human colonic tissues, which was greatly enhanced in inflamed biopsies as well as in non-inflamed biopsies from IBD patients. An elastase cDNA was cloned from human enterocytes. Immunostaining of colonic tissues showed that this elastase was only expressed in epithelial cells and secrreted into the lumen. In IBD, the expression of this elastase was enhanced in the epithelium. Tg-ELA epithelial cells exhibited defective barrier function accompanied by an increase of pro-inflammatory cytokine expression. Western blot analyses revealed that the major elements of tight junction, Occludin and Claudin-1, were targeted by elastase hyperactivity secreted in the medium. In addition, in vivo, over-expression of elastase in the intestinal epithelium (pVillin-ELA mice) for 5 weeks led to increased permeability and overexpression of antimicrobial peptides (Reg3g and Reg3b). Macrophage damage scoring highlighted intestinal inflammation, with strong adhesion phenotype.

Conclusion: We demonstrate the presence of an epithelial form of elastase in the intestine. Imbalance between elastase and its inhibitor in the epithelium participates in the generation of IBD-associated symptoms.

Disclosure: Nothing to disclose

OP156 LOSS OF PTPN2 IN DENDRITIC CELLS RESULTS IN REDUCED TUMOR BURDEN IN THE AOM/DSS COLON TUMOR MOUSE MODEL

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Disclosure: Nothing to disclose

Introduction: Protein tyrosine phosphatase non-receptor type 2 (PTPN2) has recently been identified as potential cancer immunotherapy target. We have previously recognised PTPN2 as a key regulator for inflammatory responses in the intestine. Our recent data demonstrate that loss of PTPN2 in myeloid cells using PTPN2LysMcCre conditional PTPN2 knock-out mice results in reduced tumour burden in the azoxymethane (AOM)-dextran sodium sulphate (DSS) induced model of colitis-associated colorectal cancer. However the role and mechanism of action of PTPN2 in colon carcinoma development has not yet been studied in detail. Here, we showed that the tissue specific loss of PTPN2 in dendritic cells results in reduced tumour load in AOM/DSS mouse model.

Aims and Methods: We generated a mouse line lacking PTPN2 specifically in dendritic (PTPN2−/−CD11cCre) cells. We then induced colon tumour formation in wild-type (WT) and PTPN2-deficient mice using the AOM/DSS model of colitis-associated cancer and analysed immune cells in spleen, mesenteric lymph nodes (LN) and lamina propria in PTPN2−/−CD11cCre and their WT littermate controls using flow cytometry and RNA expression levels.

Results: AOM/DSS treatment resulted in the formation of colon tumours in both WT and KO mice. Tumour burden varied between individual mice, however PTPN2−/−CD11cCre mice had less and smaller tumours comparing to their WT treated and untreated groups. This effect is likely mediated via promoting anti-cancer immune responses by modulating checkpoint inhibitor molecule expression.

Conclusion: In conclusion, our results demonstrate a role for PTPN2 in the pathogenesis of colorectal carcinoma in vivo. Loss of PTPN2 in dendritic cells exerts anti-tumour effect and results in lower colon tumour burden in AOM/DSS treated mice. This effect is likely mediated via promoting anti-cancer immune responses by modulating checkpoint inhibitor molecule expression.

Disclosure: Nothing to disclose
Introduction: In colitis-associated cancer (CAC), tumor protein p53 (TP53) mutation often occurs in the early phase of colon carcinogenesis known as dysplasia-carcinoma sequence. Although there are some reports about the relation between TP53 mutation and colonic carcinogenesis in mice model, a direct effect of TP53 mutation on colon epithelial cells and carcinogenesis in human are still unknown. We therefore aimed to assess the influence of TP53 mutation by using a CRISPR Cas9 system on human colon epithelial organoids under long-term inflammation model which we originally launched.

Aims and Methods: TP53 mutation was generated by using lentiviral CRISPR Cas9 system in 3 different epithelial organoids derived from individual human colon mucosa with wild-type TP53 (WT-TP53). Written informed consent was obtained from all included patients and this study was approved by the Ethic Committee of Tokyo Medical and Dental University. The guide RNA was designed to bind exon 10 of TP53. TP53 mutation in organoids was confirmed by direct sequencing. The expression of TP53 protein was assessed by immunohistochemical detection of TP53 with antibody by NewMillennium and the expression of TP53 target genes. Gene expression was assessed by microarray analysis and quantitative PCR. The long-term inflammation model was established by culturing organoids with inflammatory factors (TNF-α, Flagellin and IL-1β) for 2-10 weeks. Inflammatory response in the organoids was assessed by gene expression of inflammatory-related genes and the level of reactive oxygen species (ROS). Phenotypes of each organoids were assessed by MTS Assay, sphere formation assay for cell proliferation and stemness, respectively.

Results: At first, we successfully established TP53 mutation in 3 different human colon epithelial organoids. Mutant TP53 was strongly expressed in nuclei of all organoids as shown in dysplastic lesion of ulcerative colitis (UC), whereas WT-TP53 was not expressed in naive organoids. Mutant TP53 also showed Nutilin-resistance and down-regulation of TP53 target genes, indicating the loss of function of TP53. Moreover, microarray analysis revealed up-regulated genes in the organoids with mutant TP53, suggesting the gain of specific function of mutant TP53. We then assessed the effect of mutant TP53 with or without inflammatory stimulation for 60 weeks. Long-term inflammatory stimulation attenuated cell proliferation and sphere formation of the organoids with WT-TP53. Mutant TP53 however enhanced cell growth and stemness with increased gene expression of c-myc and Lgr5 compared to WT-TP53 under the inflammatory situation, nevertheless inflammatory response in the organoids with mutant TP53 was equal to that in the organoids with WT-TP53.

Conclusion: We for the first time showed TP53 mutation alone enhances cell proliferation and stemness of human colon organoids under long-term inflammation. Mutant TP53 cancelled epithelial cell damage induced inflammation, suggesting that these results might mimic the early step of colitis associated carcinogenesis.

Disclosure: Nothing to disclose
associated symptoms (hypersensitivity and barrier defects), and could constitute a new target for the treatment of colonic hypersensitivity.

Disclosure: Nothing to disclose.

OP160 NO UNCONSCIOUS ATTENTIONAL BIAS FOR GI-SALIENT TERMS IN SUBJECTS WITH FUNCTIONAL GI DISORDERS: OBJECTIVELY MEASURED BY ELECTROENCEPHALOGRAPHY (EEG)


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Introduction: Individuals suffering from functional gastrointestinal (GI) disorders have been shown to have altered central processing of visceral stimuli relative to healthy controls (1). Further such individuals appear to have selective attention to GI-related words (2) suggesting an attentional bias towards GI-relevant terms which may explain this phenomenon. They also have increased threat perception (3). However it remains unclear how much of the attention given to GI words is conscious versus unconscious. Understanding the extent to which individuals suffering from functional GI symptoms are unconsciously biased towards GI words may offer insights into therapeutic approaches to individuals in whom organic pathology has been ruled out. One previous study inferred an unconscious attentional bias for GI words through indirect means (Stroop test) (4) but its methodology was not designed to specifically measure the pre-attentional phase of central processing.

Aims and Methods: This study aimed to objectively identify differences between GI symptomatic and asymptomatic control individuals in unconscious (pre-attentional) processing of GI words using electroencephalography (EEG) which has fine temporal resolution. 26 GI symptomatic and 23 asymptomatic individuals were recruited from the community. Organic pathology and current mood disorders were ruled out by self-report. All subjects viewed 20 GI-related words, 20 negative but non-GI words and 20 neutral words from a validated word bank six times in a randomised order. Reactions were measured through ERP peak amplitude in the Occipital region in the P100 period (75-125 milliseconds) as this clearly corresponds to pre-attentional processing.

Results: Subjects generally exhibited distinctive peak amplitudes in response to all word types for the GI symptomatic subjects (p < 0.05). There was no difference in P100 peak amplitude across word type for the GI symptomatic subjects (p = 0.3). There was no difference in P100 peak amplitude for GI-relevant words between symptomatic and asymptomatic subjects (p = 0.6) nor was there an interaction between symptomatic status and word type (p = 0.8). Hence there was no suggestion of difference in P100 peak amplitude across GI-relevance of words nor symptomatic status.

Conclusion: In contrast to previous work, our data suggest that attentional bias in FGID individuals is not due to pre-attentional (unconscious) central processing and that this occurs at a later (conscious) stage. This finding has positive consequences for the development of psychological therapies targeting functional GI symptom burden since unconscious biases are much more difficult to change.

<table>
<thead>
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<th>Subject group</th>
<th>Word type</th>
<th>Symptomatic (n = 26)</th>
<th>Asymptomatic (n = 23)</th>
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<tr>
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<td>Neutral</td>
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<td>-3.75 (3.75)</td>
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<tr>
<td>Combined</td>
<td>-3.32 (2.63)</td>
<td>-3.64 (3.61)</td>
<td></td>
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</tbody>
</table>

[Table. Mean (SD) peak amplitude by subject group and word type for the P100 period in the Occipital region]

Disclosure: Nothing to disclose.

References


OP161 ANTI-TNF-A ALTERS CONNECTIVITY BETWEEN INTRINSIC SENSORY CORTEX AND AMYGDALA IN CROHN’S DISEASE PATIENTS

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Introduction: Inflammatory Bowel Disease (IBD) increases TNF-a release from peripheral mononuclear cells as the immune system responds to inflammation in mucosal tissue. This immune response is closely linked with the intensity of gastrointestinal symptoms and extra-intestinal comorbidities such as depression or anxiety. We have previously demonstrated that anti-TNF-a treatment impacts on implicit health cognition via altering brain function (Gray et al., 2018). Increased psychiatric symptoms in IBD are commonly explained as driven by an interpretative mechanism, however there is scant direct evidence to support these interpretations. To address this mechanism, we experimentally engaged core affective circuitry and then examined the influence of anti-TNF-a therapy on brain function in patients with Crohn’s disease.

Aims and Methods: 10 patients with Crohn’s disease (age 29.3 ± 13.0 yrs, 5 female, 5 ileocolonic, 2 colonic and 3 ileal disease) on stable anti-TNF therapy (6 adalimumab, 4 infliximab) were studied twice, in randomized order, before and after anti-TNF administration. On each occasion patients underwent visceral sensory testing (standardized nutrient challenge) and then functional magnetic resonance imaging (fMRI) of the brain during an interoception task. During sensory testing 600ml of enteral feeding solution was consumed over 15 minutes while the intensity of GI symptoms was quantified. We used a recognized and commonly employed experimental protocol to recruit interoceptive neural circuits, heartbeat perception (See Brener et al., 2016 for a review of experimental methods)

Results: Within 72 hrs after administration of anti-TNF-a unpleasant visceral sensation during nutrient challenge (subjective fullness) was significantly reduced. Prior to anti-TNF-a, our experimental task robustly activated core affective circuitry including the interoceptive sensory (anterior insula) cortex and interoceptive motor (anterior cingulate) cortex. Surprisingly, activation of interoceptive circuits was not significantly altered following anti-inflammatory therapy. Instead, we observed a decrease in functional connectivity between the right anterior insula and the right amygdala was significantly reduced following anti-TNF-a.

Conclusion: Anti-TNF agents significantly reduce symptoms during a standardized nutrient challenge, and alter the strength of communication between primary sensory interoceptive cortex (anterior insula) and limbic circuitry (amygdala). Our findings are consistent with previous observations that greater amygdala functional connectivity is associated with visceral hypersensitivity (Icenhour et al., 2017). Our findings however are the first to demonstrate altered amygdala connectivity specific to interoceptive processing. These findings suggest that the functional coupling between interoceptive circuits and limbic circuits may be implicated in the translation of inflammatory conditions into psychological symptoms such as depression and anxiety. These findings support further examination of how cytokines including TNF-a may impact on mental health in gastrointestinal patients.

Disclosure: Nothing to disclose.

References
OP164 GENETIC ASSOCIATIONS OF IRITABLE BOWEL SYNDROME AND DEPRESSIVE DISORDER THROUGH WHOLE EXOME POOLED-SEQUENCING

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Introduction: Irritable bowel syndrome (IBS) is the most commonly diagnosed functional gastrointestinal disorder with a psychological distress comorbidity ranging from 15.5%–39.5%, especially with depressive disorder (DD). Twins’ studies and population genome wide association studies (GWAS) suggest there is a genetic contribution to development of IBS, rare results could display the high comorbidity rate of IBS and depression.

Aims and Methods: The aim of this study was to distinguish the genetic associations of IBS and depressive disorder. 35 diarrhea dominated IBS patients (IBS) and 35 depressive disorder patients (DD) were recruited according the Rome III criteria and MINI Diagnostic, 35 matched healthy volunteer (HC) without any gastrointestinal or mental disease were also recruited at the same time in Peking university third hospital and Beijing HuiliLongGuan Hospital. Peripheral blood DNA of each sample in the same group were extracted and mixed as a pool, the whole exome single nucleotide polymorphism (SNPs) of 3 pools were measured through the pooled-sequencing (Pool-seq)[4]. The study was approved by the Ethics Committee of Peking University Health Science Center (no. 2013-112).

Results: 10 SNPs in IBS and 12 SNPs in DD significantly different from HC and located in exonic, non synonymous and damage protein structure. 7 of them are the same: COMT rs6267, SLC7A6OS rs8063446 are the risk variants in IBS while ANKRD11 rs13527563 and MBD1 rs8063446 are the risk variants in IBS while ANKRD11 rs13527563 is the protective one. RECL4 rs4251691 is reported in Rothmund-Thomson syndrome patients. Detailed clinical data were collected from 16 patients having RECL4 mutations and diarrhea was reported in 12 out of 14 patients (6, 7). For depressive disorder patients, COMT rs6267, EDN3 rs11570255 and PPBP rs201430284 are risk variants, SCARF1 rs744644 and VASN rs3810818 show some protective effect. Gene expression (COMT) associated with experimental pain sensitivity. COMT rs6267 minor alleles in the high pain sensitive haplotype coding for 20-fold reductions in COMT enzymatic activity and correlated with schizophrenia or Parkinson’s increased risk [8, 9].

Conclusion: This is the first study using whole exome pool-sequencing to look at genetic associations of IBS and depressive disorder together in Chinese population. Our results show IBS and DD patients have the same risk mutation which are associated with neural modulation or depression. Meanwhile, specific SNPs are found in IBS or DD patients respectively. The results support that some genetic variants may lead to the high comorbidity of IBS and depression.

Disclosure: Nothing to disclose.

SNPs

<table>
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<th>IBS SNPs</th>
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<td>1.56</td>
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[Odd ratio of significant variants in IBS and DD]

Disclosure: Nothing to disclose.

OP163 UNDERSTANDING THE ROLE OF NEURO-IMMUNE INTERACTIONS AND NERVE SPROUTING IN PATIENTS WITH DIVERTICULAR DISEASE

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Introduction: Colonic diverticula are an age-dependent event in Western countries characterized by nerve fiber sprouting and neuro-immune interactions which could be involved in symptom generation.

Aims and Methods: We investigated whether stress-related mediators of the pathogenesis of IBS such as tryptase and corticosterone affect enteric glial cell (EGC) on cellular activation, cell proliferation, morphological alterations, and gene induction of neurotrophic factors and axon guidance factors. EGC (CRL-2690 purchased from ATCC) were used for the consequent experiments after recruiting to sub-confluent condition. Presence of tryptase-protoaeactivated receptor-2 (PAR-2), glucocorticoid receptor, and morphological changes of EGC was evaluated by immunofluorescence method. For EGC activation, we evaluated expressions of phosphorylated extracellular signal-regulated kinase (pERK) and nucleus factor kappa-light-chain-enhancer of activated B cells (NF-kB) by real-time RT-PCR. Expression of netrin-1 was histologically evaluated. To evaluate cell proliferation, we used the MTT assay method and cell number counting.

Results: PAR-2 was localized in the nucleus of EGC, and glucocorticoid receptor was observed in the cytoplasm of EGC. Expressions of pERK1/2 were about 2-fold higher than those of the basal control, and peaked at 2 min and 5 min after stimulation and corticosterone (1 μM) and tryptase (1 mM). Tryptase significantly increased mRNA expression levels of GFAP (1.7-fold) at 30 min and 1 hr. Regarding with morphology of EGC, corticosterone (1 μM, 6 hrs) but not tryptase remarkably caused EGC process elongation and long thin process connecting with another distant EGC. Extended cytoplasm of EGC also appeared by stimulation with corticosterone alone. Tryptase increased NGF mRNA expression at 1 hr (about 2.5-fold) and GDNF mRNA expressions at 30 min (2.9-fold) and 1 hr (3.7-fold). Then, increased NGF mRNA expression was continued until 6 hrs, but GDNF mRNA expressions were gradually decreased. While, corticosterone significantly decreased mRNA expression levels of NGF by 90% (1 μM), but increased GDNF mRNA (4-fold, 1μM) at 30 min. Netrin-1 was expressed in the EGC cytoplasm of EGC. Netrin-1 mRNA expression was increased by both stimulations (2.5-fold higher, tryptase: 1.8-fold higher, corticosterone), and its expression levels continued until 6 hr.

Conclusion: There appeared different responses of EGC between proliferation and morphology stimulated by stress mediators. Immunohistochemical responses of EGC may associate with induction of neuronal factors (NGF, GDNF, netrin-1), which possibly regulates neuronal elongation under stress conditions.

Disclosure: Nothing to disclose.

Disclosure:

Nothing to disclose.
OP165 SPANISH PRIMARY CARE SURVEY ON THE MANAGEMENT OF H. PYLORI INFECTION: PREFERENCES, ACCESS TO TECHNOLOGY, AND DECISIONS
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Introduction: The H. pylori management preferences and decisions of primary care physicians, or their access to different health technologies (i.e. diagnostic methods), courses and information have not generally been taken in consideration by the literature even though they currently manage most of the infections.

Aims and Methods: To evaluate the preferences, decisions and access to health technologies of Spanish Primary Care physicians. A multidisciplinary committee was involved in the design of the survey, with representatives from different regions of Spain, assessing a broad set of elements regarding preferences on management and access to health technology. Survey was submitted via e-mail to the primary care physicians, or their access to different health technologies. A strong national program is needed to ensure adequate strategies in Spain to the real access to health technology and decisions taken by the primary care physicians. Aims and Methods: Survey was submitted via e-mail to the primary care physicians. A strong national program is needed to ensure adequate strategies in Spain to the real access to health technology and decisions taken by

Conclusion: Our survey shows there is a significant deviation from recommended strategies in Spain to the real access to health technology and decisions taken by primary care physicians. A strong national program is needed to ensure adequate access to technologies and continuous medical education by primary care physicians.

References

OP166 PCR TEST FOR HELICOBACTER PYLORI DETECTION AND CLARI THROMYCIN RESISTANCE PREDICTION ON FECAL AND BIOPIC SAMPLES: COMPARISON OF ACCURACIES
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Introduction: Helicobacter pylori (Hp) infection treatment is still a challenge for clinicians. Eradication rates of first-line clarithromycin-based regimens have fallen in the last 20 years, mainly due to the increase of clarithromycin resistant Hp strains. Hp culture is difficult, time consuming, not always successful and it requires an invasive procedure. 12 point mutations in the 23S rRNA gene related to clarithromycin resistance have been so far identified, in particular A2142C, A2142G, A2143G are present in 90% of cases. Aims and Methods: To evaluate the accuracy of RT-PCR performed on stool samples to detect the presence of Hp DNA while concurrently detecting point mutations in the 23S rRNA gene. Results were compared with RT-PCR carried on biopic samples. Methods: Between January and April 2018, 93 dyspeptic patients (30 males, 63 females, mean age 49.5 years) referred to our Unit to perform an upper endoscopy, were enrolled. Composite reference method (CRM): 1C urea breath test (1C UBT), rapid urease test, histology and culture were performed to establish Hp status. On Hp positive cultures, antibiogram was performed with the E-test method. On the day of endoscopy, stools specimens were collected and rapidly frozen at −20°C. Results: With the CRM method 69 patients resulted Hp positive and 24 Hp negative. In stools, 64 out of the 69 positive specimens were deemed true positive and all the negative specimens were detected properly (accuracy: 94.6%, 95% CI: 89.6% to 98.2%). Among the 23S rRNA positive samples, 30 out of 32 were deemed true sensitive and 22 out of 32 true resistant (accuracy: 81.3%, 95% CI: 69.9% to 89.9%). In biopsies, 66 out of the 69 positive specimens were deemed true positive and all the negative specimens were detected properly (accuracy: 97.8%, 95% CI: 92.4% to 99.7%). Among the 66 positive samples, 32 out of 33 were deemed true sensitive and 23 out of 33 true resistant (accuracy: 83.4%, 95% CI: 72.1% to 91.4%). PCR on stools and biopsies were highly concordant, being Cohen K coefficient 0.9 for Hp detection and 0.8 for resistance prediction. Conclusion: Helicobacter pylori DNA and 23S rRNA point mutations can be detected in human stool specimens with high accuracy, obtaining the same performance of DNA extraction from biopsies. RT-PCR on stools can therefore be used to determine the presence of the bacterium and the genotypic resistance to clarithromycin, facilitating the choice of the right therapeutic approach when endoscopy or culture can’t be performed.

Disclosure: Nothing to disclose.
OP167 GENOTYPIC RESISTANCE GUIDED VERSUS EMPIRICAL THERAPY FOR H. PYLORI INFECTION – A RANDOMIZED TRIAL

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Introduction: Randomized controlled trials comparing susceptibility testing guided empirical therapy for patients who fail after 2 or more eradication therapies for H. pylori are lacking.

Aims and Methods: We aimed to compare the efficacy of genotypic resistance guided therapy versus empirical therapy for eradication of refractory H. pylori infection, conducted between Oct 2012 and Sep 2017. Adult (>20 years old) patients who failed after at least 2 eradication therapies for H. pylori infection were enrolled. Eligible patients were randomized to receive either (A) genotypic resistance guided therapy for 14 days; or (B) empirical therapy according to medication history for 14 days. Eradication status was determined by 13C-urea breath test. The primary outcome was the eradication rate at least 6 weeks after eradication therapy according to intention-to-treat (ITT) analysis. Genotypic resistances of clarithromycin (23S rRNA) and levofloxacin (gyrase A) were determined by PCR with direct sequencing.

Results: Upon recruitment of 41 patients, trial 1 was terminated because of low efficacy of doxycycline sequential therapy (57.7%, 15/26). We replaced doxycycline with tetracycline in trial 2 and a total of 410 patients were randomized as the study population. Overall microbial composition as well as Shannon diversity index were determined with 16S rRNA sequencing.

Conclusion: Properly designed empirical therapy according to medication history in patients who failed more than 2 eradication therapies might improve the eradication rate.

Disclosure: Nothing to disclose

OP168 SHIFTS IN HUMAN GUT MICROBIOTA AFTER HELICOBACTER PYLORI ERADICATION THERAPY: SHORT- AND LONG-TERM EFFECTS

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Introduction: Antibiotics treatment may affect the indigenous gut microbiota and lead to probiotic microbiota. The aim of the study was to assess the human gut microbiota composition in H. pylori-positive patients before, immediately after and 1 month after eradication therapy.

Results: A total of 53 patients were enrolled. The gut microenvironment homeostasis using 16S rRNA sequencing.

Conclusion: The gut microenvironment homeostasis using 16S rRNA sequencing.

Disclosure: Nothing to disclose

OP169 THE IMPACT OF HELICOBACTER PYLORI INFECTION, ERADICATION THERAPY AND PROBIOTIC SUPPLEMENTATION ON GUT MICROENVIRONMENT HOMEOSTASIS: AN OPEN-LABEL, PROSPECTIVE CLINICAL TRIAL

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Introduction: It was estimated that approximately 4.4 billion individuals were infected with Helicobacter pylori (H. pylori) worldwide by year 2015. As we know, H. pylori is the dominant bacterial species of gastric microbiota in H. pylori-infected patients. The domination of H. pylori can change the gastric microenvironment and result in the reconstitution of gastric microbial commnity. However, the influence of H. pylori infection on gut microbiota homeostasis is still largely unknown.

As is well known, eradication therapy of H. pylori is followed by gastric and gut microbiota alterations. Whether the alterations are beneficial or detrimental, and the effect of eradication therapy on gut microbiota were not thoroughly studied. As a typical butyric acid-producing bacterium, Clostridium butyricum (C. butyricum) has been studied in several test models and human for the eradication of H. pylori. However, most studies of C. butyricum were conducted with standard triple eradication therapy, analyzed gut microbiota alterations using bacterial culture, and emphasized the long and side effect of eradication rate and side effect. Our study analyzed the effect of C. butyricum supplementation on gut microbiota homeostasis using 16S rRNA sequencing.

Aims and Methods: Our study aimed to investigate the impact of H. pylori infection, 14-day BQ therapy and probiotic supplementation on gut microbiota homeostasis and to provide suggestions for clinical decision. A total of 70 H. pylori-positive patients and 35 H. pylori-negative patients were enrolled. Patients were randomly assigned to one of the 2 groups. In Group A, patients received 14-day BQ therapy consisting of pantoprazole, amoxicillin, furazolidone and colloidal bismuth pectin. Patients in Group B were supplemented with C. butyricum. Stool samples of H. pylori-positive patients were collected on day 0, day 14 and day 56 while stool samples of H. pylori-negative patients were collected on day 0. Gut microbiota was investigated by 16S rRNA sequencing. H. pylori status was reassessed by 13C urea breath test on day 36 for patients in group A and group B. H. pylori-negative status indicated the success of eradication treatment.

Results: 63 H. pylori-positive patients and 35 H. pylori-negative patients completed this study. Several important metabolism pathways were predicted to be more abundant in H. pylori-positive community while some human diseases pathways were with higher potential in H. pylori-negative community through KEGG pathway analysis. The abundances of most butyric acid-producing bacterium significantly decreased and those of several detrimental bacteria increased immediately after 14-day BQ therapy. The gut microenvironment homeostasis was not completely reconstituted 6 weeks after treatment in spite of a recovery tendency. Although no significant improvement of eradication rate was observed, more gastrointestinal symptoms were relieved with the supplementation of C. butyricum.

Conclusion: The role of H. pylori in human disease and gut microenvironment homeostasis may not be necessarily detrimental. The eradication of H. pylori should be based on comprehensive analysis of individual patients, especially for asymptomatic H. pylori-infected patients. The gut microbiota was extremely changed immediately after eradication therapy and 6 weeks was not enough to thoroughly reconstitute gut microenvironment balance in spite of a recovery tendency. C. butyricum might promote the recovery of gut microenvironment balance through immunological and non-immunological mechanisms.

Disclosure: Nothing to disclose
This study was supported by Eisai Co., Ltd.

The results suggested that the follow-up interval could be extended after 24 weeks in patients with clinical stage I/II (Lugano staging system) under- going H. pylori eradication therapy. The primary endpoints were complete remission (CR) rate and the rate of transfer to secondary treatment. The secondary endpoints were CR maintenance duration and overall survival (OS).

Results: H. pylori eradication therapy was successful in all 97 patients of the efficacy analysis set. CR of lymphoma was achieved in 84 of the 97 patients (86.6%), during the period of 2.0–44.7 months (median, 5.3 months) following H. pylori eradication therapy. CR was maintained in 77 of 81 patients (95.1%), who were followed for 0.4–53.2 months (median, 31.0 months). Kaplan-Meier estimates for the cumulative probability of CR maintenance were 97.5% (95% CI; 89.6–99.9%) at 12 months and 94.2% (95% CI; 85.3–97.8%) at 24 months. CR remained throughout 36 months and 48 months. Secondary treatments (radiotherapy, rituximab, or gastrectomy) for gastric MALT lymphoma were needed in 10 of the 97 patients (10.31%). During follow-up, OS rate was 96.9% (94/97). 3 patients died of causes unrelated to gastric lymphoma.

Conclusion: H. pylori eradication therapy demonstrated a high CR rate, long CR maintenance for patients with localized and H. pylori-positive gastric MALT lymphoma in this prospective, practice-based, nationwide, multicenter study. The results suggested that the follow-up interval could be extended after 24 weeks in patients with localized H. pylori-positive gastric MALT lymphoma in the patients with the same clinical characteristics enrolled in this study.

Disclosure: This study was supported by Eisai Co., Ltd.

Reference

OP170 HELICOBACTER PYLORI ERADICATION THERAPY IN LOCALIZED GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA: A PROSPECTIVE, NATIONAL, MULTICENTER STUDY IN JAPAN

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Introduction: Helicobacter pylori eradication therapy induces clinical and histological regression of gastric extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) in the majority of cases and was approved for the first-line, standard treatment of H. pylori-positive gastric MALT lymphoma by Japanese government in 2010. Although several retrospective studies or small-scale single-centre studies have been reported, a prospective, large-scale, multi-center study has not yet been conducted in Japan.

Aims and Methods: We have conducted a prospective, nationwide, multicenter study to evaluate the clinical efficacy of rabeprazole-based triple H. pylori eradication therapy for localized H. pylori-positive gastric MALT lymphoma in practice-based clinical trial (ClinicalTrials.gov, NCT01264822). The 108 H. pylori-positive patients with clinical stage I/II (Lugano staging system) underwent H. pylori eradication therapy. The primary endpoints were complete remission (CR) rate and the rate of transfer to secondary treatment. The secondary endpoints were CR maintenance duration and overall survival (OS).

Results: H. pylori eradication therapy was successfully achieved in all 97 patients of the efficacy analysis set. CR of lymphoma was achieved in 84 of the 97 patients (86.6%), during the period of 2.0–44.7 months (median, 5.3 months) following H. pylori eradication therapy. CR was maintained in 77 of 81 patients (95.1%), who were followed for 0.4–53.2 months (median, 31.0 months). Kaplan-Meier estimates for the cumulative probability of CR maintenance were 97.5% (95% CI; 89.6–99.9%) at 12 months and 94.2% (95% CI; 85.3–97.8%) at 24 months. CR remained throughout 36 months and 48 months. Secondary treatments (radiotherapy, rituximab, or gastrectomy) for gastric MALT lymphoma were needed in 10 of the 97 patients (10.31%). During follow-up, OS rate was 96.9% (94/97). 3 patients died of causes unrelated to gastric lymphoma.

Conclusion: H. pylori eradication therapy demonstrated a high CR rate, long CR maintenance for patients with localized and H. pylori-positive gastric MALT lymphoma in this prospective, practice-based, nationwide, multicenter study. The results suggested that the follow-up interval could be extended after 24 weeks in patients with localized H. pylori-positive gastric MALT lymphoma in the patients with the same clinical characteristics enrolled in this study.

Disclosure: This study was supported by Eisai Co., Ltd.
those without mucosal healing (17.56 μg/ml vs 16.10 μg/ml, p = 0.682). The AUC for VDZ levels was not different from 1-day calculation.

Conclusion: In a single-centre cohort of IBD patients, there was no association between maintenance VDZ levels and clinical remission or endoscopic mucosal healing. Shortening the dosing interval achieves higher VDZ levels, but this does not correlate with improved clinical response. This finding supports our observation that dose escalation of VDZ does not improve clinical response rates in patients with IBD. Interestingly, few patients had detectable AST despite lower rates of concomitant immunomodulator use than previously studied populations, supporting the suggestion that VDZ has lower immunogenicity than other biologics.

Disclosure: Nothing to disclose

OPI73 INTREREST IN THE ADDITION OF AZATHIOPRINE (AZA) TO THE SWITCH OF ANTI-TNF IN IBD PATIENTS IN CLINICAL RELAPSE WITH UNDETECTABLE ANTI-TNF TROUGH LEVELS AND ANTI-DIUGRAB ANTIBODIES: A PROSPECTIVE RANDOMIZED TRIAL

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Introduction: In patients experiencing a loss of response to a first anti-TNF-given in monotherapy at induction or 2 months later and with an undetectable level of anti-TNF with a high level of anti-drug antibodies were included. They were randomized to receive either AZA or nothing and induction by a second anti-TNF was performed at standard doses. They were followed for 2 years after the switch, with a measurement of the clinical activity and pharmacokinetics of the second TNF at 6, 12 and 24 months. Non-primary responders after the change were excluded. A clinical failure was defined as a disease outbreak defined on a Harvey Bradshaw score >5 associated with a faecal calprotectin level >250 μg/g stool for Crohn’s disease or a Mayo score >3 with an endoscopic sub-score >1 in the case of ulcerative colitis and the need for a therapeutic change (dose intensification, change in treatment, addition of corticosteroids or AZA, use of surgery). The appearance of unfavorable phenotype was defined by the appearance of low or undetectable levels of anti-TNF with anti-drug antibodies.

Results: 90 patients (48 CD, mean age: 39.5 years, sex ratio M/W: 0.95) were included. The second anti-TNF was adalimumab (ADA) and infliximab (IFX) in 40 and 50 patients, respectively. 4 patients were of the AZA phenotype (B3) (IFX, n=1; ADA, n=1; IFX, n=1; ADA, n=1), 48.4% were women. There were 148 patients with CD and 36 with UC. 86 patients were treated with IFX (n=86, REM or CT-P13) and 98 with ADA. Median disease duration was 3.69 (IQR: 10.37) years. In CD, median Harvey-Bradshaw index was 6.27 had a penetrating phenotype (B3) (IFX, n=17; ADA, n=10) and 23 had perianal fistulas (IFX, n=18 ADA, n=6). In UC, median Mayo subscore was 6.19. 16% had extra-intestinal manifestations. Concomitant immunosuppressors were prescribed in 68% and 40% of patients treated with IFX and ADA respectively. 82% and 35% of patients treated with IFX and ADA received corticosteroids, respectively. At 1 year, 95 patients (51.6%) were in clinical remission, including 73 (40%) without optimization of anti-TNF therapy. ADA were detected in 51 patients (27.7%). The immunogenicity rate for ADA and IFX was 38.8% and 15.1%, respectively. Mean time to onset of ADA was 2.5 months, and ADA persisted over time in 72%. Drug levels at 6 weeks of therapy were significantly lower in patients who developed ADA. Immunogenicity was associated with non-remission at 1 year (58.6% in patients with ADA vs 35.7% in patients without ADA, p = 0.008). In multivariate cox regression analysis of time to ADA development, immunogenicity was associated with concomitant immunosuppressors (HR: 0.39 [95% CI 0.2–0.75]), anti-TNF levels at 6 weeks of therapy (HR: 0.86 [95% CI 0.7–0.91]), antibiotics usage during the study (HR: 0.9 [95% CI 0.14–0.65]) and vaccine in the year before start of anti-TNF therapy (HR: 5.32 [95% CI 1.5–16.3]).

Conclusion: In IBD patients, immunogenicity towards anti-TNFs is associated with a lower remission rate and lower drug levels. Concomitant immunosuppressors and antibiotics are associated with a lower risk of immunogenicity while vaccine received before the start of anti-TNF are associated with an increased risk of immunogenicity.

Disclosure: Nothing to disclose
OP175 MAGNETIC RESONANCE ENTEROGRAPHY ASSESSMENT OF MUCOSAL HEALING WITH VEDOLIZUMAB IN PATIENTS WITH MODERATE-TO-SEVERE CROHN’S DISEASE: RESULTS FROM THE VERSIFY STUDY

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Introduction: Magnetic resonance enterography (MREn) may be used in clinical practice to assess disease activity in Crohn’s disease (CD).1-2 Vedolizumab (VDZ) is clinically effective in patients (pts) with moderately to severely active CD, but healing with VDZ on MREn has not been previously measured. This study evaluated the effect of VDZ on radiologic remission using MREn at weeks (wks) 26 and 52 in pts with active CD.

Aims and Methods: VERSIFY (NCT02425111) was a Phase 3b, open-label study evaluating endoscopic remission with VDZ in 101 pts at wk 26 and in 56 eligible pts at wk 52 following a protocol amendment extending treatment duration. Only patients receiving VDZ at the time of the amendment, or enrolled after the amendment were eligible to be treated to wk 52. Pts were enrolled with moderate-severe CD (CD Activity Index 220±40; Simple Endoscopic Score for CD ≥7; ≥1 mucosal ulceration on centrally read endoscopy) and who had prior failure to a corticosteroid, immunomodulator, and/or ≥1 TNF antagonist (tumour necrosis factor inhibitor). The MREn substudy enrolled 37 pts of whom 21 were eligible to continue treatment to wk 52. The exploratory endpoint was Magnetic Resonance Index of Activity (MaRIA) score,4 quantified in 6 ileocolonic segments (1 ileal and 5 colonic). MaRIA-7 remission of all active lesions and MaRIA-11 remission of only severe lesions were defined as scores of <7 and <11, respectively, in all segments, and were assessed at wk 26 and wk 52. Data were analysed in the full analysis set (FAS; all treated pts) and in the per-protocol set (PPS; treated pts with sufficient data at baseline and post-baseline). Only pts with an abnormal MaRIA score of ≥7 or ≥11, respectively, in all segments, were included in the analysis. If no relevant post-baseline MaRIA scores were available then they were considered non-responders in the FAS. Subgroup analyses of the FAS and PPS by prior TNF exposure were performed.

Results: Of 37 pts enrolled into the MREn substudy, 32 pts had a baseline MaRIA score ≥7 in ≥1 segment and 32 had a baseline score ≥11 in ≥1 segment. These pts were included in the MaRIA-7 and MaRIA-11 remission analysis. The 5 pts who did not meet the threshold for inclusion in the MaRIA-7 remission analysis were classified as having ‘suboptimal’ MREn exams at baseline. 27/32 pts had 26 wk observations. 15/21 MREn pts had 52 wk observations. At baseline, were classified as having ‘suboptimal’ MREn exams at baseline. 27/32 pts who did not meet the threshold for inclusion in the MaRIA-7 remission analysis. These pts were included in the MaRIA-7 and MaRIA-11 remission analysis. The MaRIA-7 score was quantified in 6 ileocolonic segments (1 ileal and 5 colonic). MaRIA-7 and MaRIA-11 remission at wk 26 and wk 52.

Conclusion: VDZ can induce radiologic remission (MaRIA-7) in a difficult-to-treat population with moderately to severely active CD, both in those naive to, or who had failed, anti-TNF therapy.


References:

Abstract No: OP175
Table 1: Overall remission by MREn

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<th>FAS-MREn</th>
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<tr>
<td></td>
<td>Wk 26</td>
<td>Wk 52</td>
</tr>
<tr>
<td>Overall population</td>
<td>N=32</td>
<td>N=21</td>
</tr>
<tr>
<td>MaRIA-7 remission, n (%)</td>
<td>7 (22%)</td>
<td>8 (38%)</td>
</tr>
<tr>
<td>MaRIA-11 remission, n (%)</td>
<td>11 (34%)</td>
<td>9 (43%)</td>
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<tr>
<td>TNF naïve subgroup</td>
<td>N=20</td>
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<tr>
<td>MaRIA-7 remission, n (%)</td>
<td>5 (25%)</td>
<td>8 (62%)</td>
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<tr>
<td>MaRIA-11 remission, n (%)</td>
<td>7 (35%)</td>
<td>8 (62%)</td>
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<td>TNF failure subgroup</td>
<td>N=12</td>
<td>N=8</td>
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<tr>
<td>MaRIA-7 remission, n (%)</td>
<td>2 (17%)</td>
<td>2 (20%)</td>
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<tr>
<td>MaRIA-11 remission, n (%)</td>
<td>4 (33%)</td>
<td>1 (13%)</td>
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OP176 SOLUBLE MUCOSAL ADDRESSIN CELL ADHESION MOLECULE 1 AND RETINOIC ACID ARE POTENTIAL TOOLS FOR THERAPEUTIC DRUG MONITORING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB: A PROOF OF CONCEPT STUDY

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Introduction: Vedolizumab (VDZ), a humanized monoclonal antibody targeting α4β7 integrin, is effective in induction and maintenance therapy in patients with inflammatory bowel disease (IBD) who have not adequately responded to standard therapies, and high levels of vedolizumab trough levels (VTL) have been associated with clinical remission. The α4β7 integrin binds to endothelial MadCAM-1 and is up-regulated by retinoic acid (RA).

Aims and Methods: To determine the relations between soluble MadCAM-1 (sMadCAM-1) and RA concentrations with clinical remission during VDZ maintenance therapy. In a retrospective study performed in IBD patients treated with VDZ, we measured VTL, sMadCAM-1 and RA concentrations.

Results: Among the 62 included patients (38 Crohn’s disease) 24 relapsed and 38 stayed in remission between weeks 10 to 30 after VDZ initiation. During this maintenance therapy, median values of VTL and RA were 15.4 μg/mL and 0.97 ng/mL, whereas sMadCAM-1 was undetectable (<0.41 ng/mL) in 67.3%
of samples. The positive predictive value (PPV) of undetectable sMACAM-1 for clinical recurrence was 80%, with a corresponding sensitivity of 74.6%. On multivariate analysis undetectable sMACAM-1 and high VTL (> 19 mg/L) were independently associated with clinical recurrence (OR = 7.5, p = 0.006 and OR = 2.2, p = 0.045, respectively). The combination of sMACAM-1 < 0.41 mg/L and VTL > 19 mg/L was the best pharmacokinetic profile with an AUC of 95.2%. Median values of sMACAM-1 and RA were significantly higher (p = 0.0001) before VDZ therapy than during the follow-up (sMACAM-1: 40.5 vs. < 0.41 mg/L; RA: 1.7 vs. 0.97 mg/L). Only RA > 1.60 mg/L before VDZ therapy was predictive of clinical recurrence during the follow-up (AUROC = 80.7%).

Conclusion: Undetectable sMACAM-1 appears strongly associated with clinical recurrence during VDZ maintenance therapy. Combination of undetectable sMACAM-1 with high VTL is also potentially interesting for therapeutic drug monitoring. Baseline RA concentrations are predictive of clinical remission. These findings need to be confirmed in further prospective studies.

Disclosure: Nothing to disclose.
from chronic active ulcerative colitis received repeated fecal microbiota trans-
plantation (FMT) according to the standard protocol, using donor stool pre-
paration. 25 patients (mean age 36 ± 15) were treated with frozen donor stool (mixed with sodium chloride and glycerol, stored at -80 °C), 24 patients (mean age 44 ± 9) with freshly prepared donor stool (not older than 6 hours). Response and remission were determined by the total Mayo score (TMS) before FMT and after 90 days. Clinical response was defined as a decrease of ≥3 points in TMS from baseline, along with either a decrease of ≥1 point in the rectal bleeding subscore or the absolute rectal bleeding subscore of 0 or 1. Remission was defined as a TMS < 2 and an endoscopic subscore of 0 or 1.

Results: The mean TMS was 9.2 ± 2.2 (frozen stool) and 9.9 ± 1.8 (fresh stool) at baseline and was reduced to 5.1 ± 2.7 in the frozen donor stool group and to 5.3 ± 3.6 in the fresh donor stool group at day 90. The mean improvement in TMS between baseline and day 90 was statistically not significant different between the two groups (p = 0.691). Furthermore, remission and response rates were comparable between frozen donor stool and fresh donor stool cohorts (No response/Response/Remission: 40%/40%/20% vs. 42%/33%/25%; p = 1.00/ 0.769/0.742).

Conclusion: In chronic active ulcerative colitis frozen donor stool for FMT is as effective as fresh donor stool in inducing response and remission in ulcerative colitis. By using frozen donor stool FMT may become more available for the clinical use in this patient group.

Disclosure: Nothing to disclose

OP181 RANDOMISED CLINICAL TRIAL: SINGLE INFUSION-VERSUS MULTIPLE INFUSION FAECAL MICROBIOTA TRANSPLANTATION FOR THE TREATMENT OF SEVERE CLOSTRIDIUM DIFFICILE INFECTION REFRACTORY TO ANTIBIOTICS

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Introduction: Faecal microbiota transplantation (FMT) is a highly effective treatment against recurrent C. difficile infection. Far less evidence exists on the efficacy of FMT in treating severe C. difficile infection refractory to antibiotics.

Subjects with severe C. difficile infection refractory to antibiotics were randomly assigned to 1 of the 2 following treatment arms: 1) FMT-S, including a single faecal infusion via colonoscopy followed by a 14-day vancomycin course; 2) FMT-M, including multiple faecal infusions plus a 14-day vancomycin course. In the FMT-M group, all patients received at least 2 infusions, while with pseudomembranous colitis (PMC) underwent further infusions until the disappearance of pseudomembranes. The primary outcome was the cure of refractory C. difficile infection.

Results: 36 subjects, 2 in each treatment arm, were enrolled. 21 patients in the FMT-S group and 28 patients in the FMT-M group were cured, respectively (75% versus 100%, respectively, both in PP and ITT analyses; p = 0.01). No serious AEs were associated with any of the 2 treatment protocols. However, a pseudomembranous-associated single-shot FMT protocol in curing severe C. difficile infection refractory to antibiotics.

Disclosure: Nothing to disclose

OP182 A NON-FROZEN, LYOPHILIZED, ORAL MICROBIOTA-BASED DRUG RBX7455 IS SAFE, REDUCES CLOSTRIDIUM DIFFICILE INFECTION RECURRENT, AND RESTORES THE MICROBIOME: CLINICAL EVIDENCE FROM 3 PATIENT COHORTS

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Introduction: To broaden access to microbiota-based therapeutics therapies, RBX7455, a non-frozen, lyophilized, orally-administered microbiota-restoring therapy candidate was developed. We report interim results from an open-label Phase 1 trial of RBX7455 for preventing recurrent C. difficile infections (rCDI).

Aims and Methods: 25 patients with ≥2 CDI episodes following ≥2 courses of antibiotic therapy have been enrolled to date in 3 cohorts as follows: 1) 4 RBX7455 capsules twice daily for 4 days, n = 10; 2) 4 RBX7455 capsules twice daily for 2 days, n = 10; 3) 2 RBX7455 capsules twice daily for 2 days, n = 5. Success was defined as absence of CDI recurrence through 8 weeks after treatment completion, and adverse events were monitored during and after treatment.

Results: 9 of 10 patients in cohort 1, 8 of 10 patients in cohort 2, and 5 of 5 patients in cohort 3 were recurrence-free at the 8-week endpoint, with an overall success rate of 88% (22/25). A total of 37 non-serious adverse events (AEs) have been recorded to date, with gastrointestinal AEs being most common. No serious AEs have been observed.

Prior to treatment, the taxonomic compositions of responder microbiomes were significantly dissimilar from the RBX7455 composition and were dominated by Gammaproteobacteria and Bacilli. After treatment, patient microbiomes converged toward the RBX7455 composition, with Bacteroidia and Clostridia becoming more predominant. Microbiome changes were similar among responders from all cohorts.

Conclusion: 3 different dosing regimens of RBX7455 had a high success rate in preventing rCDI with no serious AEs. In addition, RBX7455 appears to restore patient microbiomes toward the RBX7455 composition. Microbiome and safety data collection will continue for 6 months after treatment.

Disclosure: This analysis was funded by Rebiotix Inc., Roseville, MN.
OP183 TREATMENT OF GASTRIC FUNDAL VARICES WITH EUS-GUIDED EMBOLISATION COMBINING COIL PLACEMENT WITH THROMBIN INJECTION

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Introduction: Gastric varices are present in 5-33% of patients with portal hypertension with incidence of bleeding of around 25% in 2 years1. If gastric varices are the source of bleeding, therapeutic options include endoscopic therapies, TIPSS, surgery and non-selective beta-blockade2. There are reports of EUS-guided coiling combined with cyanoacrylate glue3 but limited literature on safety and efficacy of EUS-guided coil embolisation with human thrombin injection. We report our experience.

Aims and Methods: We analysed data of all EUS-guided interventions for the management of bleeding gastric varices between 2015-2017 at a liver transplant center. Olympus EUS linear scope was used to inject human thrombin (Tissose®; 500U/ML) in gastric varices with or without coils (Nester® Embolisation Coils).

Results: A total of 10 EUS-guided interventions in 6 patients (4M & 2F), aged 55 (41-59) yrs for secondary prophylaxis. 67% had cirrhosis with MELD score of 14 (10-21) and 75% were Child-Pugh class C. The remainder had non-cirrhotic portal hypertension. All patients had previous bleeding from gastric varices and 2/3rd were intolerant of beta-blockers. 67% had previous thrombin injection that had failed to obliterate the gastric varices. EUS-guided coil embolisation was performed in 6 patients (2 had thrombin injection in situ, and thrombolytic agent that had failed previous coiling embolisation). The largest feeding vessel was 120 (7-16) mm with a median 5 (2-10) coils placement followed by thrombin injection of 3500 (2500-5000) IU.

Most (8/10) stayed overnight after intervention and only 2 required longer stays, Median F U was 9 (3-20) months with zero 30-day mortality. 1 patient had fever 2 days post procedure requiring IV antibiotics. No reported episodes of re-bleeding except in 1 patient at 23 months. 4 had follow up EUS (5-7 months) and showed no flow at the level of the coils. 1 patient died within 3 months of procedure secondary to hepatic decompensation.

Conclusion: In our experience EUS-guided coil embolisation and injection of thrombin is a technically safe and well-tolerated procedure even in patients with significant comorbidities especially who have failed eradication of gastric varices from single modality therapy. Due to the lower incidence of gastric variceal bleeding in comparison to oesophageal varices bleeding, we recommend multi-center prospective data collection evaluating the modalities being used and reporting of outcome data to help inform national guidelines.

Disclosure: Nothing to disclose

References
1. Garcia-Tsao G, Abraldes J, Berzigotti A, Bosch J. (2017) Treatment of esophageal varices in one of the dreadful complications of portal hypertension [1]. Upper endoscopy is the gold standard for diagnosing esophageal varices [2]. Noninvasive methods were applied in order to predict the presence of esophageal varices and their response to medical treatment [3]. One method is the splenic stiffness measurement [4]. Many studies were carried out for evaluating this technique, all of them agreed on the benefit, however, their results were different regarding a specific unified cut-off value and the capability of identifying the size of the varices [5]. These differences were thought to be due to readings exceeding the maximum value (75 kPa) of the machine [6].

Carvedilol is a nonselective b-blocker used to reduce portal pressure in order to prevent variceal bleeding [7], being a potent therapeutic agent with dual action (non-selective b-blocker and adrenoergic blocker) [8]. Effective dose of carvedilol for reducing portal pressure with the least arterial hypotension was found to be 12.5mg d-1 [9].

Aims and Methods: The aim of this study is to investigate the possibility of using the spleen stiffness measurement by transient elastography as a noninvasive approach to detect esophageal varices, and comparing the results obtained to liver stiffness measurement and platelet count to spleen diameter ratio in detecting and grading the size of varices. The study also aims to monitor changes in spleen stiffness before and after carvedilol therapy.

This was a single-center, prospective cross-sectional study, conducted on 110 individuals (90 chronic HCV patients and 20 healthy controls). Patients were divided into 4 groups: Group 1: Healthy controls, Group 2: Chronic Hepatitis, Group 3: Cirrhosis without varices, Group 4: Cirrhosis with varices.

All patients enrolled were over 18 years of age. Patients with transient elastography technical difficulty, contraindication to b-blockers, pregnant females, thrombocytopenia, portal hypertension requiring medications, and those undergone previous endoscopic management of esophageal varices were excluded from the beginning. Each patient underwent abdominal ultrasound and laboratory investigations, cirrhotic patients (60) were furtherly subjected to doppler ultrasonography to confirm portal hypertension, then upper endoscopy to verify the presence of esophageal varices, patients with esophageal varices were prescribed carvedilol (6.25mg twice daily) (30). Liver and spleen stiffness was done for all patients once and it was repeated again for patients who received carvedilol after three month of treatment as described.

Results: There was statistical significant difference between all groups in terms of both liver and spleen stiffness (p < 0.001). An inverse correlation was found in group 4 between spleen stiffness before treatment and the spleen size (R-value = 0.438, p = 0.016). Patients in group 4 showed a statistical significant difference in spleen stiffness measurement before and after treatment (p < 0.001). Spleen stiffness measurement was capable of predicting the presence of esophageal varices at cut off 59.85 kPa with AUC 0.768, showing sensitivity 80% and specificity 70%.

Conclusion: Spleen stiffness measurement by transient elastography is a reliable noninvasive method in predicting the presence of esophageal varices compared to other noninvasive methods and monitoring of treatment by carvedilol; however, it was not capable of identifying the size nor the risk of variceal bleeding.

Disclosure: Nothing to disclose

References

United European Gastroenterology Journal 6(8S) A71
2-year survival rates of 69.6% and 86.3%, respectively. There was no difference in survival with estimated 1-year survival rates for C. Shekhar

**Introduction:** Gastric variceal bleeding is less common than esophageal variceal bleeding; however, it is associated with a high morbidity and mortality rate. The aim of our study was to compare the balloon-occluded retrograde transvenous obliteration (BROTO) with cyanoacrylate injection for the prophylaxis of recurrent gastric variceal bleeding.

**Aims and Methods:** Between June 2015 and June 2018, 64 patients with variceal bleeding were assigned either balloon-occluded retrograde transvenous obliteration (n = 32) or cyanoacrylate injection (n = 32). The mean duration of follow-up period was 415 ± 250 days in the BROTO group and 404 ± 210 days in the cyanoacrylate group. Foam sclerotherapy using lauromacrogol by BROTO was performed.

**Results:** The technical success rate was 100% (32/32 patients) in the BROTO group. The amount of lauromacrogol used was 12.5 ± 4.5 ml (range, 3-20 ml). Significant rebleeding occurred in 1 patient (21.9%) of the BROTO group, and 7 patients (21.9%) of cyanoacrylate injection group (p = 0.023). The cumulative probability of remaining free of all-cause rebleeding was significantly higher in the BROTO group than in the cyanoacrylate group; the probability at 1 year was 88.9% in the BROTO group and 78.1% in the cyanoacrylate group (p = 0.024). There was no difference in survival with estimated 1-year survival rates for BROTO and cyanoacrylate injection treated patients of 90.5% and 86.3%, and 2-year survival rates of 69.6% and 83.6%, respectively.

**Conclusion:** These results suggest that the BROTO is more effective than cyanoacrylate injection in prevention of gastric variceal rebleeding. Survival is similar in the 2 groups.

**Disclosure:** Nothing to disclose

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**References**


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**Disclosure:** Nothing to disclose

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**References**

OP191 LIPIDOMICS ANALYSES INBILE IDENTIFIED SEVERAL CANDIDATE BIOMARKERS FOR DIAGNOSIS AND DISEASE PROGRESSION OF PRIMARY SCLEORIS CHOLANGITIS AND BILIARY DYSPLASIA
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Introduction: Primary sclerosing cholangitis (PSC) is a chronic, progressive struc-
turing disease of bile ducts that may eventually lead to cirrhosis and cholangio-
carcinoma (CCA). The etiopathogenesis is heterogeneous, involving both genetic and
environmental factors. Early diagnosis and better tools for monitoring pro-
gression of PSC and detection of biliary dysplasia is a major medical challenge. Novel biomarkers enabling a more precise diagnostic and prognostic markers of both PSC and biliary dysplasia are urgently needed.

Aims and Methods: This study aimed identifying a set of lipids in bile that would
serve as biomarkers for detection and prognosis of PSC and biliary dysplasia.
After informed consent, bile samples (n = 131) were drawn from participants
(n = 147) distributed across 4 experimental groups: non-advanced PSC (n = 63),
advanced PSC with biliary dysplasia (n = 24), and healthy controls (n = 60).
The samples were subsequently analyzed using a novel lipid-screening platform
(LipidyzerTM, Sciex) to determine the concentration of 1134 lipids species across 13 lipid classes.

Results: Model based analyses (Generalized Estimating Equations) pinpointed the following set of lipids as altered in PSC patients with respect to healthy controls, after correcting for type-I error: lysophosphatidylcholines (LPC(18:3),
LPC(20:4), LPC(20:5), and LPC(22:5),; lowest p = 0.4610^-3), lysophosphatidyl-
ethanolamines (LPE(20:3)); lowest p = 0.3060^-3), sphingomyelins (SM(14:0/16:1),
SM(14:0/18:1), SM(16:0/18:1), SM(18:0/18:1), and SM(18:0/18:2),; lowest p = 0.2371^-3),
phosphatidylethanolamines (total PE, PE(16:0/16:1), PE(16:0/18:1), PE(16:0/18:2), PE(16:0/18:3), PE(16:0/20:4),
PE(18:0/18:1), PE(18:0/18:2), PE(18:0/18:3); total PC, PC(14:0/16:1), PC(16:0/18:1), PC(17:0/18:1),
PC(17:0/20:4), PC(18:0/18:1), and PC(18:0/18:3); lowest p = 0.3271^-3),
phosphatidylserines (PS, PS(14:0/16:1), PS(14:0/18:1), PS(16:0/18:1),
PS(16:0/20:4), and PS(18:0/20:4); lowest p = 0.3271^-3), and complex lipids (fatty
acids, triglycerides, cholesterol esters, and sterol esters) (lowest p = 0.3271^-3),
respectively, and PE (hexadecanoyl PE, heptadecanoyl PE, oleic PE,)
acidic PE, eicosanoyl acid, eicosapentaenoic acid; lowest p = 0.4610^-3),
PE (eicosanoyl acid; p = 0.3271^-3), PC (16:0/16:1), PE(16:0/18:1) and
PC(18:0/18:2); lowest p = 1.8510^-3).

Conclusion: From the extensive lipid panel initially screened, this study was cap-
able of detecting a set of 34 candidate bile biomarkers that allowed differentiating between persons affected with PSC and biliary dysplasia from the healthy controls.

Disclosure: Nothing to disclose

OP192 INFLUENCE OF ANTIBIOTIC DURATION IN CHOLANGITIS AFTER SUCCESSFUL DRAINAGE BY ERCP
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Introduction: The cornerstone of treatment in cholangitis is successful drainage of the biliary tract by means of an ERCP in combination with antibiotics. Recommendations in current international guidelines regarding the duration of antibiotic treatment after adequate drainage vary from 3 days or less up to 10 days. The Dutch (SWAB) guideline recommends antibiotics for 3 days or less. However, high level of evidence to justify this recommendation is lacking. Our aim was to assess the incidence of infectious complications after adequate drainage of ascending cholangitis and to evaluate the potential influence of the antibiotic duration.

Aims and Methods: We performed a retrospective multicenter study in 7 medical centers in the Amsterdam region. Patients with cholangitis due to choledocholithiasis between January 2012 and January 2017 were extracted from local pro-
spective endoscopy databases. Adequate drainage by means of ERCP was required. The primary outcome was number of infectious complications within 3 months after the initial ERCP. An infectious complication was defined as the need for antibiotics within 3 months after ERCP. Secondary outcomes included development of hospital stay and infection.

Results: 427 patients were identified (disease between 1972 and 2018); 321/472 (68%) male, median age at diagnosis 51 (11-92) years. The null model showed evidence of disease clustering with areas of high and low disease prevalence (controlled for population size). The areas of highest risk were in rural Cumbria (RR 1.755) and lowest risk in urban Durham and Teeside (RR 0.6243).
Models using single spatial covariates: urban-ness, traffic, landfill sites, coal mines, lead mines, sandstone quarries, limestone quarries, Townsend score (a measure of social deprivation) and water hardness (concentration of calcium, magnesium, iron, silicon, pH) and a multi-covariate model containing covariates showed to be significant at 95% Bayesian Credibility Intervals (BCIs). Deviance Information Criterion (DIC) was used to compare the fits of models. All models were performed after controlling for the area size of each postcode district. There were 3 main questions:
1. Is the prevalence of PSC in a defined area greater than that expected by chance i.e. disease clustering?
2. If so, is elevated risk associated with any environmental risk factors local to the case?
3. If elevated risk dependent on socio-economic status?

Results: 472 patients were identified (disease between 1972 and 2018); 321/472 (68%) male, median age at diagnosis 51 (11-92) years. The null model showed evidence of disease clustering with areas of high and low disease prevalence (controlled for population size). The areas of highest risk were in rural Cumbria (RR 1.755) and lowest risk in urban Darlington and Teeside (RR 0.6243).
Models using single spatial covariates showed that only urban-ness and Townsend score significantly improved the null model with 2.5% and 95% confidence intervals not crossing 0. A multi-covariate model (combining urban-ness and Townsend score) did not improve the model further. There was a statistically significant difference in the Townsend scores of the 20 patients living in areas of highest and lowest prevalence (p < 0.0001) with lower Townsend scores (i.e. less social deprivation) seen in areas of high disease prevalence.

Conclusion: A higher prevalence of PSC was seen in more rural, less deprived areas. This inverse association with social deprivation is the opposite to that seen in other geographical studies of many other diseases, including liver disease, and warrants further investigation into potential disease triggers. The association between rurality raises the possibility of an association with processes in these areas e.g. farming, pesticide use.

Disclosure: JKJ-D is supported by the NIHR Rare Diseases Translational Research Collaboration and NIHR Newcastle Biomedical Research Centre.
OP194 DURABLE RESPONSE IN THE MARKERS OF CHOLESTASIS THROUGH 36 MONTHS OF OPEN-LABEL EXTENSION STUDY OF OBETICHLIC ACID IN PRIMARY BILLIARY CHOLANGITIS


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Introduction: Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor agonist indicated for treatment of primary biliary cholangitis (PBC). POISE is a 12-month double-blind (DB), placebo (PBO)-controlled, Phase 3 PBC study including an open-label extension (OLE).

Aims and Methods: The purpose of the OLE is to assess safety and durability of the OCA effect on serum markers of cholestasis. Key POISE inclusion criteria: PBC diagnosis, ALP ≥ 1.67x ULN and/or total bilirubin (TB) > ULN to < 2x ULN, stable UDCA dose or unable to tolerate UDCA. During the DB phase, pruritus was the most common side effect of OCA, but discontinuation due to pruritus continues to be infrequent.

Results: 193 of 198 (97%) patients completing the DB phase of the study enrolled in the OLE: 165 reached 36 months of the OLE. PBO, n = 49; OCA 5-10 mg, n = 59; OCA 10 mg, n = 57. At the end of the DB phase, patients on OCA had significant reductions in ALP and patients on PBO did not (Table 1). ALP reduction observed in OCA-treated patients was durable through 36 months OLE. PBO-treated patients experienced a significant reduction in ALP after switching to OCA, which was durable through 36 months OLE. Similar durable improvements were seen for GGT, ALT, and AST (data not shown). For OCA-treated patients, mean TB remained below BL through 36 months OLE. For PBO-treated patients, mean TB increased at 12 months DB, but trended back toward baseline (BL) with 36 months of OCA during OLE. During the OLE, 28 (15%) patients discontinued treatment, 7 (4%) patients for pruritus.

Conclusion: OCA treatment results in improvement in liver biochemistry; this improvement is durable in this analysis. For patients initially treated with PBO, switching to OCA is also associated with a durable biochemical response. Consistent with the DB phase, pruritus was the most common side effect of OCA, but discontinuation due to pruritus continues to be infrequent.

DB Phase Treatment Group PBO OCA 5-10 mg OCA 10 mg
ALP (U/L) 327 (115) 326 (116) 316 (104)
ΔALP 12 Mo 9 (88) -104 (87)*** -118 (75)***
ΔALP 24 Mo -101 (87)*** -121 (97)*** -103 (79)***
ΔALP 36 Mo -113 (90)*** -101 (110)*** -85 (137)***
TB (μmol/L) DB BL 11.8 (7.2) 10.2 (5.5) 11.3 (6.6)
ΔTB 12 Mo 1.5 (4.1) -0.3 (3.4)** -1.2 (4.3)**
ΔTB 24 Mo 1.9 (7.6) -0.4 (3.6) -0.6 (4.8)
ΔTB 36 Mo 0.5 (3.6) -0.5 (3.4) -0.9 (4.1)

*p<0.05, **p<0.01, ***p<0.001. Values are Mean (SD). DB: P-value for comparing active treatments to PBO is obtained using an ANCOVA model with BL value as a covariate and fixed effects for treatment and randomization strata factor. OLE: P-value for the within treatment comparisons are obtained using the Student’s t-test.

Disclosure: This study was funded by Intercept Pharmaceuticals, Inc.

Tuesday, October 23, 2018
14:00-15:30
IBD clinical trials I – Room F1

OP195 EFFICACY AND SAFETY OF UPADACITINIB AS AN INDUCTION THERAPY FOR PATIENTS WITH MODERATELY-TO-SEVERELY ACTIVE ULCERATIVE COLITIS: DATA FROM THE PHASE 2B STUDY U-AChEIVE


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Introduction: Janus Kinase (JAK) inhibitors are emerging as a promising treatment option for ulcerative colitis (UC). The efficacy and safety of upadacitinib (UPA), a JAK1-selective inhibitor, was assessed in an 8-week double-blind placebo (PBO)-controlled dose-ranging Phase 2b induction study in patients (pts) with moderately-to-severely active UC who had inadequate response, loss of response or intolerance to corticosteroids (CS), immunosuppressants (IS), or biologic therapies.

Aims and Methods: Adult pts with moderately-to-severely active UC (Adapted Mayo Score [Mayo score without Physician Global Assessment] 5-9 points and centrally-read endoscopic subscore ≥2-3) were randomized to receive extended-release UPA 7.5, 15, 30, 45 mg once daily (QD) or PBO for 8 weeks. Pts were stratified by previous biologic use, baseline (BL) CS use, and BL Adapted Mayo score (≤5). A dose-response relationship between UPA doses and PBO for the primary endpoint, clinical remission per Adapted Mayo Score at week 8 (defined as stool frequency subscore [SFS]≤1, rectal bleeding subscore [RBS] = 0, endoscopic subscore [ES]≤1), was tested by Multiple Comparison Procedures Modeling (MCP-Mod) using pre-specified candidate models in the intent-to-treat population. Pairwise comparisons between UPA doses and PBO for the primary and ranked secondary endpoints were also conducted using the Cochran-Mantel-Haenszel test stratified by randomization factors. Non-responder and last observation carried forward imputations were utilized for missing data.

Abstract No: OP195

Endpoints Placebo UPA 7.5 mg QD UPA 15 mg QD UPA 30 mg QD UPA 45 mg QD
n = 46 n = 47 n = 49 n = 52 n = 56
Clinical remission per Adapted Mayo Score at week 8 (stool frequency subscore ≤1, rectal bleeding score = 0, endoscopic score ≤1)* 0 4 (8.5) 7 (14.3)* 7 (13.5)* 11 (19.6)*
Endoscopic Improvement (endoscopic subscore ≤1) at week 8* 1 (2.2) 7 (14.9)* 15 (30.6)*** 14 (26.9)*** 20 (35.7)***
Clinical remission per Full Mayo (Full Mayo ≤2 with no subscore >1) at week 8# 0 4 (8.5) 5 (10.2)* 6 (11.5)* 11 (19.6)*
Clinical response per Adapted Mayo (decrease from baseline ≥2 points and ≥30% and in RBS ≥1 or RBS = 0 or 1) at week 8* 6 (13.0) 14 (29.8)* 22 (44.9)*** 23 (44.2)*** 28 (50.0)***

*Primary Endpoint; #Ranked Secondary Endpoints; ***, **, * significant at 0.001, 0.01, and 0.05 levels, respectively
values in categorical and continuous efficacy variables. Treatment-emergent adverse events (AEs) were reported from first dose of study drug up to 30 days after last dose.

Results: A total of 250 pts were randomised with a mean (SD) age of 42.3 (14.2) years and a disease duration of 8.2 (2.5) years. At BL, 77.6% had prior use of biological modulators or tumour necrosis factor inhibitors. Remission (total Mayo score <2, no subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

OP196 CANNABIS INDUCES CLINICAL RESPONSE BUT NO ENDOSCOPIC IMPROVEMENT IN CROHN’S DISEASE PATIENTS

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Introduction: Many patients with Crohn’s disease (CD) report that the use of medical cannabis improves their symptoms, however studies evaluating objective disease parameters including inflammatory markers and endoscopic score are lacking.

Aims and Methods: To assess the effect of cannabis treatment on Crohn’s disease patients.

Methods: In a double blind, randomized, placebo-controlled trial on CD patients with active disease Patients were randomized to receive either cannabis oil with 15% Cannabidiol (CBD) and 4% tetrahydrocannabinol (THC) or placebo for 8 weeks. All other medications remained unchanged. Disease-related outcome measures including Crohn’s disease activity index (CDAI), C-reactive protein (CRP), fecal calprotectin, simple endoscopic score for Crohn’s disease (SES-CD) and SF-36 quality of life (QOL) were assessed before, during and after treatment.

Results: A total of 46 patients, 31 males (67%), mean age ± 35±12, were investigated. Each study group included 23 patients. CDAI before the treatment was 288.4 ± 78.0 and 298.5 ± 112.2 (p = 0.71), after 8 weeks of treatment the CDAI was 143.1 ± 96.0 and 209.5 ± 131.0 in the cannabis and placebo groups, respectively (p = 0.05). Remission rate (defined as CDAI < 150) was achieved in 65% (29/46) and 55.6% (25/45) of patients, respectively (p = 0.40). The potential anti-inflammatory properties of cannabis treatment in IBD/Crohn’s disease requires further investigation.

Disclosure: Bar-Lev Schleider Lhi is an employee of Tikun Olam, a supplier of medical cannabis.

OP197 TOFACITINIB IS MILLIGRAMS TWICE DAILY FOR PATIENTS WITH MILD TO SEVERE ULCERATIVE COLITIS: RESULTS FROM 8-WEEK INDUCTION STUDIES OCTAVE INDUCTION 1 & 2


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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). The efficacy and safety of tofacitinib in patients with ulcerative colitis disease severity score (UCDSS) C10 were previously reported in a 2-week, Phase II study (NCT01465763 & NCT01465764). The current study trial protocols called for patients to be randomised to either tofacitinib 10 or 15 mg BID or placebo. The primary endpoint of interest was the proportion of patients achieving a primary clinical response (PCI) at Week 8.

Results: 77 patients (44 males, 33 females) with an average age of 38.3 years and a disease duration of 8.2 (2.5) years. At BL, 77.6% had prior use of biological modulators or tumour necrosis factor inhibitors. Remission (total Mayo score <2, no subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

Aims and Methods: We report pooled efficacy and safety analyses from OCTAVE Induction 1 & 2 for the tofacitinib 15 mg BID dose alongside data from the tofacitinib 10 mg BID groups previously reported. Patients were ≥18 years of age and had failed, or were intolerant to, corticosteroids, immunomodulators or tumour necrosis factor inhibitors. Remission (total Mayo score ≤2, no subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

Results: Baseline demographics and disease characteristics of the 22 patients who received tofacitinib 15 mg BID during OCTAVE Induction 1 & 2 were generally consistent with the overall study population. At Week 8 in the tofacitinib 15 mg BID group, the primary efficacy point of remission was achieved by 9 (40.9%) patients, mucosal healing by 13 (59.1%) patients, and clinical response by 19 patients (86.4%). Treatment effect sizes (ie difference from placebo [95% CI]) were 34.9% (15.6, 54.6) for remission, 45.4% (23.5, 65.3) for mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

Disclosure: The authors declare that they have no conflicts of interest.

Results: 18 patients (9 males, 9 females) with an average age of 38.3 years and a disease duration of 8.2 (2.5) years. At BL, 77.6% had prior use of biological modulators or tumour necrosis factor inhibitors. Remission (total Mayo score ≤2, no subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

Disclosure: The authors declare that they have no conflicts of interest.

Results: 18 patients (9 males, 9 females) with an average age of 38.3 years and a disease duration of 8.2 (2.5) years. At BL, 77.6% had prior use of biological modulators or tumour necrosis factor inhibitors. Remission (total Mayo score ≤2, no subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

Disclosure: The authors declare that they have no conflicts of interest.

Results: 18 patients (9 males, 9 females) with an average age of 38.3 years and a disease duration of 8.2 (2.5) years. At BL, 77.6% had prior use of biological modulators or tumour necrosis factor inhibitors. Remission (total Mayo score ≤2, no subscore >1 and rectal bleeding subscore of 0), mucosal healing (Mayo endoscopic subscore ≤1) and clinical response (decrease from baseline total Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) were evaluated based on central reading of endoscopic subscore. Differences from placebo and 95% confidence intervals (CI) were calculated using an exact method.

Disclosure: The authors declare that they have no conflicts of interest.
**Table. Baseline demographics and disease characteristics, and summary of efficacy and safety at Week 8, in OCTAVE Induction 1 & 2**

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Tolactamin 10 mg BID</th>
<th>Tolactamin 15 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 234</td>
<td>N = 905</td>
<td>N = 22</td>
</tr>
</tbody>
</table>

**Baseline demographics and disease characteristics**
- **Age in years, mean (SD)**: Placebo 41.1 (14.4), Tolactamin 42.0 (13.8), Tolactamin 38.8 (12.7)
- **Male, n (%):** Placebo 132 (56.4), Tolactamin 53 (59.2), Tolactamin 12 (54.5)
- **Disease duration in years, median (range):** Placebo 6.1 (0.4-36.2), Tolactamin 6.3 (0.4-42.5), Tolactamin 6.9 (0.5-21.9)
- **Total Mayo score, mean (SD):** Placebo 9.0 (1.5), Tolactamin 9.0 (1.4), Tolactamin 9.0 (1.5)
- **Prior TNFi Failure, n (%):** Placebo 124 (53.0), Tolactamin 465 (51.4), Tolactamin 10 (45.5)

**Efficacy outcomes at Week 8, n (%)**
- **Remission:** Placebo 14 (6.0), Tolactamin 159 (17.6), Tolactamin 9 (40.9)
- **Difference (95% CI) from placebo:** Tolactamin -11.6 (7.7, 15.5), Tolactamin 34.9 (15.6, 56.4)
- **Mucosal healing:** Placebo 32 (13.7), Tolactamin 271 (29.9), Tolactamin 13 (59.1)
- **Difference (95% CI) from placebo:** Tolactamin -16.3 (11.0, 21.6), Tolactamin 45.4 (23.5, 65.3)
- **Clinical response:** Placebo 72 (30.8), Tolactamin 521 (57.6), Tolactamin 19 (86.4)
- **Difference (95% CI) from placebo:** Tolactamin -26.8 (20.1, 33.5), Tolactamin 55.6 (32.3, 76.7)

**Summary of safety up to Week 8, n (%)**
- **AEs:** Placebo 132 (56.4), Tolactamin 501 (55.4), Tolactamin 16 (72.7)
- **SAEs:** Placebo 14 (6.0), Tolactamin 34 (3.8), Tolactamin 0 (0.0)
- **Discontinuations due to AEs:** Placebo 10 (4.3), Tolactamin 35 (3.9), Tolactamin 0 (0.0)
- **SAEs:** Placebo 14 (6.0), Tolactamin 34 (3.8), Tolactamin 0 (0.0)
- **AEs 132 (56.4), Tolactamin 501 (55.4), Tolactamin 16 (72.7)**

**Efficacy data are full analysis set with non-responder imputation based on central read endoscopy.**

**Disclosure:** DT Rubin has received research support from AbbVie, Genentech, Janssen, Takeda, UCBD; and consultancy fees from AbbVie, Amgen, Janssen, Pfizer Inc, Takeda, UCBD; S Motoya has received research support from Janssen, Takeda, UCB; and consultancy fees from AbbVie, Amgen, Janssen, Pfizer Inc, Pfizer Inc employees and shareholders; PDR Higgins has received consultancy fees from AbbVie, Amgen, Genentech, JBR Pharma, Lyerca.

**Reference**

**OP198 EFFICACY AND SAFETY OF GASTRO-RESISTANT PHOSPHATIDYLCHOLINE (LT-02) FOR INDUCTION OF REMISSION IN PATIENTS WITH MILD-TO-MODERATE ULCERATIVE COLITIS REFRACTORY TO MESALAZINE: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY (PCG-2)**

**Introduction:** An observed deficiency of phosphatidylcholine (PC) in the intestinal mucus in patients with ulcerative colitis (UC) [1] led to the hypothesis that daily oral administration and subsequent gastro-resistant release of PC into the ileum could restore the protective mucus barrier function.

**Aims and Methods:** This was a prospective, double-blind, randomised, multicentre phase 3 trial to compare the efficacy and safety of 2 different dosing regimen of LT-02 (LT-02 0.8 g QID, LT-02 1.6 g BID) with placebo over 12 weeks for induction of remission in patients with active ulcerative colitis (mDAI score 4-10, <10% 1 point in each of the four subscores) refractory to mesalazine despite either continued treatment with oral 5-ASA ≥ 2.4 g/d or ≥ 6 weeks or combination of oral 5-ASA ≥ 2.4 g/d and a rectal 5-ASA preparation for ≥10-14 days. Subjects had to have fecal calprotectin (FCP) ≥ 250 μg/g at screening or FCP ≥ 100 μg/g and Histological Index (HI) ≥ 1. Primary endpoint was the percentage of patients in deep remission defined as mDAI Score ≤ 1 with a score of 0 points for rectal bleeding and stool frequency, and ≥ 1 point reduction from baseline in the mucosal appearance score. After a pre-specified interim-analysis, the study was stopped for futility.

**Results:** The full analysis set (FAS) comprised 465 patients. Both the primary and the secondary efficacy endpoints did not show significant differences across treatment groups.

**Reference**
OP199 A PHASE 3 STUDY OF VEDOLIZUMAB IN JAPANESE PATIENTS WITH INTESTINAL CROHN’S DISEASE: EFFECTS ON TIME TO DISEASE WORSENING AND TREATMENT FAILURE

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Introduction: Vedolizumab (VDZ), a humanized monoclonal antibody inhibiting α4β7 integrin, is approved globally for the treatment of ulcerative colitis (UC). However, data on its safety and efficacy is limited in the Asian population. We conducted a phase 3, randomized, double-blind, placebo (PBO)-controlled study in Japanese patients (pts) with UC (NCT02039505), where 1 of 2 primary end-points was remission clinical response at Week 10 (induction phase, IP) was numerically greater but not significant, and clinical remission at Week 6 (maintenance phase, MP) was statistically superior, in the VDZ compared with the PBO arm. Here we report the results of predefined exploratory end-points for the MP: the effect of VDZ on time to disease worsening (TDW) and time to treatment failure (TTF).

Aims and Methods: Japanese pts with moderate-to-severe UC received 300mg VDZ or PBO at Weeks 0, 2 and 6 in the IP. Pts showing a clinical response to VDZ at Week 10 were then randomized 1:1 to receive VDZ (N = 41) or PBO (N = 42) in the MP, at Weeks 14, 22, 30, 38, 46 and 54. Disease worsening in the MP was defined as an increase of the partial Mayo score (range: 0-9 points) by ≥3 points compared with that of Week 10 for 2 successive visits, and a partial Mayo score of ≤5 points (or ≥6 points in 2 successive visits, in the case of >6 points at Week 10). Treatment failure was defined as any of the following: disease worsening, use of rescue medication, or study discontinuation due to drug-related adverse events.

Results: A Kaplan-Meier analysis of TDW showed that at Month 6, the proportion of pts without disease worsening was higher for the VDZ group (82.5%) compared with the PBO group (61.5%); this difference was sustained at Month 12 (89.6% vs 61.5%). The Kaplan-Meier analysis of TTD showed that at Month 6, the proportion of pts without treatment failure was 74.4%; this difference was maintained at Month 12 (74.4% vs 44.2%). Disease worsening in the VDZ group at Week 10 were then randomized 1:1 to receive VDZ (N = 73) or PBO (N = 71). The difference between the treatment groups for both TDW (p = 0.0446) and TTD (p = 0.0166).

Conclusion: VDZ showed statistically significant difference between treatment groups on TDW and TTD in Japanese pts with UC.

Disclosure: Motoya S; Advisory council or committee: Kyorin Pharma, Board of directors: Pfizer, Honoraria: Mitsubishi Tanabe Pharma, Grants or funds; Janssen, EA Pharma Watanabe K; Honoraria & Grants or funds: Takeda Pharmaceutical* Ogata H; Honoraria & Grant or funds: ZERIA Pharmaceutical*, Asua Kasei Medical*, Zeria Pharmaceutical*, Takeda Pharmaceutical*, JIMRO*, MP was defined as an increase of the partial Mayo score (range: 0-9 points) by ≥3 points compared with that of Week 10 for 2 successive visits, and a partial Mayo score of ≤5 points (or ≥6 points in 2 successive visits, in the case of >6 points at Week 10). Treatment failure was defined as any of the following: disease worsening, use of rescue medication, or study discontinuation due to drug-related adverse events.

OP200 ROLE OF CONCOMITANT IMMUNOSUPPRESSION IN THE EFFICACY AND SAFETY OF USTEKINUMAB: POST-HOC ANALYSES OF UNITI

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Introduction: Unlike anti-TNFs, ustekinumab (UST, an anti-IL-12/23 monoclonal antibody) appears minimally immunogenic, and therefore may not require combination with immunosuppressants (IS) AZA, 6-MP, or MTX to achieve maximum efficacy. As previously reported, UST is superior to PBO across a wide range of subgroups, including combo & mono therapy. In this post hoc

Abstract No: OP200

Table 1: Role of concomitant immunosuppression in the efficacy of UST induction

<table>
<thead>
<tr>
<th>No AZA/6-MP/MTX</th>
<th>With AZA/6-MP/MTX</th>
<th>Difference mono</th>
<th>Difference combo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNITI-1: UST ≤ 6 mg/kg (TNF-failures)</td>
<td>PBO (n = 137)</td>
<td>UST (n = 138)</td>
<td>UST-PBO</td>
<td>UST-PBO</td>
</tr>
<tr>
<td>CR-100 Week 6</td>
<td>21.0</td>
<td>36.3</td>
<td>22.5</td>
<td>28.2</td>
</tr>
<tr>
<td>Remission Week 8</td>
<td>6.6</td>
<td>19.9</td>
<td>8.8</td>
<td>23.1</td>
</tr>
<tr>
<td>UNITI-2: UST ≤ 6 mg/kg (Conventional failures)</td>
<td>PBO (n = 167)</td>
<td>UST (n = 171)</td>
<td>UST-PBO</td>
<td>UST-PBO</td>
</tr>
<tr>
<td>CR-100 Week 6</td>
<td>28.7</td>
<td>50.0</td>
<td>28.8</td>
<td>66.2</td>
</tr>
<tr>
<td>Remission Week 8</td>
<td>18.3</td>
<td>37.7</td>
<td>21.9</td>
<td>45.1</td>
</tr>
<tr>
<td>IM-UNITI: UST 90 mg Q8W</td>
<td>PBO (n = 87)</td>
<td>UST (n = 85)</td>
<td>UST-PBO</td>
<td>UST-PBO</td>
</tr>
<tr>
<td>CR-100 Week 44</td>
<td>41.3</td>
<td>57.0</td>
<td>50.0</td>
<td>62.8</td>
</tr>
<tr>
<td>Remission Week 44</td>
<td>32.2</td>
<td>51.8</td>
<td>43.2</td>
<td>55.8</td>
</tr>
<tr>
<td>IM-UNITI: UST 90 mg Q12W</td>
<td>PBO (n = 87)</td>
<td>UST (n = 78)</td>
<td>UST-PBO</td>
<td>UST-PBO</td>
</tr>
<tr>
<td>CR-100 Week 44</td>
<td>41.3</td>
<td>55.1</td>
<td>50.0</td>
<td>62.8</td>
</tr>
<tr>
<td>Remission Week 44</td>
<td>32.2</td>
<td>46.2</td>
<td>43.2</td>
<td>52.9</td>
</tr>
</tbody>
</table>
Disclosure: Nothing to disclose

The efficacy of UST in induction and maintenance was stratified according to IS use, then tested for potential correlation between the effect size of the response of UST and the use of IS (Chi-square, without correction for multiple comparison). For the safety population, we created odds ratios for all AEs and infections, for combo and mono groups. Safety data was corrected for follow-up and stratified by concomitant IS use.

**Results:** We compared the efficacy of UST and PBO at primary and major secondary endpoints for the induction and maintenance phase3 trials. During the induction trials (UNITI-1 & -2) we could not detect an association between concomitant IS use and efficacy at any endpoint (Data for approved -6mg/kg induction dose in Table 1), nor was there any consistently obvious benefit for combo over mono therapy during maintenance therapy (IM-UNITI, we failed to detect significant interactions between concomitant IS use and efficacy in either QSW or Q12W UST groups (Table1). Rates of total AEs were not obviously different between groups, though combo therapy tended to have lower rates than monotherapy, in terms of bleeding rates of infections, there were no trends when contrasting dose groups or IS use. PBO pts treated with concomitant IS had infection rates of 156, 182, and 114 per 100 pt-yrs (PBO, UST 90mg Q12W, and UST 30mg Q8W) vs. 167, 130, 173 per 100 pt-yrs (PBO, UST 90mg Q12W, and UST 90mg Q8W) without IS. Odds ratios did not appear different when contrasting mono and combo therapy, with 95% CI’s were broadly overlapping and crossing 1.0.

**Conclusion:** In our analysis, we were unable to detect a significant interaction between any dosage of UST and IS. Taken with previously presented data on serum [UST] being independent of IS use, and low overall immunogenicity; these data suggest that similar benefit is achieved when UST is administered as mono-therapy, or given as combination therapy with IS in patients with moderate to severe CD.

Disclosure: This study was supported by Janssen Research & Development, LLC.

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**Aims and Methods:**

Over 9 years to April 2017 analysis of LSL resected by EMR from a prospectively collected database at 8 Australian Tertiary Referral Centres was performed. LSL ≤ 25mm in the left colon and ≤ 20mm in the right colon were included. Multiple LSL in the same patient were excluded. Standard inject and resect EMR was performed. LSL resections were identified as piecemeal or en bloc (single snare resection) and their outcomes were compared. Scheduled surveillance colonoscopy was performed at desired intervals of 4-6 months and 18 months after EMR. Late recurrence described adenoma recurrence after a negative surveillance procedure.

**Results:** 587 LSL were included of which 267 (46.1%) were resected en bloc, with histologic clear margins in 80.4%. Larger and previously attempted LSL were more likely to be removed piecemeal (p=0.015 and p<0.001 respectively). Neither colonic location nor morphology predicted en bloc resection. En bloc resection took less time, median 10 versus 20 minutes, p<0.001. Muscularis propria injury was more common with en bloc resection (p=0.038). Other adverse events were not more common between the groups (table 1). LSL underwent first surveillance in rectum in 5 (2.6%) LSL which were resected en bloc and 23 (9.3%) resected piecemeal (p=0.004). 251 (63%) LSL underwent second surveillance at median 19.5 months (interquartile range 15.5–25). Recurrence was present in 1 (0.8%) EMR scar where the LSL was resected en bloc and 7 (2.7%) LSL which were resected piecemeal (p=0.066). In the piecemeal group 4/7 of these recurrences were after treatment of a previous recurrence. Need for surgery was infrequent in both groups during surveillance and was due to inability to resect recurrence in all cases.

**Disclosure:** Nothing to disclose

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**Disclosure:** Nothing to disclose

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**Disclosure:** Nothing to disclose
Op203 A NEW METHOD OF ENDOSCOPIC RESECTION FOR COLORECTAL ADENOMA, "UNDERWATER COLD SNARE POLYPECTOMY": A PROPENSITY SCORE MATCHING ANALYSIS WITH CONVENTIONAL COLD SNARE POLYPECTOMY

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Introduction: Cold snare polypectomy (CSP) for colorectal adenomas is used worldwide because of its excellent safety. However, the rate of R0 resection is not adequately high [1]. Few studies have reported on the efficacy of underwater endoscopic mucosal resection for colorectal adenomas [2]. We hypothesized that CSP for colorectal adenoma in underwater environment may combine high safety and high R0 resection rate; we named this procedure underwater CSP (UCSP). We prospectively analyzed the safety and efficacy of UCSP.

Aims and Methods: [Study 1] Between May 2017 and January 2018, 161 lesions from 53 patients were resected using UCSP. UCSP was carried out by two endoscopists who confirmed adenomas underwent follow-up colonoscopy 3 weeks after UCSP whether or not they achieved R0 resection. Any post-UCSP scars were biopsied to confirm the presence of residual adenomas.

[Study 2] We used propensity score-matching (PSM) analysis to compare the safety and efficacy of UCSP in the resection of 175 adenomas and to confirm the presence of residual adenomas in the 102 lesions resected using conventional CSP, between March 2015 and April 2017; the follow-up schedule for both groups was the same. The location, macroscopic type, and size of the lesions were used as covariates.

Results: [Study 1] The patients included 33 men and 20 women (mean age, 68.0 ± 8.1 years). The mean lesions in the colon, ascending colon, transverse colon, descending colon, sigmoidal colon, and rectum, was 15, 51, 53, 22, 35, and 15, respectively. The number of lesions with type Ip, Isp, Is, and H macroscopic appearance was 3, 49, 62, and 78, respectively. The mean lesion size was 4.5 ± 1.5 mm; median, 4mm. The en bloc resection and complete retrieval rates of specimens were 100% and 99.5%, respectively. In the final pathological diagnoses, 13, 157, 6, 8, 1, 1, and 4 lesions were non-tumor, low-grade tubular adenoma, low-grade tubulo-villous adenoma, high-grade tubular adenoma, high-grade tubulo-villous adenoma, intra-mucosal carcinoma, and SSA/P, respectively. The R0 resection rate of 177 tumorous lesions was 74.0% (131/177). No cases of perforation or delayed bleeding were found. Of the 177 scars post-CSP for adenomas, 175 (98.9%) were identified, and one residual scar was identified at UCSP site.

Conclusion: The R0 resection rate of UCSP was significantly higher than that of conventional CSP, with both procedures showing similar safety. Therefore, UCSP may be adequate therapy for small colorectal adenomas.

Disclosure: Nothing to disclose

Reference

Op204 ENDOSCOPIC FULL THICKNESS RESECTION IN THE COLON: 3-YEAR MULTICENTRE UK EXPERIENCE

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Introduction: Endoscopic full thickness resection (eFTR) of the colon using the full thickness resection device (FTRD) is a novel method for removing lesions involving, or tethered to, deeper layers of the colonic wall. The UK FTRD registry collects data from multiple centres performing this procedure. We describe the feasibility and early outcomes of this technique.

Aims and Methods: Registry data from April 2013 – January 2018 was analysed. Main outcome measures were technical success, procedural time, specimen size, R0 resection, endoscopic clearance, and adverse events. Reported technical difficulties were collated.

Results: 38 cases were performed across 8 centres (median 2 cases per centre, range 1-23). Mean patient age was 70 years (39-93). Indications for eFTR include non-lifting adenoma (18 cases), T1 tumour resection (10), submucosal tumour (7), and appendix base adenoma (3).

In 94.7% (37/38) of patients the lesion was reached with the FTRD. 1 caecal lesion could not be reached due to sigmoid diverticulitis. The procedure was technically successful in 91.9% of patients (34/37). Median procedure time was 41 minutes (11-86), median resection time 6 minutes (2-36), and median specimen size 22mm (10-30). R0 resection was achieved in 76.5% of patients (26/34). R0 resection was not achieved in 8 patients, of which 5 had no residual lesion on follow up, giving a total endoscopic clearance rate of 91.2% (31/34).

Technical difficulty occurred in 9 patients; due to snare failure and 3 due to lesion slippage on clip deployment. Of these 9 cases, 7 achieved R0 resection by using further snare.

Complications occurred in 2 patients; 1 acute appendicitis at day 6 after resection of appendix base adenoma, and 1 mild asymptomatic stricture at eFTR site at follow-up. There were no cases of bleeding, perforation, or fistula.

Conclusion: eFTR has a high success rate in treating lesions not previously amenable to endoscopic therapy. Whilst technical difficulties may arise, complication rates are low and outcomes acceptable, making eFTR a viable alternative to surgery.

Disclosure: Nothing to disclose

Reference

Op205 LIMITATIONS OF ENDOSCOPIC RESECTION FOR COLORECTAL SUBMUCOSAL INVASIVE CARCINOMA ARISING IN SESSILE SERRATED ADENOMA/POLYP

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Introduction: Among early colorectal carcinomas, lesions with little possibility of lymph node metastasis are usually treated endoscopically [1]. However, to the best of our knowledge, no report has described the problem with endoscopic treatment for early carcinomas arising in sessile serrated adenoma/polyp (SSA/Ps). Although invasive carcinomas with SSA/Ps (CA-SSA/Ps) are rare, these tumours are critical because SSA/Ps may grow into subsequent SSA/Ps with high-grade dysplasia or those with submucosal carcinoma more rapidly [2]. Furthermore, mucinous histology has also been found in CA-SSA/Ps [3, 4].

Aims and Methods: The aim of this study was to elucidate the clinicopathological features of CA-SSA/Ps and to investigate the possibility of endoscopic resection for these lesions. We reviewed all lesions pathologically diagnosed as T1 colorectal carcinomas that were endoscopically or surgically resected at Juntendo University Hospital and our affiliated hospitals between 2006 and 2017. We identified 45 CA-SSA/P lesions (from 45 patients) that were endoscopically (n = 18) or surgically resected (n = 27). For comparison, we randomly selected 200 invasive carcinomas with adenomas (CA-ADs) that were endoscopically (n = 87) or surgically resected (n = 113) from 200 patients.

Results: The clinicopathological characteristics of the studied lesions are summarized in Table 1. The patients with CA-SSA/P were older than those with CA-ADs (median age, 74 years vs. 57 years). Although the R0 resection rate of UCSP was significantly higher than that of CSP (75.5% vs. 32.4%; p < 0.001), the rate of pathological residual adenomas 3 weeks after resection was 0.98% in both groups (1/102).

In 97.4% (37/38) of patients the lesion was reached with the FTRD. 1 caecal lesion exhibited a higher potential for lymphatic invasion and lymph node metastasis. Therefore, the risk of lymph node metastasis should be considered when perform-
Table 1: Clinico pathological characteristics of colorectal lesions studied.

Disclosure: Nothing to disclose

References


OP206 ENDOSCOPIC RESECTIONS IN INFLAMMATORY BOWEL DISEASE


1, A. Alkandari1, M. Bhandari1, A. Przybysz2, M. Bugajski2, K. Kandiah3, S. Subramaniam1, R. Maselli4, P. Galtieri4, M. Spychalski5, S. Lof8, F. Giovinazzo8, J. van Dam9, T. Kent2, O.R.C. Busch10, B. Groot Koerkamp11, M. Abu Hilal11, C. Bassi12, J. Tseng7, M.G.H. Besselink13

Aims and Methods: The aim of this study was to assess the need for surgery in the management of neoplasia in colitis. This is a multicentre cohort study of all neoplasia endoscopically resected in patients with colitis from 5 tertiary European centres between 2008-2017. The following endoscopic resection techniques were used: endoscopic mucosal resection (EMR) and hybrid endoscopic submucosal dissection (ESD).

Results: 101 neoplasia were resected in 85 patients at 5 European centres. Mean age 61 years (range 28-82). Mean size of lesions 34 mm (range 8-120mm). 40% of the lesions were treated by hybrid ESD. There was no difference in lesion location between EMR and hybrid ESD. Lesions >20mm in size were removed more by hybrid ESD than EMR. More of the lesions removed by hybrid ESD (26) had fibrosis compared to EMR (15). 7 complications occurred in the cohort; 3 cases of bleeding and 4 perforations. Bleeding was controlled endoscopically, 3 perforations were managed endoscopically and 1 required surgery. 7/86 (8.1%) lesions with follow up data had recurrence.

Multi-variate regression analysis concluded;
- EMR leads to higher recurrence rates, irrespective of size, location and fibrosis (p-value of 0.048)
- Hybrid ESD leads to higher complication rates in the colon compared to the rectum (p-value of 0.045)
- Hybrid ESD shows a trend towards better en-bloc resection (p-value 0.063)
- 5 lesions underwent surgery; 3 due to cancer; 1 due to perforation; 1 due to failure of endoscopic resection. Histology: 88 adenomas (low-grade dysplasia), 6 adenomas (high-grade dysplasia), 3 cancers and 4 sessile serrated polyps.

Conclusion: This is the largest reported cohort of endoscopic resections of neoplasia in colitis. We demonstrate that both hybrid ESD and EMR are feasible in colitis with only 5% of patients requiring surgery. Fibrosis is very common in colitis. Recurrence is higher with EMR and complications higher with hybrid ESD. Our data shows that lesions with fibrosis are best treated by hybrid ESD, and those without fibrosis and <20mm in size can be managed by EMR.

Disclosure: Nothing to disclose

From bench to the bedside in pancreatic cancer – Room L7

OP207 INTERNATIONAL VALIDATION OF THE 5TH EDITION AMERICAN JOINT COMMITTEE ON CANCER (AJCC) TNM STAGING SYSTEM IN PATIENTS WITH RESECTED Pancreatic CANCER

S. van Roessl1, G. Kasumova2, J. Verheij3, R. Najarian1, L. Magnino1, M. De Pustena1, G. Malleo1, G. Marchegiani2, R. Salvia3, S.C. Ng4, S. de Geus2, M. Abu Hilal8, C. Bassi12, J. Tseng7, M.G.H. Besselink13

1, A. Alkandari1, M. Bhandari1, A. Przybysz2, M. Bugajski2, K. Kandiah3, S. Subramaniam1, R. Maselli4, P. Galtieri4, M. Spychalski5, S. Lof8, F. Giovinazzo8, J. van Dam9, T. Kent2, O.R.C. Busch10, B. Groot Koerkamp11, M. Abu Hilal11, C. Bassi12, J. Tseng7, M.G.H. Besselink13

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Conclusion: This is the largest reported cohort of endoscopic resections of neoplasia in colitis. We demonstrate that both hybrid ESD and EMR are feasible in colitis with only 5% of patients requiring surgery. Fibrosis is very common in colitis. Recurrence is higher with EMR and complications higher with hybrid ESD. Our data shows that lesions with fibrosis are best treated by hybrid ESD, and those without fibrosis and <20mm in size can be managed by EMR.

Disclosure: Nothing to disclose

From bench to the bedside in pancreatic cancer – Room L7

TUESDAY, OCTOBER 23, 2018 14:00-15:30

From bench to the bedside in pancreatic cancer – Room L7

Abstract No: OP206

Table 1: Endoscopic Resections According to Location, Presence of Fibrosis and Size.

<table>
<thead>
<tr>
<th>LESION LOCATION</th>
<th>Hybrid ESD Colon (26)</th>
<th>Hybrid ESD Rectum (13)</th>
<th>EMR Colon (54)</th>
<th>EMR Rectum (8)</th>
<th>Total (101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Complications</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>En-bloc</td>
<td>14</td>
<td>11</td>
<td>33</td>
<td>5</td>
<td>63</td>
</tr>
<tr>
<td>FIBROSIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hybrid ESD Fibrosis (26)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Hybrid ESD No Fibrosis (13)</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>En-bloc</td>
<td>15</td>
<td>10</td>
<td>8</td>
<td>30</td>
<td>63</td>
</tr>
<tr>
<td>LESION SIZE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hybrid ESD 0-20mm</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Hybrid ESD &gt;20mm</td>
<td>15</td>
<td>10</td>
<td>8</td>
<td>30</td>
<td>63</td>
</tr>
<tr>
<td>Recurrence</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Complications</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>En-bloc</td>
<td>4</td>
<td>21</td>
<td>37</td>
<td>7</td>
<td>63</td>
</tr>
</tbody>
</table>
Thorough analysis of human and mouse pancreatic tissues showed that GKN1 expression is absent in healthy pancreatic cells and on malignant tumors. Furthermore, GKN1 expression is restricted to low-grade premalignant lesions, it is abundant in the cytoplasm of dysplastic epithelium. Proteomic analysis in KC mice confirmed the secretion of GKNs into pancreatic juice but not in the serum. Analysis of pancreatic tissue from GKN1−/− KC mice, at 3 months, showed faster development of PanIN with accelerated tumor development. Investigating the cellular and molecular mechanisms focused on tissue remodeling (epithelial mesenchymal transition, tight junctions), apoptosis, senescence and inflammatory environment. GKN1−/− mice injected with Pan02 cells developed significantly smaller subcutaneous tumors, possibly due to increased CD8+/CD4+ T cells ratio within tumors.

Conclusion: Collectively, our data establishes a role for Gastrokine 1 in PanIN and PDAC development. The accelerated PanIN development in the absence of GKN1 in vivo suggest that gaskrokines expression can delay PanIN formation and molecular tumor markers focused on tissue remodeling (epithelial mesenchymal transition, tight junctions), apoptosis, senescence and inflammatory environment during carcinogenesis could make them potential early biomarker(s) to detect PDAC.

Disclosure: Nothing to disclose.

References:

Disclosure: No conflict of interest.

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Disclosure: Nothing to disclose.
Disclosure: may be among the key mediators.

Conclusion: lung endothelium and not of the liver endothelium. Comparative secretomic the selective promotion of lung endothelial growth by cancer cell subgroups. In human PCa patients and from the genetically engineered KPC ( introduction: Pancreatic cancer is characterised by an unparalleled degree of neural invasion (NI). NI is associated with reduced overall survival, increased local recurrence rate, and with neuropathic pain. One of the major mechanisms leading to NI is the specific affinity of tumor cells to neurons. This affinity can be mimicked by means of 3-dimensional migration assays that include neurons and cancer cells.

Aims and Methods: The aim of the study was to identify genetic alterations that specifically promotes neural invasion in pancreatic cancer by means of in vivo piggyback-transposon mutation. A set of genetically pre-characterized mouse pancreatic cancer cell lines, which were generated by means of piggyback-transposon mediated mutagenesis, was used in three-dimensional migration assays with neurons. The cell lines with the highest affinity to neurons were analyzed for the sites of transposon integration in a pre-existing sequencing data base. The identified loci were functionally analyzed in the cells by means of Cre/ Cso9 gene editing.

Results: In the genetically pre-characterized group of 22 mouse pancreatic cancer cell lines, 3 cell lines were identified to exhibit a high neuroaffinity. In the analysis of the transposon insertion sites, we found a specific pleckstrin domain in the gene. In accordance, Crisp/Cas9-mediated gene editing resulted in increased migration of pancreatic cancer cell to Neurons.

Conclusion: The in vivo mutation screen allows identification of neural invasion-promoting genetic alterations in pancreatic cancer. These results suggest that galactoaminyltransferases may promote neural invasion in pancreatic cancer.

Disclosure: This abstract was previously presented at the BVC 2017 congress in Germany.

TUESDAY, OCTOBER 23, 2018 14:00–15:30
Barrett’s oesophagus: Pathogenesis and biomarkers – Room L8

Barrett’s metaplasia originates from HOXA13-positive cells in the gastro-oesophageal junction
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5Jagiellonian University Medical College, Department of Physiology, Cracow, Poland
6Queens Health & Science University, Portland, United States
7Technische Universität Dresden, DFG-Center for Regenerative Therapies, Dresden, Germany
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Introduction: Barrett’s oesophagus (BE) is an intestinal metaplasia characterized by crypt-structured columnar epithelium with distal gastrointestinal (GI)-tract characteristics. This hemochronic transformation predisposes to adenocarcinoma of the esophagus. HOX genes are known mediators of hemochronic transformations. Certain HOX genes of anterior to posterior progression in organogenesis and tissue homeostasis. The 3 to 5’ sequence of HOX genes corresponds to the sequence in which they act along the anterior toward posterior axes of the body. This property termed collinearity and links clustering of HOX genes with anterior to posterior progression in organogenesis and tissue homeostasis. Recent evidence from human and mouse studies has shown BE might originate from the glands at the gastro-oesophageal junction (see refs). It can be shown that these glands contain elements associated with positional misspecifica-

Disclosure: This abstract was previously presented at the VBC 2017 congress in Germany.

OP211 SITE-SPECIFIC ANGIogenesis MAY PROMOTE ISOLATED PULMONARY METASTASIS IN PANCREATIC CANCER T. Krauss, S. Teller, H. Friess, G.O. Ceyhan, E.I Demir Klinikum rechts der Isar, Technische Universität München, Department of Surgery, München, Germany

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Introduction: Pancreatic cancer (PCa) has the worst prognosis among all gastro-intestinal cancers. Recent studies identified a remarkably better prognosis of PCa patients with isolated pulmonary metastasis. The reason behind this peculiarly better prognosis of this interesting patient subgroup is yet unknown.

Aims and Methods: In the present study, we hypothesized that some subtypes of PCa might preferentially foster the growth of endothelial cells in the lung, and lead to the growth of lung and thereby lead to isolated pulmonary metastases. For this purpose, we made use of endothelial cells specifically isolated from the human lung and liver, and treated these with several types of human pancreatic cancer cell lines. The proliferation and the tube formation rate by each PCa cell line was shown in cancer cells within lung metastases and relatively higher levels of Angpt2. In vitro, certain types of PCa cell lines preferentially induced the growth of lung endothelium and not of the liver endothelium. Comparative screctomic analysis of lung and liver endothelium growth-promoting molecules showed selectively increased secretion of plasminogen and transferrin from cancer cells that specifically promote lung endothelial growth.

Conclusion: Occurrence of isolated pulmonary metastasis in PCa may be due to the selective promotion of lung endothelial growth by cancer cell subgroups. In this pulmonary pro-angiogenic capacity of PCa cells, plasminogen and transferrin may be among the key mediators.

Disclosure: Nothing to disclose.

Disclosure: may be among the key mediators.
Conclusion: HOXA13 expression is epithelial and is not upregulated in squamous epithelium in vitro and in vivo. The HOXA13 promoter is regulated bipartially by the Wellman and the non-Wnt mediated pathway. These findings point to a novel role of Notch signaling in NFkB dependent stem cell expansion during esophageal carcinogenesis and introduce Notch activation as a novel biomarker for BE to EAC progression.

Disclosure: Nothing to disclose.

References

Disclosure: Nothing to disclose.

References
1. F. Wein1, B. Kunze1, H.-Y. Fang1, A. Anand1, T. Baumeister1, J. Ingenm1, T.C. Wang2, J.A. Abrams3, M. Quante4
1Technical University of Munich, Department of Internal Medicine, Munich, Germany
2Columbia University Medical Center, Irvine Cancer Research Center, New York, United States
3Columbia University Medical Center, New York, Department of Medicine, Division of Digestive and Liver Diseases, New York, United States

Contact E-Mail Address: frederik.wein@tum.de

Introduction: Barrett’s esophagus (BE) is a premalignant, inflammation-dependent condition of the esophagus and a known precursor of esophageal adenocarcinoma (EAC). The incidence of EAC has increased at a rate of 4 to 10% annually in parts of the Western World. Though endoscopic surveillance is utilized to detect and treat dysplasia and early malignancy, it may not detect early cancers in nearly half of patients. Furthermore, endoscopic therapy shows decreased ability in only up to 75% of cases and treatment specific risks have to be factored in. Novel biomarkers would ideally help in identifying patients with BE at increased risk of disease progression, prompting extended surveillance programs. A number of predictive markers have been reported in the literature including DNA content abnormalities. Genomic instability is a known driver for carcinogenesis and can occur with impaired telomere function. However, the functional role of short telomeres has not been evaluated during esophageal carcinogenesis.

Aims and Methods: Here we utilize the L2-IL-1β1/2 transgenic mouse model of BE that recapitulates the human histopathologic progression to EAC while inducing chronic inflammation in the esophagus. To study the role of telomere dysfunction and shortening of telomeres we crossed a telomerase k.o. mouse model (mTerc-/-) into our IL-1β1/2 model and analyzed progression to dysplasia as well as its implication for cellular differentiation in different backcrossed IL-1β1/2 generations. Telomere length was measured quantitatively with in situ Hybridization (FISH) on a per cell basis. Results were compared to a human cohort of which full-length resected surgical esophagi were histopathologically scored and epithelial telomere length was measured at different stages of disease for each individual (27 samples of 9 individuals).

Results: In the mouse model, significant dysfunction of telomeres was observed in the second generation (H1-mTerc-/- G2). Therefore, we compared IL-1β1/2 mTerc-/- G2 mice (n=16) with IL-1β1/2 mice (n=16). IL-1β1/2 mTerc-/- G2 mice exhibited significantly shorter telomeres (p=0.02) and a significantly higher grade of dysplasia (p=0.02) than their age-matched IL-1β1/2 counterparts. These length assessment of human biopsies of EAC precursor lesions confirmed prior findings that BE- and LGD- epithelial cells possess significantly shorter telomeres than epithelial control cells of the gastric cardia with reduced ratios in BE and LGD. Furthermore, telomeres (p<0.01) and LGD-Cardia (p<0.01) samples, suggesting a progressive shortening with accelerated malignant transformation. Importantly, discrimination of epithelial cells into columnar cells and goblet cells displayed significantly shorter telomeres in columnar lined cells than in goblet cells of human BE tissue (p<0.01) and LGD tissue (p=0.01).

Conclusion: Shortening of telomeres accelerated dysplasia in our mouse model of BE. This proves for the first time the functional importance of dysfunctional telomeres as a potential driver in early stages of esophageal carcinogenesis. In addition epithelial telomere shortness was correlated with disease progression and cellular de-differentiation in murine and human EAC precursor lesions. Thus telomere length qualifies as a potential biomarker in EAC precursor lesions and should therefore be further tested in large human cohorts to prove its validity. Remarkably the result that goblet cells possess longer telomeres than columnar cells within the same histologically defined samples complements earlier findings that higher goblet-to-columnar-cell ratios are more likely to be found in stages of metaplasia than dysplasia.

Disclosure: Nothing to disclose.

References
to differentiating patients with a normal oesophagus from those with DBE and OAC. We demonstrate that raised MCM5 expression in exfoliated cells of patients in the NDBE group demonstrated very high expression compared to the DBE/OAC group, although 2 patients in the NDBE group showed a trend towards higher mean MCM5 expression in patients with DBE/OAC (2.72 pg/ml IQR 5.4–9.9) of 628 patients included (69% male, median age 60 years, 76% length of BE ≥ 3 cm); 48 developed HGD or EAC. If a patient would have only 2 FU moments, 1 with normal (0) expression of the biomarker, 1 with aberrant (1), the hazard ratio (HR) of neoplastic progression was 1.2 for LGD (p = 0.06). There was no significant difference between patients with a macroscopically normal oesophagus (NE), non-dysplastic Barrett’s oesophagus (NDBE), dysplastic Barrett’s oesophagus (DBE) and OAC.

**Aims and Methods:** Patients were recruited from a UK referral centre between Aug 2017 and Apr 2018. All patients with NDBE, DBE or OAC had endoscopic and histological confirmation of the diagnosis. High-grade dysplasia was considered DBE. Patients previously treated with radiofrequency ablation, chemotherapy or chemo-radiotherapy, with systemic inflammatory disease, BE low-grade dysplasia, BE high-grade dysplasia or other malignancy were excluded. The oesophagus was carefully intubated to stratify symptomatic patients presenting to clinicians. We assess whether MCM5 expression, quantified using a proprietary assay, can be used to discriminate between patients undergoing endoscopy with a macroscopically normal oesophagus (NE), non-dysplastic Barrett’s oesophagus (NDBE), dysplastic Barrett’s oesophagus (DBE) and OAC.

**Results:** 61 patients were recruited (15 NE, 14 NDBE, 18 HGD and 14 OAC). We demonstrate a stepwise increase in MCM5 expression for patients with acid reflux, NDBE, DBE and BE associated OAC. The median expression for each group was 47 pg/ml (IQR 32.8 [26.92–59.77]) for NE, 116 pg/ml (IQR 411.3 [17.23–428.54]) for NDBE, 229 pg/ml (IQR 1070.4 [29.59–1099.96]) for DBE and 279 pg/ml (IQR 1462.7 [10.09–1500]) for OAC. There was a significant difference in MCM5 expression between patients with a macroscopically normal oesophagus and those with DBE or adenocarcinoma (p < 0.001). We also observed a trend towards higher mean MCM5 expression in patients with NDBE compared to those with a normal oesophagus (p = 0.06). There was no significant difference between patients with NDBE and DBE/OAC, although 2 patients in the NDBE group demonstrated very high expression compared to the rest of the group.

**Conclusion:** We demonstrate that raised MCM5 expression in exfoliated cells obtained from aspirating gastric fluid at upper endoscopy is a feasible approach to differentiating patients with a normal oesophagus from those with DBE and OAC. Further work should focus on appropriately powered multi-centre trials to assess for significant differences in MCM5 expression in patients with AR (NE), NDBE, DBE and BE associated OAC.

**Disclosure:** Materials and assays were performed by Arquer.
A new class of acid-suppressing agents, and takes only 3 hours to inhibit gastric acid secretion. Therefore, VPZ should be first administered shortly after ESD for pre-ESD bleeding.

Results:


Conclusion: Vonoprazan should be first administered shortly after ESD for preventing post-ESD bleeding.

Disclosure: Nothing to disclose

References


Disclosure: Nothing to disclose
administration of anticoagulants after April 2013. The clinical outcomes of ESD were retrospectively compared between the non-continuous and continuous groups.

Results: The study population included 60 men and 16 women (median age, 77.5 years). Varifarin was taken by all 49 patients in the non-continuous group and 16 patients in the continuous group. The remaining 11 patients received DOACs (dabigatran, n = 3; apixaban, n = 4; and rivaroxaban, n = 4). The clinical characteristics (including age, gender, tumor location, macroscopic appearance, tumor size, presence of ulcer scar and tumor depth) did not differ between the two groups to a statistically significant extent. En-bloc resection was achieved in all patients with a complete resection rate of 96% in the non-continuous group (47 of 49 patients) and 100% in the continuous group (27 of 27 patients). The median procedure time was 78 minutes in the non-continuous group and 70 minutes in the continuous group (p = 0.09). Postoperative bleeding occurred in 4 patients in the non-continuous group (8.2%) and 2 patients in the continuous group (7.4%); the difference was not statistically significant (p = 1.00). None of the patients developed perforation during the study period. One patient in the non-continuous group suffered from cerebrovascular disease.

Conclusion: The continuous administration of anticoagulants did not significantly increase the incidence of adverse events in our cases. Considering the risk of cerebrovascular disease, the continuous administration of anticoagulants might be feasible and safe in gastric ESD.

Disclosure: Nothing to disclose.

OP223. EFFICACY OF ORAL MIXTURE OF HYDROCORTISONE SODIUM SUCCINATE AND ALUMINUM PHOSPHATE GEL FOR THE PREVENTION OF STRICTION AFTER ≥2/3 CIRCUMFERENTIAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR ESOPHAGEAL CANCER

Y. Huang, X. Yan, D. Nie
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Introduction: ESD has been performed on many patients with early esophageal cancer. However, postoperative stricture after ≥2/3 circumferential ESD is the most important issues for quality of life in patients which is drastically decreased and repeat, periodic endoscopic balloon dilation (ESD) is usually required. We explored an innovative strategy of oral mixture of hydrocortisone sodium succinate and aluminum phosphate gel for prevention of the stricture and evaluate the efficacy of this mixture in single center of Beijing, China.

Aims and Methods: 27 patients who underwent more than 2/3-circular ESD between September 2014 and December 2017 were enrolled. They were randomized into control and study groups. 13 patients received endoscopic intraluminal steroid injection accompanied with systemic steroid treatment (IT + ST, group control); 14 patients received oral mixture of hydrocortisone sodium succinate and aluminum phosphate gel (IT + ST group. Start with 0.5g oral mixture hydrocortisone sodium succinate and aluminum phosphate gel 20g qid, qid 2 weeks and continued with a gradually tapering dose of OHA on the second day post-ESD. ESD was performed when patients experienced persistent dysphagia. If the patient had no complaint of dysphagia, esophageal gastroduodenoscopy (EGDY) was performed 8 weeks after ESD to evaluate any possible stricture. The primary end point in this study was the stricture rate after ESD. The secondary end point was the number of EBD sessions required to resolve the stricture. A stricture was defined as a difficulty in swallowing solids or an inability to pass an EGD (9.2mm diameter endoscope).

Results: No significant differences were seen among the 2 groups in terms of demographic parameters including age, sex, tumor location, resection size. The stricture rates of IT + ST, OHA group after ESD were 53.8% (7 of 13 patients), 71.4% (1 of 14 patients), respectively (95% confidence interval, p = 0.013). OHA group needed less EBD sessions than IT + ST group (median 0, interquartile range 0 to 0 vs. median 1, interquartile range 0 to 5, p = 0.019).

Conclusion: Oral mixture of hydrocortisone sodium succinate and aluminum phosphate gel showed promising results for the prevention of stricture after ESD for early esophageal cancer.

Disclosure: Nothing to disclose.

OP224. A RANDOMIZED CONTROLLED ANIMAL STUDY TO EVALUATE THE TECHNICAL FEASIBILITY OF CHEMICALLY INHIBITED SUBMUCOSAL DISSECTION TECHNIQUE WITH THE CONTINUOUS APPLICATION OF MESNA

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Introduction: Mesna is a mucolytic agent, which chemically dissolves disulfide ESD procedure to create a submucosal fluid bleb, which dramatically reduces the need for electrosurgical dissection. However, the chemical effect of mesna is inactivated within a short period of time and the substance with a low osmotic pressure quickly dissipates into surrounding tissues. A novel infusion pump system was recently developed to enable mesna to be continuously applied onto tissues while dissection the submucosal tissue plane.

Aims and Methods: To explore the procedural feasibility of ESD with the chemical blunt dissection technique (COLD ESD) using the newly developed mesna infusion pump system (CADISS Remote System, Auxin surgery) in vivo porcine models evaluating the effect of mesna as a chemical tissue dissector comparing with saline. In this study, 5 porcine models were used under general anesthesia. We created 2 tentacles sized about 20mm in the body and the antrum of the stomach respectively. A total of 4 lesions were created for each pig. Then, each lesion was randomly assigned into the mesna group or the saline group as a control. After the circumscription around the lesion was made, mesna or saline was injected into the submucosal layer underneath the isolated lesion with the CADISS Remote System. The information of the injectate used was blinded to the operator. First, the blunt cleavage of the submucosa was attempted while continuously applying one of the injectates using a Hook Knife J (Olympus medical systems), connected to the pump. However, the use of electrosurgical dissection was allowed when the operator felt excessive tissue resistance ad lib. We counted the number of electrosurgical incisions used with the VIO Doku software in real-time (ERBE). All endoscopic procedures were performed by experienced endoscopists. The levels of procedural difficulty were evaluated with a 5-point analogue scale. The burned area ratio (burned area/specimen area) of the excised specimen was evaluated with a picture of the specimen using Image J software (NIH).

Results: En bloc resection rate was 100% in both groups. The total procedure time (mesna group 18.1 ± 7.9 min vs. saline group 20.9 ± 12.5 min, p = 0.54), the submucosal dissection time (mesna group 11.1 ± 8.0 vs saline group 12.5 ± 9.4
TUESDAY, OCTOBER 23, 2018 15:45-17:15
Champion session in surgery and endoscopy – Room E1

OP225 LAPAROSCOPIC VERSUS OPEN PANCREATODUODENECTOMY (LEOPARD-2): A MULTICENTER, PATIENT-BLINDED, RANDOMIZED CONTROLLED TRIAL
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Introduction: Laparoscopic pancreatoduodenectomy (LPD) is gaining popularity because of potential advantages including less operative blood loss, less delayed gastric emptying, and shorter hospital stay but concerns exist regarding increased pancreatic fistula rates and, in low-volume centers, increased postoperative mortality. Multicenter randomized trials investigating this subject are lacking. In the Netherlands, LPD was introduced according to the IDEAL framework for surgical innovation including a training program (LAELAPS-2) with a 3.5% 90-day mortality. Multicenter randomized trials investigating this subject are lacking. In the Netherlands, LPD was introduced according to the IDEAL framework for surgical innovation including a training program (LAELAPS-2) with a 3.5% 90-day mortality. Multicenter randomized trials investigating this subject are lacking. In the Netherlands, LPD was introduced according to the IDEAL framework for surgical innovation including a training program (LAELAPS-2) with a 3.5% 90-day mortality. Multicenter randomized trials investigating this subject are lacking. In the Netherlands, LPD was introduced according to the IDEAL framework for surgical innovation including a training program (LAELAPS-2) with a 3.5% 90-day mortality. According to the IDEAL framework, we hereafter initiated an RCT to assess whether LPD could reduce time to functional recovery.

Aims and Methods: A multicenter randomized controlled, patient-blinded, trial comparing LPD with OPD was performed in 4 centers that each perform ≥20 pancreatoduodenectomies annually (median 37 (range 23-77)), completed the LPD training program, and had performed at least 20 LPDs during the 18 months prior to the start of the trial (range 23-34). Adult patients with an indication for pancreatectomy because of a neoplasm without signs of vascular involvement were included. Primary outcome was time (days) to functional recovery.

Results: The data safety monitoring board (DSMB) recommended early termination were included. Primary outcome was time (days) to functional recovery. The results of this study indicated that the continuous topical application of mesna would minimize the thermal damage on the tissues, which may provide optimal tissue sampling for accurate histological evaluation of specimens and reduce bystander tissue burns associated with electrosurgical incisions.

Disclosure: Nothing to disclose.
**OP227** WIRE-GUIDED BILIARY CANNULATION IN ENDOSCOPIC RETROGRADE CHolangiopancreatography (ERCP): A PROSPECTIVE RANDOMIZED COMPARISON BETWEEN MICRO AND CONVENTIONAL GUIDEWIRE

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**Introduction:** Wire-guided biliary cannulation is reported to be an appropriate first attempt treatment technique, since it is associated with a high success rate and low risk of post-ERCP pancreatitis (PEP). However, the conventional guidewire (CGW) (0.025 inch) is sometimes too rigid to pass through the long curved narrow segment, resulting in increased biliary cannulation time and even an unsuccessful biliary cannulation. At UEWG 2017, we reported that a micro guidewire (GTW; GT wire; 0.016 inch, 300 cm, TERUMO, Japan) designed for selective angiography was helpful in such cases. Rapid biliary cannulation is desirable because a prolonged procedure may induce PEP. The use of GTW-assisted cannulation as the first-time cannulation technique for ERCP could reduce biliary cannulation time.

**Aims and Methods:** We aimed to evaluate whether biliary cannulation was achieved in lesser time using GTW than when using CGW in ERCP. In total, 118 consecutive ERCP-naive patients were randomly assigned to undergo biliary cannulation with GTW (GTW group) or CGW (CGW group). We measured the cannulation time (from the time the cannula advanced out of the endoscope channel to the time successful deep cannulation was confirmed) and the serum amylase level on the following day. The endoscopist performed ERCP with the designated guidewire for less than 10 min and was permitted to switch to the other guidewire to achieve cannulation after 10 min from initiation of the procedure. The secondary outcome was the overall success rate of biliary cannulation as well as the incidence of PEP and asymptomatic hyperamylasemia in both groups. Additionally, among patients in whom biliary cannulation was successful, we compared the frequency of switching to the other guidewire and the biliary cannulation success rate between both groups.

**Results:** The biliary cannulation success rate within the first 10 min was significantly higher in the GTW group than in the CGW group (39/59 patients, 66% and 29/59 patients, 49%, respectively; p = 0.047 by Fisher’s exact test). The overall biliary cannulation success rate (57/59 patients, 97% and 57/59 patients, 97%) and incidence of PEP (1/59 patients, 1.7% and 1/59 patients, 1.7%) was equal in both groups. The overall asymptomatic hyperamylasemia was 13.6% (8/59 patients) in the GTW group and 15.3% (9/59 patients) in the CGW group. Among the 114 patients in whom biliary cannulation was successfully achieved, 32% (18/57 patients) in the CGW group were switched to GTW. No patients in the GTW group were switched to CGW after 10 min from initiation of the procedure. The biliary cannulation success rate in the GTW group was significantly higher than that in the CGW group (p = 0.036, by the Kaplan-Meier method and log rank test).

**Conclusion:** The use of GTW-assisted cannulation as the first-time cannulation technique for ERCP significantly improved the biliary cannulation success rate and reduced biliary cannulation time.

**Disclosure:** Nothing to disclose

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**OP229** REAL-TIME ARTIFICIAL INTELLIGENCE “FULL COLONOSCOPY WORKFLOW” FOR AUTOMATIC DETECTION FOLLOWED BY OPTICAL BIOPSY OF COLORECTAL POLYS

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**Introduction:** Colon polyp detection and optical biopsy are key performance indicators in colonoscopy. Artificial Intelligence (AI) has the potential to greatly improve both. However, practical real-time applications with standard scopes are lacking.

**Aims and Methods:** We have published on real-time optical biopsy of diminutive colon polyps using AI, surpassing the 90% negative predictive value (NPV) for adenomas, as per PIVI guidelines. We sought to use latest AI techniques to further improve our optical biopsy performance. In relation to polyp detection, most AI detection tools are trained using still images or videos with obvious polyps. In contrast, we planned our tool around difficult sequences from clinical screening videos that start when the polyp first becomes visible. Finally, an AI model capable of detecting NBI light was the cornerstone that allowed us to propose a “full clinical workflow” for colon polyp detection immediately followed by optical biopsy. Our workflow was optimized to allow for real-time clinical use, a first in this field.

The workflow captures the video feed from a tower and consists of 3 distinct AI models: a NBI light detector, a polyp detector, and an optical biopsy. The NBI light detector runs continuously and triggers either the detection mode (white light) or the optical biopsy mode (NBI). This allows a seamless interface without the need for a switching signal from either the tower or operator.

**Results:** The NBI light model was tested on 21,804 unseen frames and achieved a near-perfect accuracy of 99.94%.

The polyp detection model was tested on the polyp approach sequence part of 30 previously unseen colonoscopy videos (>20min each). The model detected polyps with a sensitivity of 79.6% while triggering on 13.7% of frames without polyps. Notably, polyps are detected, on average, 403 milliseconds after their first appearance.

The optical biopsy was tested on videos of 125 previously unseen polyps and achieved a sensitivity of 95.95%, specificity of 91.66%, and NPV of 93.6%. Even if the model can abstain when unsure, it committed to a prediction for 97.6% of polyps, an absolute increase of 12.8% over our previous work.

Finally, results are displayed in real-time and the user interface is updated 30 times per second.

**Conclusion:** We propose the first real-time AI full colonoscopy workflow for automatic detection followed by optical biopsy of colorectal polyps. It consists of three separate AI models allowing for real-time detection of colon polyps, automatic recognition of the switch from white light to NBI, followed by immediate optical biopsy of detected polyps. Detection shows very promising results, especially on difficult approach sequences, and our AI optical biopsy has been even further improved. A clinical trial is planned for the near future.

**Disclosure:** M.F. Byrne—founder “asgi”, shareholder Satis Operations Inc. N Chapados, F Chandelier—shareholders Imagia Cybernetics Inc.

Reference
OP230  
OPTICAL DIAGNOSIS OF DIMINUTIVE POLYS IN THE DUTC H CRC SCREENING PROGRAM: ARE WE READY TO START?

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Introduction: Implementation of the optical diagnosis of diminutive polyps increases the efficacy and reduces the economic burden of a colorectal cancer (CRC) screening program. To adopt such strategy in clinical practice, the ASGE PIVI thresholds should be met: >90% negative predictive value (NPV) for diagnosis of adenomatous histology and >90% agreement between optical diagnosis and histological diagnosis in determining the post-polypectomy surveillance intervals. We evaluated these performance parameters in the Dutch CRC screening program.

Aims and Methods: We measured the agreement between optical diagnosis and histological diagnosis in determining the post-polypectomy surveillance intervals. We evaluated the diagnostic performance of optical diagnosis compared with histological diagnosis in 2390 index colonoscopy procedures in 2015/2016. Agreement on surveillance intervals was calculated using kappa statistics. Diagnostic performance of optical diagnosis and histological diagnosis was compared using the McNemar test and the Methodological Index for Research Quality (MIRQ) tool was used to rate studies.

Results: Overall agreement on surveillance intervals was 0.666 (95% CI 0.634-0.698). Baseline characteristics of patients included in this study were: median age: 65 years (50-75), 54% male, 33% patients had a personal history of colorectal cancer, 5% smokers, and 42% were on aspirin therapy. The diagnostic performance of optical diagnosis compared with histological diagnosis is shown in Table 1.

Conclusion: The optical diagnosis of diminutive polyps is feasible in routine clinical practice. However, the diagnostic performance and decision-making algorithm on surveillance intervals need improvement. Further studies are indicated to improve the diagnostic performance and to optimize the efficacy of our nationwide CRC screening program.

Disclosure: Roel M.M. Bogie and S. Sanduleanu-Dascălescu received an unrestricted research grant from Gentex Europe.

Reference

A89

OP231  
HIGH-DEFINITION CHROMOENDOSCOPY (HDCE) USING 0.2% IC VS. 0.2% INDIGO CARMIN FOR DETERMINING DYSPLASIA IN PATIENTS UNDERGOING IB D COLITIS SURVEILLANCE. A RANDOMIZED CONTROLLED TRIAL – INTERIM ANALYSIS

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Introduction: Patients with ulcerative colitis (UC) and Crohn’s colitis are known to have an increased risk of colorectal cancer compared with that of the background population. The recent National Institute for Health and Care Excellence (NICE) guidelines for colorectal cancer screening in patients with inflammatory bowel disease (IBD) recommend colonoscopic surveillance of patients with IBD, based on its definition of high-risk groups, without defining specific colorectal cancer surveillance intervals or strategies. We present the interim analysis of a randomized clinical trial investigating the efficacy of different methods of surveillance in patients with IBD.

Aims and Methods: A parallel group randomized controlled trial (ClinicalTrials.gov id: NCT03250708) in which patients undergoing surveillance for IBD colitis were randomized to receive: 0.2% IC using a spray catheter or HDCE using 0.3% IC via a foot pump. HDCE was performed using the Olympus CF-HQ290i and processors (Elite CV 290). A total of 221 patients were randomized to 0.2% IC and 0.3% IC arms in the study.

Results: There were 75 patients in each arm (total n = 150). Baseline characteristics were similar between the two arms except for sex distribution which was significantly different: 58% male in the 0.2% IC arm and 42% male in the 0.3% IC arm (p = 0.012). Dysplasia was reported in 5 (3.3%) cases in the 0.2% IC arm and 2 (1.3%) in the 0.3% IC arm (p = 0.083). Dysplasia on random biopsies, only, was found in 3 (2%) of the cohort. Histopathologists confirmed presence of dysplasia. Time of withdrawal and ampoules of IC were also recorded.

Conclusion: There is no significant difference in dysplasia detection between 0.2% and 0.3% IC, which suggests that a reduction in cost of surveillance is possible. A definitive trial is needed to confirm these preliminary results.

Disclosure: Nothing to disclose

OP232  
SIMPLE ENDOCOSCOPIC TREATMENT OF ADENOMA RECURRENT AFTER WIDE FIELD ENDOSCOPIC MUCOSAL RESECTION IS EFFECTIVE: A PROSPECTIVE STUDY OF 1558 LESIONS WITH LONG-TERM FOLLOW-UP

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Introduction: Adenoma recurrence after wide field endoscopic mucosal resection (EMR) of laterally spreading colorectal lesions ≥ 20mm (LSLs) is a major limitation. Data on the optimal methods and outcomes of endoscopic treatment of recurrence (ETOR) is absent and no evidence based standard exists. We examined the techniques and success of ETOR over time in a large prospective cohort.

Aims and Methods: Over 100 months to January 2017 data on all recurrences after consecutive EMR procedures for LSLs at the lead centre of the Australian Colonic Endoscopic Resection Study (ACE) were recorded. Recurrence at the EMR site was deemed a 1st recurrence. Further hand-drawn high definition endoscopic imaging as previously described. ETOR comprised coagulation snare resection 2 recurrence (ERBE Effect 2, 30W), cold avulsion forceps with adjuvant snare tip soft coagulation [CAST] (ERBE Effect 4, 80W) or a combination of the two. The primary outcome were complete adenoma clearance using ETOR at first surveillance (desired interval 4-6 months) and absence of recurrence at subsequent surveillance procedures.

Results: 1558 patients with 1558 LSLs were included. 150 LSLs (9.6%) had recurrence at first surveillance colonoscopy. The mean age of patients with recurrence was 68 years and 55% were male. Recurrent LSLs were median 50mm in size (IQR 35-60mm) and located distal to the hepatic flexure in 52.7%. They were commonly Paris 0-IIa+Is morphology (46.7%) and displayed tubulovillous architecture (75.3%), with high grade dysplasia in 23.4%. 3 (2.7%) were resected en-bloc. Recurrence at the EMR scar was ≤ 2mm in size (64%), uni-focal (75%) and within the scar (55%) or at the edge (45%). The commonest modality used to resect recurrence was hot snare with adjuvant snare tip soft coagulation (CAST) used in 30% and was also used in combination with hot snare (9%). CAST was more commonly used in the second temporal half (62.5%) than the first half (10.6%, p < 0.001) of the cohort. Prior injection was performed in a minority (16%). In 124 cases (86.7%) cases where tissue was retrieved, there was histologic confirmation of recurrence. ETOR achieved complete clearance of recurrent adenoma in 94.7% of cases at first surveillance colonoscopy with 5 (5.3%) referred for surgery primarily due to an

[Table 1.]

Disclosure: Roel M.M. Bogie and S. Sanduleanu-Dascălescu received an unrestricted research grant from Gentex Europe.

Reference
A90

United European Gastroenterology Journal 6(8S)

inability to resect recurrence. For LSLs that underwent further surveillance, 89%
(1 further surveillance), 86.5% (2 further surveillances) and 89.5% (3 further
surveillances) respectively showed no evidence of recurrence.

First Half
of Cohort

Second Half Whole
of Cohort
Cohort

Number of recurrences
69/785 (8.8) 81/773 (10.5)
Size of recurrence (%) 52mm 9 (13.0)
17 (21.0)
2.1–5mm
34 (49.3)
36 (44.4)
5.1–10mm
22 (31.9)
18 (22.2)
410mm
4 (5.8)
10 (12.3)
Recurrence treatment
N ¼ 146
Use of CAST (%)
7 (10.6)
50 (62.5)
Histologic correlate of
62 (95.4)
62 (79.5)
recurrence/n ¼ 143 (%)
Endoscopic cure at
64 (92.8)
78 (96.3)
SC1 (%) n ¼ 150
1 negative FU after
55 (91.7)
42 (85.7)
treatment/109 (%)
2 negative FU after
26 (92.9)
6 (66.7)
treatment /37 (%)

P

150/1558 (9.6) 0.259
26 (17.3)
0.226
70 (46.7)
40 (26.7)
14 (9.3)
57 (39.0)
124 (86.7)

50.001
0.006

142 (94.7)

0.471

97 (89.0)

0.323

32 (86.5)

0.081

[Table 1: Features of LSLs that demonstrated recurrence at first surveillance
colonoscopy and their outcomes, FU – follow up, SC1 – first surveillance]
Conclusion: Adenoma recurrence after EMR of LSLs is commonly diminutive
and can be effectively treated using simple endoscopic techniques with rates of
long-term remission approaching 90%. Based on this data, more technically
complex, morbid and resource intensive endoscopic or surgical techniques are
unnecessary to resect LSL recurrence after EMR.
Disclosure: Nothing to disclose

Continued

Number and % of bleeds treated with Purastat and heat
Mean length of time taken for
haemostasis per bleed
(seconds)
Total procedure time (minutes)

Purastat
group
(n ¼ 46)

Control
group
(n ¼ 45)

Significance

121 (54.8%)

N/A

N/A

70.0

77.6

p ¼ 0.67

74.2

80.7

p ¼ 0.56

[Intraprocedural bleeding during ESD]
Both groups were well matched in terms of baseline characteristics (mean lesion
size 33.7mm in the PurastatÕ group and 36.6mm in the control group, age 68.6 vs
71.5 years, adenocarcinoma and high-grade dysplasia 60.9% vs 53.3%). There
were 221 bleeds requiring haemostasis in the PurastatÕ group compared to 262 in
the control group with no significant difference in the mean number of bleeds per
patient. There was a significant reduction in the proportion of bleeds treated with
heat therapy in the patients receiving PurastatÕ compared to controls (110/221 or
49.8% vs 261/262 or 99.6%, p 5 0.001). PurastatÕ was used in 54.8% of bleeds in
the interventional group and haemostasis was achieved with this device as a
single agent in 91.7% (111/121) of cases when used.
All bleeds were managed endoscopically with no blood transfusion or hospital
admission for management required. There were no complications related to the
application of PurastatÕ in this study and it did not interfere with subsequent use
of diathermy for haemostasis if required.
Conclusion: This is the first randomised controlled trial of this haemostatic device
and our results show that PurastatÕ successfully reduced the use of intraprocedural heat therapy for haemostasis in ESD by almost 50%. The device was easy
to use and did not prolong the time taken for haemostasis or the total procedure
time. This study supports its use as a safe and effective haemostat for bleeding
during endoscopic resection.
Disclosure: Nothing to disclose

References

TUESDAY, OCTOBER 23, 2018


OP233 BLEEDING DURING ENDOSCOPIC SUBMUCOSAL
DISSECTION: A RANDOMISED CONTROLLED TRIAL OF A NOVEL
HAEMOSTATIC AGENT
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Introduction: Endoscopic submucosal dissection (ESD) is associated with intraprocedural bleeding which is usually treated with heat applied to the visible
bleeding vessel. Prolonged and repeated applications of heat can increase the
risk of perforation. PurastatÕ is a transparent gel with a novel extracellular
scaffold matrix which forms a mechanical barrier over the bleeding point. It
may be an alternative non diathermic option for intraprocedural bleeding.
Aims and Methods: The aim of this study was to assess the efficacy of PurastatÕ
in reducing the use of intraprocedural heat therapy during ESD.
This was a randomised controlled trial conducted in a tertiary referral centre
between May 2016 to April 2018. Patients undergoing ESD in the oesophagus or
colorectum were randomised in equal proportions to receive PurastatÕ as the
primary haemostat during intraprocedural bleeding (intervention) or heat therapy (control). Patients in the PurastatÕ arm were not excluded from heat therapy
treatment when required to achieve haemostasis. The primary endpoint was the
reduction in the amount of heat therapy required for intraprocedural haemostasis between PurastatÕ and control groups.
Results: 100 patients were recruited to the study. There were 2 withdrawals (ESD
aborted) and 7 had no bleeds. An intention to treat analysis was performed on 91
patients (see table).

Total number of bleeds
Total number of bleeds requiring treatment
Mean number of bleeds per
patient
Number and % of bleeds treated with heat
Number and % of bleeds treated with Purastat alone

15:45–17:15

IBD on fire – Room F1____________________

Purastat
group
(n ¼ 46)

Control
group
(n ¼ 45)

Significance

232
221 (95.3%)

269
262 (97.4%)

p ¼ 0.20

5.04

5.96

p ¼ 0.29

110 (49.8%)

261 (99.6%)

p50.001

111 (50.2%)

N/A

N/A
(continued)

OP234 DEVELOPMENT OF A SUBCUTANEOUS FORMULATION
OF CT-P13 (INFLIXIMAB): MAINTENANCE SUBCUTANEOUS
ADMINISTRATION MAY ELICIT LOWER IMMUNOGENICITY
COMPARED TO INTRAVENOUS TREATMENT
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Introduction: Intravenous (IV) use of CT-P13, an infliximab biosimilar, has
resulted in comparable efficacy, safety and immunogenicity as innovator infliximab in various indications including Crohn’s disease (CD)1 and rheumatoid
arthritis (RA)2. A subcutaneous (SC) formulation of CT-P13 is developed to
provide patients with opportunities for self-injection, thereby enhancing convenience and flexibility in treatment.
Aims and Methods: This work aimed to investigate immunogenicity by post-hoc
analysis of 2 randomised controlled trials comparing pharmacokinetics of CTP13 IV and CT-P13 SC. Patients with active CD (Crohn’s Disease Activity Index
[CDAI] score of 220–450) and RA (presence of 6 or more swollen and tender
joints [of 28 assessed], and serum C-reactive protein [CRP] concentration 40.6
mg/dL) were treated with CT-P13 IV at Weeks 0 and 2. At Week 6, patients were
randomised for continuation with IV or SC administration. The IV cohorts
received CT-P13 IV (5 mg/kg for CD and 3 mg/kg for RA) every 8 weeks and
the SC cohorts were treated with CT-P13 SC (120, 180 and 240 mg for CD and
90, 120, 180 mg for RA) every 2 weeks up to Week 30. Trough serum concentrations (Ctrough) were assessed at Weeks 6, 14 and 22 for IV and Weeks 6, 8, 10, 14,
22, 24, 26 and 28 for SC. Target exposure level was considered as 5 mg/mL for
CD3,4 and 1 mg/mL for RA5,6. Anti-drug antibody (ADA) was assessed before
study drug administration at Weeks 0, 6, 14, 22 and 30 by a drug-sensitive,
enzyme-linked immunosorbent assay (ELISA).
Results: In total, 92 CD (n ¼ 44) and RA (n ¼ 48) patients were randomised at
Week 6 to IV (CD: n ¼ 13, RA: n ¼ 13) or SC (CD: n ¼ 31, RA: n ¼ 35). Among
CD patients, immunomodulators (azathioprine, 6-mercaptopurine or methotrexate) were used at Week 6 by 9 (69.2%) and 15 (48.4%) patients in IV and SC
cohorts, respectively. All RA patients used methotrexate as concomitant medication throughout the study. Efficacy results in each indication (CDAI-70 responder rate for CD and EULAR [CRP] responder rate for RA) were comparable
between the IV and SC cohorts. Systemic safety profiles observed from CT-P13
SC after randomisation were also comparable to those of IV. A sub-therapeutic
Ctrough level below target exposure was detected at least once in 23 (92.0%) and 9
(14.1%) patients in IV and SC cohorts, respectively. ADA were detected at least
once in 16 (64.0%) versus 11 (18.1%) of patients in the IV and SC cohorts
(p 5 0.0001), respectively.


Efficacy

<table>
<thead>
<tr>
<th></th>
<th>IV cohort</th>
<th>SC cohort</th>
<th>( p ) value</th>
<th>( \text{CDAI-70 responder rate at Week 30 in CD patients} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8/10 (80.0%)</td>
<td>24/26 (92.3%)</td>
<td>0.3048</td>
<td>12/13 (92.3%)</td>
</tr>
<tr>
<td></td>
<td>32/32 (100%)</td>
<td>0.2889</td>
<td></td>
<td>15/15 (100%)</td>
</tr>
<tr>
<td>C\textsubscript{ trough} ( &lt; ) target exposure at least once</td>
<td>23 (92.0%)</td>
<td>9 (14.1%)</td>
<td>&lt;0.0001</td>
<td>15/15 (100%)</td>
</tr>
<tr>
<td>C\textsubscript{ trough} ( \geq ) target exposure throughout the study</td>
<td>2 (8.0%)</td>
<td>55 (85.9%)</td>
<td></td>
<td>0.0019</td>
</tr>
</tbody>
</table>

Immunogenicity

<table>
<thead>
<tr>
<th></th>
<th>IV cohort</th>
<th>SC cohort</th>
<th>( p ) value</th>
<th>( \text{Anti-drug antibody positive at least once} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16/25 b (64.0%)</td>
<td>11/61 b (18.1%)</td>
<td>&lt;0.0001</td>
<td>12/13 (92.3%)</td>
</tr>
<tr>
<td></td>
<td>3/28 b (10.7%)</td>
<td>55 (85.9%)</td>
<td></td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>0.0002</td>
<td></td>
<td>0.3048</td>
<td>12/13 (92.3%)</td>
</tr>
<tr>
<td></td>
<td>0.2889</td>
<td></td>
<td>0.2889</td>
<td>12/13 (92.3%)</td>
</tr>
</tbody>
</table>

Note: \( p \) value was derived from Fisher’s exact test. \( \text{aPatients who reported ADA positive at Week 0 or 6 (before randomization) were excluded.} \)

\[\text{Efficacy, Compliance, and immunogenicity among CD and RA patients} \]

Conclusion: After initial loading two doses of infliximab IV, patients subsequently receiving biweekly maintenance treatment with injections of CT-P13 SC achieve more stable steady state therapeutic levels of infliximab and have lower rate of anti-infliximab antibodies compared with patients receiving continued IV treatment. Further work to corroborate these findings is ongoing.

Disclosure: S. Ben-Horin received consultancy and/or advisory board fees from Celltrion, Inc., R. Westhovens grant/research support from Celltrion, Inc., BMS and Pfizer, Pfizer speaker/consultant/or advisory board for Celltrion, Inc., Abbvie Korea, Pfizer, Procter & Gamble, Prometheus, Sandoz, Schering-Plough, Second condo, Grünenthal, Inova, Johnson & Johnson, Kyowa Hakko Kirin Pharma, Boehringer-Ingelheim, Bristol-Myers Squibb, Cellerix, Chemocentryx, Celgene, Centocor, Celltrion, Inc., Danone Austria, Elian, Ferring, Galapagos, Genentech, Grüntenhal, Inova, Janssen, Johnson & Johnson, Kyowa Hakko Kirin Pharma, Lipid Therapeutics, MedImmune, Millenium, Mitsubishi Tanabe Pharma Corporation, MSD, Nestle, Novartis, Otera, Otsuka, PDL, Pharmacosms, Pfizer, Procter & Gamble, Prometheus, Sandoz, Schering-Plough, Second Genome, Setpointmedicinal, Takeda, Theraoks, Tigitens, UCB, Zealand, Zynegena, and ASC. Additional disclosures available on request. B. D. Ye is speaker/consultant/or advisory board for Celltrion, Inc., Abbvie Korea, Ferring Korea, Janssen Korea, Kangstam Biotech, Kuhlmi Pharm, Shire Korea, Takeda Korea, Cornerstones Health, IQVIA, Roberts Clinical Trials Inc. R. Westhovens grant/research support from Celltrion, Inc., IMS and Roche, consultant for Celltrion, Inc., Galapagos/Gilead and Janssen. D. H. Yoo grant/research support from Celltrion, Inc., S. J. Lee, S. Y. Lee and M. R. Kim are employees of Celltrion, Inc. S. Schruber received consultancies and/or lecture fees from Abbvie, Allergan, Biogen, Boehringer, Celltrion, Inc., Janssen, Merck, Pfizer, Takeda, UCB.

References


OP225 NOVEL PROTEIN BIOMARKERS IN SERUM EXTRACELLULAR VESICLES FOR THE DIAGNOSIS OF PRIMARY SCLEROSING CHOLANGITIS (PSC) IN PATIENTS WITH ULCERATIVE COLITIS (UC)

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic cholestatic biliary disease of unknown etiology, which increases the risk of developing cholangiocarcinoma (CCA). Currently, PSC patients frequently (80%) present inflammatory bowel disease, mainly ulcerative colitis (UC) (PSC-UC). Therefore, we propose serum extracellular vesicles (EVs) as a novel biomarker for the differential diagnosis of PSC and UC.

Aims and Methods: The aim of this study was to investigate the usefulness of protein biomarkers in serum EVs for the differential diagnosis of PSC-UC and UC patients, which could help in the early diagnosis of PSC in UC patients.

Methods: Serum EVs were isolated from PSC-UC (n = 21), UC (n = 64), and healthy individuals (n = 62) using ultracentrifugation/filtration methods. EV characterization was performed by transmission electron microscopy (TEM), nanoparticle tracking analysis (NTA) and immunoblot. The proteome of EVs was analyzed by mass spectrometry-based proteomics.

Results: Serum EVs showed round morphology by TEM, similar size (180 nm in diameter by NTA) and markers (CD9, CD63 and CD81 by immunoblotting) consistent with exosomes and small-size microvesicles. The proteomic profiles of serum EVs revealed 45 proteins to be differentially expressed in UC vs. controls, 66 in PSC-UC vs. UC patients with high diagnostic performance(sensitivity and specificity). In particular, proteins such as Aminoepinpeptidase N (AMPN), Polymeric immunoglobulin receptor (PIGR), G-protein coupled receptor family C group 5 member C (GPC5C) and Panethinease (VNN1) were exclusively upregulated (p < 0.05) in PSC-UC patients compared to UC and healthy controls. In contrast, proteins such as Complement factor I (CF1A), Ficolin-2 (FCN2) and Fibronectin (FCN1) were downregulated (p < 0.05) in PSC-UC patients compared to UC and healthy controls.

Conclusion: Proteomic signatures found in serum EVs of PSC-UC and UC patients show potential as non-invasive tools for diagnosis and follow-up.

Disclosure: Nothing to disclose

Reference

Aims and Methods: The 52-week data from the phase 2, randomised, double-blind CELEST study (M13-740; NCT02365649) were analysed for long-term effects of 4 UPA regimens on PROs. All patients who completed the 16-week induction period were re-randomised 1:1:1 into an Extension Phase to receive UPA 3 mg twice daily (BID), 12 mg BID or 24 mg daily (QD) for 36 weeks. The 24 mg QD arm was later stopped and a 6 mg BID arm was initiated to evaluate an intermediate maintenance dose. Patients completed the Inflammatory Bowel Disease Questionnaire (IBDQ), EuroQol (EQ-5D) and Work Productivity and Activity Impairment (WPAI) PROs at baseline, week 16, and week 22. Outcomes at week 52 for patients who received UPA induction therapy and achieved clinical response at week 16 were assessed. Percentages of patients who achieved IBDQ response (defined as minimum clinically important differences (MCID) ≥16-point increase in IBDQ score from baseline) and who achieved IBDQ remission (IBDQ score ≥170) at week 52 were determined using non-responder imputation (NRI). Changes from baseline to week 52 were calculated using observed cases and analysis of covariance for IBDQ score, EQ-5D visual analogue score (VAS) and WPAI.

Results: Among 220 patients enrolled in CELEST, 180 were re-randomized into the Extension Phase. Of these, 153 patients received UPA induction therapy, of whom 94 achieved clinical response at week 16. Among week-16 clinical responders, a greater proportion of patients in the BID dose groups attained IBDQ response (43.8% vs 78.6%) and achieved IBDQ remission (43.8% vs 50.0%) at week 52 than those in the 24mg QD dose group (Table). Dose-related improvements in mean IBDQ scores (range 43-71) and EQ-5D VAS (range 18-36) were observed in the 3mg, 6mg and 12mg BID dose groups at week 52. At week 52, improvements in WPAI including reduction of activity impairment (26-42%) and work impairment (23-38%) were numerically greater for the BID dose groups.

Mean ± SD (n)

<table>
<thead>
<tr>
<th>IBDQ at week 52 (NRI, n (%))</th>
<th>UPA 3mg BID</th>
<th>UPA 6mg BID</th>
<th>UPA 12mg BID</th>
<th>UPA 24mg QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response (IBDQ ≥170)</td>
<td>44 (14.3)</td>
<td>7 (50.0)</td>
<td>12 (41.4)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Response (A≥16)</td>
<td>43 (14.8)</td>
<td>78 (66.0)</td>
<td>6 (31.6)</td>
<td></td>
</tr>
<tr>
<td>Mean change from baseline to week 52 (observed cases)</td>
<td>47 ± 44</td>
<td>47 ± 28</td>
<td>71 ± 47</td>
<td>27 ± 53</td>
</tr>
<tr>
<td>IBDQ</td>
<td>(n = 22)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>18 ± 19</td>
<td>22 ± 17</td>
<td>36 ± 26*</td>
<td>9 ± 18*</td>
</tr>
<tr>
<td>(n = 22)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
</tr>
<tr>
<td>WPAI: % activity impairment</td>
<td>−29 ± 12</td>
<td>−26 ± 22</td>
<td>−42 ± 28</td>
<td>−15 ± 27*</td>
</tr>
<tr>
<td>(n = 22)</td>
<td>(n = 21)</td>
<td>(n = 21)</td>
<td>(n = 21)</td>
<td>(n = 14)</td>
</tr>
<tr>
<td>WPAI: % overall work impairment*</td>
<td>−33 ± 6</td>
<td>−37 ± 32</td>
<td>−38 ± 35</td>
<td>−21 ± 26</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(n = 5)</td>
<td>(n = 15)</td>
<td>(n = 16)</td>
<td></td>
</tr>
</tbody>
</table>

*, ** statistically significant at 0.05 and 0.1 level for each group vs 3 mg BID for mean change from baseline.

*Only employed patients.

<table>
<thead>
<tr>
<th>Table. Patient-Reported Outcomes Results for Week-16 Clinical Responders</th>
</tr>
</thead>
</table>

Conclusion: Treatment with UPA among week-16 clinical responders resulted in improved quality of life based on IBDQ, EQ-5D and work productivity over 52 weeks. Numerically greater improvements were reported in the patients who received 12 mg BID.

Disclosure: Financial support for the study and medical writing services (Rebecca Wylie, Fishawack) was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. L Peyrin-Biroulet, email: s.ghosh@abbvie.com; AbbVie, Research support: AbbVie, Pfizer, Janssen, AbbVie, BMS, Celgene, Healthcare. Research support: AbbVie, Takeda, Chiesi, Pfizer, Janssen, BMS, Celgene, Boehringer-Ingelheim, Lilly, Pfizer, HAC-Pharma, Index Pharmaceuticals, Aegerion, Sandoz, Forward Pharma GmbH, Celgene, Biogen, Lycera, Samsung Bioepis. Lecture fees: Merck, AbbVie, Chiesi, Pfizer, Janssen, Takeda, Ferring, Norgine, Tilotts, Vifor, Therakos, Pharmacemos, Pilge, BMS, UCBE Pharma, Hospira, Celltrion, Takeda, Biogaran, Boehringer-Ingelheim, Lilly, Pfizer, HAC-Pharma, Index Pharmaceuticals, Aegerion, Sandoz, Forward Pharma GmbH, Celgene, Biogen, Lycera, Samsung Bioepis. Lecture fees: Merck, AbbVie, Janssen, Takeda, Ferring, Norgine, Tilotts, Vifor, Therakos, Pharmaceuticals, Lilly, Pfizer, HAC-Pharma. E Louiss: Educational grants: MSD, AbbVie, Takeda, Speaker fees: AbbVie, Ferring, MSD, Chiesi, Mitsubishi Pharma, Hospira, Janssen, Takeda. Advisory board: AbbVie, Ferring, MSD, Takeda, Hospira, Mitsubishi Pharma, Celltrion, Prometheus. EV Lotus Jr: Consulting: AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Eli Lilly, Celgene, Celltrion Healthcare. Research support: AbbVie, Takeda, Janssen, UCB, Amgen, Pfizer, Genentech, Receptos, Gilead, Celgene, Sereis, MedImmune, Robert's Clinical Trials, C-Bio, Pfizer, Janssen, AbbVie, BMS, Celgene, Boehringer-Ingelheim. Speaker honorarium: AbbVie, Janssen, Takeda, Shield, Ferring, Falk Pharma, WJ Lee, A Lacerda, F Cataldi: Employees, stock: AbbVie.

Reference
Aims and Methods: Long-term follow-up data was retrospectively collected for patients who participated in the LIRIC trial; a multicenter, randomized controlled trial that compared laparoscopic ICR with IFX induction and maintenance therapy for adult patients with non-stricturing and immunomodulator refractory ileocecal Crohn’s disease (≥20cm). Primary outcome was the time to therapeutic intervention defined by the initiation or modification of medical therapy or surgery for disease flare or intolerance to treatment. Time to intervention was analyzed by Kaplan-Meier survival analysis. Potential predictive factors were defined a priori, identified through Cox proportional hazards regression analysis and expressed as hazard ratio (HR) [95% CI]. Tissue samples were taken from the surgical specimen (M0) and at time of recurrence (M1). The presence of mucosa-associated Enterobacteriaceae on the surgical specimen was an independent risk factor for severe post-operative recurrence of Crohn’s disease. Thus, the detection of AIEC at the time of surgery appears essential to adapt the postoperative treatment.

Disclosure: No disclosure to disclose

Reference

OP239 PRESENCE OF MUCOSA-ASSOCIATED ESCHERICHA COLI, ESPECIALLY ADHERENT-INVASIVE E. COLI, ON THE SURGICAL SPECIMEN IN ILEAL CROHN’S DISEASE AS A GOOD PREDICTOR OF POST-OPERATIVE RECURRENCE: A STUDY FROM THE REMIND GROUP
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Introduction: The majority of patients with ileal Crohn’s disease (CD) undergo at least one intestinal resection during the course of their disease. Postoperative recurrence is a major issue, as up to 70% of them develop new lesions in their colorectal stump within 1 year of surgery. We aim to determine whether the presence of adherent and invasive Escherichia coli (AIEC) bacteria at the time of surgery was associated with endoscopic post-operative recurrence at 6 months.

Aims and Methods: The REMIND group (9 centers) has established a homogeneous, prospective, multicenter cohort (POP-REMIND) of operated CD patients. Tissue samples were taken from the surgical specimen (M0) and at endoscopy (M6), and stored centrally in a biobank. The inclusion criteria were: age ≥18 years, ileal or ileocecal CD requiring intestinal resection. Post-operative treatment was prescribed according to a standardized algorithm. Clinical outcome, therapeutic, biological and endoscopic data (Rutgeerts score) were collected 6 months after surgery. Clinical factors (demographic variables, phenotypic and postoperative treatments) associated with endoscopic recurrence were investigated by univariate and logistic regressions. The search for mucosa-associated E. coli bacteria was carried out by culturing on Drigalski medium, and adherent-invasive characteristics of E. coli was performed using hnt-407 cells, and survival within THP-1 macrophages.

Results: The presence of mucosa-associated E. coli strains was determined on the surgical specimen in 241 patients; 110 harbored mucosa-associated E. coli (45.6%). The presence of mucosa-associated E. coli on the surgical specimen was not correlated with age, disease duration, smoking, previous surgical resection, or corticosteroid use. In the IFX group (HR 0.21, 3e-8, 0.58). The presence of mucosa-associated E. coli on the surgical specimen was associated with increase risk of endoscopic post-operative recurrence (defined as Rutgeerts scores ≥12, 13 and ≥14; p = 0.01). Towards the endoscopic post-operative recurrence of Crohn’s disease, thus the detection of AIEC at the time of surgery appears essential to adapt the postoperative treatment.

Disclosure: No disclosure to disclose

Reference

OP240 MOLECULAR PROFILING OF ULCERATIVE COLITIS PATIENTS FROM THE TURANDOT TRIAL UNCOVERS NOVEL PHARMACODYNAMIC AND CLINICAL EFFICACY BIOMARKERS AND A MECHANISTIC RATIONAL FOR A NON-MONOTONIC DOSE RESPONSE
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2Fizer Inc., Cambridge, United States
3Fizer Inc., Cambridge, United States

Introduction: FPPS-4765 (SHP647) is a human anti-mucosal addressin cell adhesion molecule-1 (MAdCAM-1) IgG monoclonal antibody that decreases intestinal inflammation through inhibition of MAdCAM-1-dependent lymphocyte recruitment. A phase 2 study (NCT 01602255), in patients with moderate to severe, active ulcerative colitis in the TURANDOT study showed the therapeutic efficacy of FFPS-476579 in a non-monotonic dose responsive manner, with the improved response in 225 mg dose cohort demonstrating greater efficacy than the highest 225 mg dose cohort1.

Aims and Methods: We aimed to define novel pharmacodynamic and efficacy biomarkers and to elucidate potential mechanisms underlying the observed non-monomeric dose response.

Transcriptome (RNA seq), protein (Olink), and immunohistochemistry (IHC) data were generated from the peripheral blood and intestinal biopsies of 310 patients from this phase 2 trial.

Results: Compared to the placebo group, C-C Motif Chemokine Receptor 9 (CCR9) gene expression demonstrated a 1.2, 2.0, 3.0 and 2.5-fold increase in the 7.5 mg, 22.5mg, 75mg, and 225mg cohorts, respectively (p = 0.21, 3e-8, 7.5e-18 and 1.8e-12) in peripheral blood, while in inflamed intestinal tissue, it demonstrated a 0.3, 0.4, 0.5 and 0.5-fold decrease in the 7.5 mg, 22.5mg, 75mg and 225mg cohorts, respectively (p = 0.046, 0.007, 0.0051, 0.028). Osteoclast M (OSM) gene or protein expression in peripheral blood or intestinal tissue demonstrated a 0.2 to 0.9-fold decrease among patients who showed efficacy (response, remission, or mucosal healing, p = 0.01 to 2.6e-8). Compared to the placebo group, intestinal T regulatory cells measured by IHC demonstrated a 0.2 to 0.9-fold decrease among patients who showed efficacy (response, remission, or mucosal healing, p = 0.01 to 2.6e-8).

Conclusion: These results reveal CCR9 and OSM as pharmacodynamic and efficacy biomarkers, respectively. Furthermore, the increased number of regulatory cells in the intestinal cohort at 225 mg dose cohort could suggest a greater sensitivity for T effector versus T regulatory cells to FFPS-4765-mediated blockade, implicating a potential mechanistic rationale for the observed non-monotonic efficacy response. Taken together, these findings may have significant implications for our understanding of UC disease pathophysiology and the development of future therapeutic approaches.
1. P. Salvador Escribano1, D.C. Macías-Ceja2, F. Navarro-Vicente2, R. Alonso2, L. Peyrin-Biroulet2, J. Cosín Roger2, S. Cañaitaya3, M.D. Barrachina3, D. Ortiz Masía1
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Introduction: Macrophages contribute to fibrosis through the release of different mediators and the pattern of secretion may vary according to their phenotype. Strong evidence identifies the Wnt signalling pathway as an emerging modulator of fibrosis. We have recently reported differences in the Wnt signalling pathway in surgical resections from Crohn’s disease patients presenting a strictureing (B2) or a non-stricturing (B3) behavior (1).

Aims and Methods: The aim of the present study is to analyze the pattern of expression of macrophages and the expression of Wnt ligands in surgical resections from Crohn’s disease (CD, n = 43) patients with different disease behavior. CD patients were categorized according to Montreal classification (B2 or B3) and an unaffected mucosa of patients with colorectal cancer was used as control. mRNA was isolated and the expression of macrophage markers, pro-inflammatory cytokines and Wnt2b was analyzed by RT-PCR (Gene-b-actin) mRNA expression; fold induction vs control group). The number of macrophages positive for the different markers (CD206, CD68, CD16 and CD61) was analysed by flow cytometry. Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy donors and treated with secretomies from control, B2 or B3 surgical resections for 48 hours. mRNA from PBMCs was isolated and the expression of macrophage markers and Wnt2b was determined. Results are expressed by mean ± SEM (n≥5). Statistical analysis was performed by ANOVA + Newman-Keuls test. Correlations between data were analysed using Pearson’s correlation coefficient (p<0.05).

Results: The expression of pro-inflammatory cytokines, IL-1b and IL-6 and Wnt2b was significantly higher in intestinal samples from B3 CD patients (8.9±2.0, 8.7±1.8 and 2.3±0.4 respectively) than in controls (2.3±0.4, 2.4±0.6 and 1.1±0.1 respectively) or B2 CD patients (3.0±1.0, 3.9±0.8 and 0.7±0.1 respectively). The number of CD16 or CD68 positive macrophages was significantly higher in intestinal tissue from B3 CD patients (69.7±24.4% and 88.8±18.4%, respectively) than in that from B2 CD patients (56.12±5.8% and 30.58±10.9%, respectively). A high percentage of CD16 positive macrophages were also positive for Wnt2b in intestinal tissue from B3 CD patients (24.7±8.8%). A significant and positive correlation between WNT2b and CD16 (r=0.8, p=0.001) or CD68 (r=0.7, p=0.001) as well as CD16+ cells and CD61+ cells (r=0.7, p=0.002) was detected in intestinal tissue from B3 CD patients. The mRNA expression of CD16, CD68 and WNT2b was significantly higher in PBMCs treated with B3-secretomes (138.6±20.9, 33.8±0.0 and 12±3.2, respectively) than in those treated with B2- (3.3±1.8, 3.3±1.8 and 3.3±1.8, respectively) or control (1.2±0.5, 1.2±0.5 and 1.2±0.5, respectively) secretomes.

Conclusion: A pro-inflammatory/profibrotic macrophage phenotype may act as a source of Wnt2b in intestinal tissue from Crohn’s disease patients with a penetrating (B3) behavior.

Disclosure: Nothing to disclose

References
1. P008-Differences in macrophage infiltration and Wnt ligands expression in surgical resections from Crohn’s disease patients presenting a strictureing (B2) or a non-stricturing (B3) behavior. P. Salvador Escribano1, D.C. Macías-Ceja2, F. Navarro-Vicente2, R. Alonso2, L. Peyrin-Biroulet2, J. Cosín Roger2, S. Cañaitaya3, M.D. Barrachina3, D. Ortiz Masía1
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Disclosure: Nothing to disclose

Reference
1. P008-Differences in macrophage infiltration and Wnt ligands expression in surgical resections from Crohn’s disease patients presenting a strictureing (B2) or a non-stricturing (B3) behavior. P. Salvador Escribano1, D.C. Macías-Ceja2, F. Navarro-Vicente2, R. Alonso2, L. Peyrin-Biroulet2, J. Cosín Roger2, S. Cañaitaya3, M.D. Barrachina3, D. Ortiz Masía1
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Disclosure: Nothing to disclose

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1. P008-Differences in macrophage infiltration and Wnt ligands expression in surgical resections from Crohn’s disease patients presenting a strictureing (B2) or a non-stricturing (B3) behavior. P. Salvador Escribano1, D.C. Macías-Ceja2, F. Navarro-Vicente2, R. Alonso2, L. Peyrin-Biroulet2, J. Cosín Roger2, S. Cañaitaya3, M.D. Barrachina3, D. Ortiz Masía1
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Disclosure: Nothing to disclose

Reference
A. Dunlop1, R. Arasaradnam1 showed the proportion presenting at Dukes A \( \equiv 6.9–8.5 \). Cancer stage at diagnosis was reported in 28.5% of papers. Pooled data weighting mean was calculated with a cancer conversion rate of 7.7% (95% CI 36.7% and 6.6% respectively1. The results provoke a reconsideration of the benefits of the TWW pathway for CR screening. Recal-evaluation of the criteria needs consideration with focus on symptoms with higher positive predictive value (PPV) in cancer.

Disclosure: Nothing to disclose

Introduction:


Abstract No: OP244

Table 1: Age, Participation rate, Positivity rate, Detection rate and Positive Predictive Value per screened subgroup in 2016.

<table>
<thead>
<tr>
<th>Age</th>
<th>First-time invitees (n=1038998)</th>
<th>Second-time invitees previously invited for FIT at 15 µg Hb/g feces (n=57936)</th>
<th>Second-time invitees, previously invited for FIT at 47 µg Hb/g feces (n=400657)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median years (IQR)</td>
<td>63 (61-71)</td>
<td>67 (65-69)</td>
<td>4.3 (4.3-4.4)</td>
</tr>
<tr>
<td>Participation rate (%)</td>
<td>71.8 (71.7-71.9)</td>
<td>76.2 (76.0-76.3)</td>
<td>15.0 (14.5-15.4)</td>
</tr>
<tr>
<td>Positivity rate (%)</td>
<td>6.0 (5.9-6.1)</td>
<td>3.3 (3.1-3.5)</td>
<td>4.3 (4.3-4.4)</td>
</tr>
<tr>
<td>Detection rate per 1,000</td>
<td>26.4 (26.0-26.8)</td>
<td>10.4 (9.4-11.4)</td>
<td>15.0 (14.5-15.4)</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>53.7 (51.5-54.2)</td>
<td>36.8 (34.0-40.0)</td>
<td>41.0 (40.0-41.9)</td>
</tr>
</tbody>
</table>

Notes:

1. First-time invitees, 57,936 second-time invitees with a previous FIT cut-off level to increase the PPV and to alleviate the colonoscopy capacity. This study presents the impact of the increased FIT cut-off level on the results of the second round of the CRC screening program.

Aim: To investigate the impact of increasing the cut-off level on participation and yield in the second round.

Methods:

We present outcomes of the Dutch national CRC screening program in 2016. The target population for this year consisted of 3 groups of individuals: first-time invitees; second-time invitees that had been invited to FIT at a cut-off level of 15 µg Hb/g feces in 2014; and second-time invitees invited to a FIT at a cut-off level of 47 µg Hb/g feces in 2014. All participants in 2016 underwent screening with a 47 µg Hb/g feces FIT cut-off level. The FIT positivity rate and PPV for detecting CRC and/or Advanced Adenoma (AA) among FIT positive participants was compared between the three groups of individuals. Data were collected from Screen-IT, the national screening database covering the whole Dutch CRC screening program from selection of individuals for invitation to the colonoscopy and pathology reports.

Results:

A total of 1,497,591 individuals were invited for FIT in 2016: 1,038,998 first-time invitees, 57,936 second-time invitees with a previous 15 µg Hb/g feces cut-off level and 400,657 second-time invitees with a previous 47 µg Hb/g feces cut-off level (Table). Participation was high in both first- and second-time invitees: 71.8% and 76.2% respectively. As expected, FIT positivity was highest among first-time invitees (6.0%, 95%CI: 5.9-6.1). In second-time invitees, positivity rate was lower in those previously invited for a FIT with cut-off of 15 µg Hb/g feces (3.3%, 95%CI: 3.1-3.5), compared to those previously invited for a FIT with cut-off of 47 µg Hb/g feces (4.3%, 95%CI: 4.3-4.4). Results for detection rates and PPV showed a similar pattern (Table).

Conclusion:

Participation in the Dutch CRC screening program remains the highest in the world. The increase in FIT cut-off level in 2014 has not jeopardized participation. As expected, an increased FIT cut-off level in the first screening round resulted in relatively more positive FIT results and higher PPV the second round of the CRC screening program.
in the subsequent screening round. This suggests that most of the missed findings due to use of an increased FIT cut-off level are detected in the subsequent round, emphasizing the importance of repeated screening, especially within screening settings with high cut-off levels.

Disclosure: Nothing to disclose

OP245 COST-UTILITY ANALYSIS OF COLONOSCOPY OR FAEAL IMMUNOCHEMICAL TEST FOR COLORECTAL CANCER SCREENING

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Introduction: Organized programs for colorectal cancer (CRC) screening have been associated with a substantial degree of CRC prevention in terms of its incidence and mortality. However, these programs demand a high burden of medical and economic resources. The 2 preferred screening methods are faecal immunochromatographic test (FIT) and primary colonoscopy. Our aim was to perform a cost-utility analysis between these 2 tests in an European setting.

Aims and Methods: A Markov cost-utility analysis was performed for the Portuguese population from a societal perspective comparing FIT or colonoscopy screening versus non-screening. Clinical data and utilities were collected from a systematic review and costs from published national data. Population was screened from 50 to 74 years-old by biennial FIT or colonscopy every 10 years and efficacy was evaluated in quality-adjusted life years (QALY). For the base case scenario, FIT cost was €3, with 50% acceptance, sensitivity 70% and specificity 95%; colonoscopy cost was €397 with 38% acceptance. An annual discount of 3% was used and the threshold was set at €39,760/QALY. The primary outcomes were the cost-effectiveness ratio (ICER), deterministic and probabilistic sensitivity analysis was done and colonoscopy burden was addressed according to the screening option.

Results: Biennial FIT screening and primary colonoscopy every 10 years screening resulted in a degree of CRC incidence and mortality prevention of 30% and 30%, and 38% and 38%, respectively. This translated in an incremental utility of 0.00157 QALY and 0.00185 QALY, as compared with no screening. The overall cost was €17.9 for FIT and €199.4 for colonoscopy, resulting in an additional cost of €10 and €191 vs. no screening, respectively. At cost-effectiveness analysis, FIT was the most cost-effective option providing an ICER of €6,383/QALY while colonoscopy every 10 years provided an ICER of €103,633/QALY. FIT screening was the most cost-effective option in 90% of simulations in sensitivity analysis and colonoscopy would have to increase 1.3% for a FIT program (26,000 colonoscopies/year, million screened) or 31% for a colonoscopy programme (48,000 colonoscopies/year, million screened).

Conclusion: Biennial FIT is a more suitable choice compared to primary colonoscopy screening resulting in a more rational exploitation of the limited endoscopic capacity. This further supports the progressive implementation of FIT-based programs in Europe.

Disclosure: Nothing to disclose

OP246 PREDICTION OF ADVANCED COLONIC NEOPLASM IN SYMPTOMATIC PATIENTS: A SCORING SYSTEM BASED ON THE FAecal IMMUNOCHEMICAL TEST TO PRIORITIZE COLONSCOPY IN THE FAST-TRACK REFERRAL SYSTEM (COLONOFIT STUDY)

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Introduction: The fast-track colonoscopy program to detect patients with colorectal cancer (CRC) based on high-risk symptoms is associated with low sensitivity and specificity.

Aims and Methods: Define a predictive score of advanced colonic neoplasia (ACN) in symptomatic patients with indication of a fast-track colonoscopy.

All the patients referred for colonoscopy with fast-track indication were evaluated. We performed a retrospective analysis of patients included in the faecal immunological occult haemoglobin test (FIT) (samples) considering positive > 4 µg Hb/g faeces and a face-to-face survey to register clinical variables of interest. The main outcome was ACN defined as CRC or advanced adenoma (> 1 cm or high-grade dysplasia or villous component). The overall maximum faecal haemoglobin (MAXFIT) value, which maximizes the probability of ACN through the assessment of the diagnostic odds ratio (OR) was calculated, and was 11 µg Hb/g faeces. We assumed 3 categories for the MAXFIT variable: < 4, > 4 to 11, > 11 µg Hb/g faeces. A minimum sample size of 600 individuals was calculated for each phase of the study: Phase 1 (derivation cohort) and Phase 2 (validation cohort). A Bayesian logistic regression analysis using R software was performed to derive a predictive score and stratify the risk of ACN.

Results: 1495 patients were included (Phase 1 = 2). Differences were found between the derivation and the validation cohort in the variables related to the FIT (colorectal cancer screening resulted in a more rational exploitation of the faecal immunochemical test (FIT) (samples) considering positive > 4 µg Hb/g faeces and a face-to-face survey to register clinical variables of interest. The main outcome was ACN defined as CRC or advanced adenoma (> 1 cm or high-grade dysplasia or villous component). The overall maximum faecal haemoglobin (MAXFIT) value, which maximizes the probability of ACN through the assessment of the diagnostic odds ratio (OR) was calculated, and was 11 µg Hb/g faeces. We assumed 3 categories for the MAXFIT variable: < 4, > 4 to 11, > 11 µg Hb/g faeces. A minimum sample size of 600 individuals was calculated for each phase of the study: Phase 1 (derivation cohort) and Phase 2 (validation cohort). A Bayesian logistic regression analysis using R software was performed to derive a predictive score and stratify the risk of ACN.

Conclusion: A scoring system was derived and validated to prioritize fast-track colonoscopies according to risk, which was shown to be efficient, simple and robust.

Disclosure: Sponsored by a Grant ‘Fundació la Marató de TV3’ (785/U/2013). This sponsor had no role in the study design, nor in the acquisition, analysis, or interpretation of the data, or the writing of the report.

OP247 POST-COLONOSCOPY COLORECTAL CANCER IN THE ENGLISH NATIONAL HEALTH SERVICE BOWEL CANCER SCREENING PROGRAMME

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Introduction: Post-Colonoscopy Colorectal Cancer (PCCRC) rate is a key quality indicator in colorectal screening. The Word Endoscopy Organization has reached consensus agreement to use one method for calculating 3-year PCCRC rates (termed PCCRC-3y) to enable international benchmarking of rates (1). This methodology, used previously by Morris et al (2), showed a PCCRC-3y rate of 8.6% across the English National Health Service (NHS) from 2001-2007(2) with a rate of 7.3% in 2007. This study aimed to determine the rate of PCCRC-3y in the English NHS Bowel Cancer Screening Programme (BCSP).

Aim and Methods: Data from each colonoscopy in the BCSP is entered into a national database, the Bowel Cancer Screening System. All colorectal adenocarcinomas, within and outside the BCSP, are validated and registered by the National Cancer Registration and Analysis Service. This retrospective observational study interrogated these databases to identify BCSP colorectal cancers and detect colorectal cancers within 6 months (true positive colonoscopies) and those BCSP colonoscopies in patients who subsequently developed a colorectal cancer 6 months – 3 years after the colonoscopy (false negatives) between 2006 and 2013.

Results: Of the 200 PCCRCs, 115 were detected at a subsequent BCSP procedure and 85 detected outside the BCSP.
2. Despite the high quality of colonoscopy in the BCSP, PCCRCs still occur, showing the importance of vigilance during all colonoscopies.
3. Diagnosis of >2000 colorectal cancers (true positive colonoscopies) each year indicates there is an adequate sample size for annual reporting of PCCRC-3y rate within the BCSP and comparison with PCCRC-yr rates in symptomatic services.

Disclosure: Nothing to disclose

References

OP248 HIGH-RISK LESIONS ARE A STRONGER PREDICTOR FOR INTERVAL CANCER THAN ADENOMA DETECTION RATE
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Introduction: After index colonoscopy patients with high-risk adenomas (> 2 polyps or ≥ 10 mm or high-grade dysplasia or villous or tubulovillous histology) should undergo surveillance colonoscopy after 3 years, patients with low-risk adenomas after 10 years. Although endoscopic screening reached high quality standards, interval cancers still occur in a significant number of patients and the underlying risk factors are poorly understood.

Aims and Methods: To evaluate if patients with high-risk adenomas are at increased risk for interval cancers. Screening colonoscopies performed between 1/2009 and 6/2015 within a nationwide quality assurance program were included. An interval cancer was defined as colorectal cancer diagnosed at least 6 months after screening colonoscopy and the scheduled time of surveillance colonoscopy.

Results: 146,894 colonoscopies were included (50.8% women, median age 60 years) of which 19% were classified as high risk. During a median follow up of 36 months, 572 interval cancers were identified. Patients with high-risk lesions had significantly higher incidence rates of interval cancers than those in the low-risk group (HR 1.77 [1.18–2.66]; p = 0.006). Other factors associated with interval cancer were older age (HR per 10 years 1.87 [1.52–2.29]; p < 0.001) and adenoma detection rate (HR 0.65 [0.44–0.95]; p = 0.025). Interestingly, there was no association with female sex.

Conclusion: High-risk lesions are a stronger predictor for the occurrence of interval cancer than poor adenoma detection rate. In contrast to previous studies there was no association with female sex.

Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018
15:45-17:15
Artificial intelligence: The rise of the machines – Room N2

OP249 AUTOMATIC DETECTION OF EARLY GASTRIC CANCER IN ENDOSCOPIC IMAGES USING A TRANSFERRING CONVOLUTIONAL NEURAL NETWORK
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Introduction: Detection of gastric cancer is difficult even for well-trained endoscopists, therefore machine learning is expected to be useful for reducing misdiagnosis and interobserver variability in endoscopic diagnosis. Dramatic changes in detection accuracy in machine learning have been occurring since the availability of the utility of convolutional neural network (CNN). Although many results have been reported, there are relatively few effective methods to automatically detect early gastric cancer with small morphological features, which implies that automatic detection methods can be extremely difficult to construct. Additionally, it is well-known that CNN-based methods require the learning about each normal structure and benign lesion, which will surely reduce the ability of AI to detect esophageal cancer including squamous cell carcinoma (SCC) and adenocarcinoma.

Aims and Methods: We collected 8428 training images of esophageal cancer lesions that were histologically proven to be SCC or adenocarcinoma in 384 patients in Cancer Institute Hospital, Tokyo, Japan from 2014 to 2017. The training esophageal cancer image included 397 lesions of esophageal SCCs (SCCs) which consisted of 332 lesions of superficial cancer and 65 lesions of advanced cancer. A total of 32 lesions of esophageal adenocarcinomas (EACs) were also included for training and consisted of 19 lesions of superficial cancers and 13 lesions of advanced cancers. With these training images, we developed deep learning through convolutional neural networks (CNNs). We also prepared 1118 test images in 47 patients with 49 esophageal cancers, including 41 SCCs and 8 EACs (169 images of esophageal cancer and 376 images without cancer), and 50 patients without esophageal cancer (573 images of the non-cancerous part of the esophagus) to evaluate the diagnostic accuracy. All cases of esophageal cancer were confirmed to have no other cancer using WLI, NBI, iodine staining, and follow-up endoscopy after the treatment.

Results: The CNN took 27 seconds to analyze 1118 test images and correctly detected esophageal cancer cases with a sensitivity of 98% (48/49). CNN could detect all 7 small cancer lesions less than 10 mm in size. In contrast the CNN misdetect 42 non-cancerous lesions, which caused low positive predictive value (54%). However, the PPV of NBI with magnification was reported to be 45% in experienced endoscopists and 35% in less experienced endoscopists, which was not so different from our outcomes. The misdiagnosed lesions included scars of esophagitis, small size endoscopic images were successfully done with showing detected cancers area as pseudo colored heatmap, and detection success was accomplished in a total of 106 images (82.8%) out of 128 cancer images. Conversely, a total of 491 identified (40.8%) out of 698 normal images were misdetect. The processing time was 4 ms per image, except for the time required to input/output the image.

Conclusion: Our preliminary CNN-based prediction scheme achieved high accuracy of early gastric cancer detection from the small amount of learning datasets. Automatic detection of early gastric cancer may offer sufficient assistance to endoscopists in decision making.

Disclosure: Nothing to disclose
Conclusion: Percentage of recognized neoplastic images where the algorithm detected the soft spot and sweet spot; 3) Red-flag indication: Percentage of recognized neoplastic images where the algorithm recognized the location of the neoplastic area and a ‘red-flag’ indication of only the most suspicious part of the neoplastic area. These results are promising and show feasibility of computer-aided detection as a red-flag detection technique in BE surveillance. Future steps of early BE neoplasia, thereby improving efficacy of BE surveillance. Recently, several deep learning techniques using Transfer Learning in Convolutional Neural Networks (CNNs) have shown promising results in other fields. CAD systems using deep learning techniques allow for faster execution time than the conventional clinically inspired algorithms, which will be essential for real-time operation. The aim of this study was to evaluate feasibility of a deep learning algorithm for detection of BE neoplasia using high-quality endoscopic images. Aims and Methods: Endoscopic overview images of 40 subtle early neoplastic BE lesions and 20 non-neoplastic BE patients were prospectively collected in White Light Endoscopy (WLE) in three tertiary referral centers. To establish a ground truth for detection and delineation, 6 international BE experts delineated all neoplastic images using a proprietary online delineation module. The area with at least 1 expert delineation was labelled as the soft spot. Positive samples were extracted from the sweet spot of the neoplastic images, while negative samples were taken from the area outside of the soft spot and from the NDBE images. The deep learning algorithm was trained using transfer learning on a ResNet50 model pre-trained on ImageNet. The images were divided in blocks of 128 x 128 pixels that were used as input to the CNN. Based on their location, each image block was then classified as neoplastic or non-neoplastic separately and aggregated to obtain a segmentation mask. For each detected neoplastic image, the algorithm produced 2 separate delineations: A complete delineation of the neoplastic area and a ‘red-flag’ indication of only the most suspicious part of the lesion. Outcome parameters: 1) Detection scores: Diagnostic accuracy of the algorithm per image in terms of accuracy, sensitivity, specificity, NPV and PPV; 2) Localization scores: Percentage of recognized neoplastic images where the delineation of the algorithm detected the soft spot and sweet spot; 3) Red-flag indication: Percentage of recognized neoplastic images where the algorithm red-flagged the soft spot and sweet spot. Performance was evaluated using 4-fold cross-validation. Results: Accuracy, sensitivity, specificity, PPV, NPV for detection per image were 92%, 95%, 85%, 93% and 90%, respectively. On the detected neoplastic images, the algorithm identified both the soft- and sweet spot to be neoplastic in all cases (100%). On these images the algorithm furthermore red-flagged the soft spot and sweet spot to be neoplastic in 97% and 87%, respectively. Conclusion: Detection scores of the first version of this deep learning algorithm were high. On all detected images, the algorithm recognized the location of the neoplastic lesion. These results are promising and show feasibility of computer-aided detection of early neoplasia in BE surveillance. Future steps will focus on further development of the algorithm towards video- and real-time analyses.

Disclosure: Nothing to disclose

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Introduction: Clinically significant post-endoscopic bleeding (CSPEB) is the most common complication following colonoscopic endoscopic mucosal resection (EMR). Current prediction tools are based on peri-procedural patient and lesion characteristics and do not account for the post-EMR mucosal defect appearance. We hypothesized that CSPEB may be predicted by analyzing the morphometric characteristics of blood vessels within the post-EMR mucosal defect. Our aim was to create a tool that will allow real-time identification of high-risk patients, thereby benefit from prophylactic treatment and close follow-up. Aims and Methods: Patients from the Australian prospective EMR cohort (ACE) were assigned to 2 groups based on presence or absence of CSPEB. The groups were matched in a 1:1 ratio for the clinical variables known to be associated with CSPEB (Age, aspirin use, lesion location in the colon, lesion size, histological subtype and intraprocedural bleeding). Standard EMR was performed, detailed patient lesion and procedural characteristics were recorded and meticulous photo-documentation prior to, during and after the procedure was obtained. A telephone interview was conducted 14 days after the procedure as part of the ACE study protocol, to record adverse events. Computerized morphometric analysis was used to quantify various morphologic characteristics of the blood vessels within the post-EMR mucosal defect. Multivariate Discriminant Regression Analysis and neural network were used as prediction models. Results: Over the course of 6 years, until 2015, 1332 colonic lateral spreading lesions (LSL) >20 mm under EMR at Westmead Hospital Sydney were analyzed. On the trains of the ACE study, 88/1332 (6.6%) had CSPEB. 43 cases and 43 matched controls with high quality images of the post EMR mucosal defect were selected for the analysis (median lesion size 40 mm (IQR 30-51.25)). Of 30 blood vessel characteristics, 5 morphometric characteristics were independently associated with CSPEB (table 1). Discernant analysis using the 5 independent predictors yielded 86% sensitivity and 76.7% specificity in correctly identifying patients at risk of CSPEB. A Neural Network (NNET) classifier using same independent predictors was trained on data of 60 subjects (30 controls and 30 cases) and subsequently tested on 26 subjects (13 controls and 13 cases). Training and testing subjects were chosen by computer randomization. The validated NNET yielded an sensitivity of 100% and specificity of 76.9% for correctly identifying patients at risk of CSPEB. Conclusion: Morphological characteristics of blood vessels in post-EMR defects can be used to predict delayed bleeding following colonic EMR. Future applications may include real-time computerized image analysis of blood vessels, which may assist in clinical decision-making regarding high-risk patients.

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Introduction: Recently the American Society for Gastrointestinal Endoscopy (ASGE) addressed the “reject and discard” strategy, which suggests that diminutive polyps can be rejected and discarded without submitting pathological assessment, when it is estimated not as adenomatos polyps with high confidence. This strategy can reduce the physician’s burden, complications caused by biopsies, and medical costs. However, endoscopists need specific training until they can precisely detect and classify colorectal polyps, and in this regard computer-assisted diagnose (CAD) system may be of help. Previous studies have suggested promising application of artificial intelligence (AI), using deep learning in object recognition.

Aims and Methods: We aimed to construct a CAD using deep learning method that can accurately identify and classify CP in stored colonoscopy images. A deep convolutional neural network (CNN) architecture called Single Shot MultiBox Detector was utilized to develop and validate the CAD system in the present study. We trained the CNN using 16,418 images: 4,752 of CP and 4,013 of normal colorectum, and subsequently validated the performance of the trained CNN in 7,077 colonoscopy images, including 1,172 CP images from 309 various types of CP. Diagnostic speed and yields for the detection and classification of CP were evaluated as a measure of performance of the trained CNN.

Results: The processing speed of the CNN was 20 ms per frame. The trained CNN identified 1,247 CP with a sensitivity of 92% and a positive predictive value (PPV) of 86%. Among the correctly detected polyps, 83% of the CP were accurately classified, and furthermore, 97% of adenomas were precisely identified.

Conclusion: Our CNN showed robust performance to detect and classify CP through colonoscopy images, highlighting its high potential for future application as a CAD system of CP during colonoscopy.

Disclosure: T. Tada and K. Aoyama are employed by AI Medical Service Inc.
Aims and Methods: The study was performed as randomized, cross-over trial. 12 healthy lean male subjects received an intragastric glucose (ig-gluc) load with or without intravenous (iv) exendin-39-39 (ex9-39; specific GLP-1 receptor antagonist). Functional magnetic resonance imaging was used to investigate the effect of endogenous GLP-1 on resting state functional connectivity (rsfC) between homeostatic and reward-related brain regions. Visual analogue scales were used to rate appetite-related sensations. Blood samples were collected for insulin and glucose measurements.

Results: The main findings can be summarized as follow: i) after iv-ex9-39/ig-gluc a significantly higher rsfC was found relative to ig-gluc between the hypothalamus and the left lateral orbitofrontal cortex (OFC) as well as the left amygdala (p<0.001, respectively); ii) after iv-ex9-39/ig-gluc a significantly higher rsfC was found relative to ig-gluc between the midbrain (VTA) and the right caudate nucleus (p<0.001); iii) iv-gluc significantly decreased prospective food consumption and increased fullness sensations compared to the pre-infusion baseline (p=0.028 and p=0.019, respectively), these effects were not present in the iv-ex9-39/ig-gluc condition v) after iv-ex9-39/ig-gluc an attenuated increase in plasma glucose concentration was relative to ig-gluc (p=0.012).

Conclusion: In conclusion, this trial in healthy lean individuals indicates that glucose-induced endogenous GLP-1 release affects central regulation of appetite by modulating rsfC in homeostatic and reward-related brain regions in a GLP-1 receptor-mediated fashion.

Disclosure: Nothing to disclose

**OP254 NOVEL COMPUTER-AIDED DIAGNOSIS SYSTEM USING CONVOLUTIONAL NEURAL NETWORKS FOR ENDOSCOPIC DISEASE ACTIVITY IN PATIENTS WITH UC**


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**Introduction:** Endoscopic findings for patients with Ulcerative Colitis (UC) are important to evaluate the extent and severity of the disease, as well as to determine the management of UC. However, since endoscopic diagnosis is an observer-dependent method, a certain period of training time is necessary for endoscopists to acquire sufficient ability to accurately evaluate the inflammatory disease activity. Inter-observer variability is known to exist in endoscopic diagnosis. An image recognition system with artificial intelligence (AI) has great potential to support physicians' clinical practices by providing objective and specialist-level diagnoses in the field of gastrointestinal endoscopy (1), including in the diagnosis of UC.

**Aims and Methods:** In this study, we constructed a computer-assisted diagnosis (CAD) system with a convolutional neural network (CNN) and evaluated its performance with a large dataset of endoscopic images from UC patients. A retrospective review was performed of patients with UC who underwent colonoscopy at a single center in Japan from October 2006 to June 2017. A CNN-based CAD system, constructed based on GoogleLeNet architecture, was trained with 26,304 colonoscopy images from 841 UC patients that were tagged with both anatomical locations and Mayo endoscopic scores (Mayo 0, Mayo 1, and Mayo 2-3). The performance of the CNN to identify mucosal healing state (Mayo endoscopic score 0 or 1) was evaluated in an independent test set of 4,589 images from 117 UC patients using receiver operating characteristic (ROC) curves and calculating the area under the receiver operating characteristic curves (AUCs). Additionally, AUCs in each location of the colorectum (right-sided colon, left-sided colon, and rectum) were evaluated.

**Results:** Of the 4,589 images, 65% (1237 of 1890 images) of the Mayo 0 images, 56% (1295 of 2293 images) of the Mayo 1 images, and 51% (206 of 406 images) of the Mayo 2-3 images were correctly classified as each class of Mayo scores by the CNN-based CAD system. ROC curves of the CNN-based CAD system showed high performance with an AUCROC value of 0.95 to identify Mayo endoscopic score 0 or 1 vs. 2 or 3. The performance of the CNN was better in right-sided colon and left sided-colon than in rectum (AUCROC = 0.96, 0.97, and 0.88, respectively).

**Conclusion:** The CNN-based CAD system showed robust performance in identifying endoscopic inflammation severity in patients with UC, highlighting its capacity to support immature endoscopists and reduce inter-observer variability.

**Disclosure:** The authors declare no conflict of interest. T. Tada and K. Aoyama are employed by AI Medical Service Inc.

**Reference**


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**OP255 ENDGENOUS GLP-1 AFFECTS CENTRAL REGULATION OF APPETITE IN HEALTHY LEAN MALES**

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**Introduction:** Endogenous infusion of glucagon-like peptide-1 (GLP-1) triggers appetite responses and can affect brain activity in areas involved in the regulation of appetite, including hypothalamic and reward-related brain regions. In contrast, the physiological role of endogenous GLP-1 in the central regulation of appetite has hardly been investigated.

**Aims and Methods:** The study was performed as randomized, cross-over trial. 12 healthy lean male subjects received an intragastric glucose (ig-gluc) load with or without intravenous (iv) exendin-39-39 (ex9-39; specific GLP-1 receptor antagonist). Functional magnetic resonance imaging was used to investigate the effect of endogenous GLP-1 on resting state functional connectivity (rsfC) between homeostatic and reward-related brain regions. Visual analogue scales were used to rate appetite-related sensations. Blood samples were collected for insulin and glucose measurements.

**Results:** The main findings can be summarized as follow: i) after iv-ex9-39/ig-gluc a significantly higher rsfC was found relative to ig-gluc between the hypothalamus and the left lateral orbitofrontal cortex (OFC) as well as the left amygdala (p<0.001, respectively); ii) after iv-ex9-39/ig-gluc a significantly higher rsfC was found relative to ig-gluc between the midbrain (VTA) and the right caudate nucleus (p<0.001); iii) iv-gluc significantly decreased prospective food consumption and increased fullness sensations compared to the pre-infusion baseline (p=0.028 and p=0.019, respectively), these effects were not present in the iv-ex9-39/ig-gluc condition v) after iv-ex9-39/ig-gluc an attenuated increase in plasma glucose concentration was relative to ig-gluc (p=0.012).

**Conclusion:** In conclusion, this trial in healthy lean individuals indicates that glucose-induced endogenous GLP-1 release affects central regulation of appetite by modulating rsfC in homeostatic and reward-related brain regions in a GLP-1 receptor-mediated fashion.

**Disclosure:** Nothing to disclose

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**OP256 ENDOSCOPIC SLEEVE GASTROPLASTY (ESG): A METABOLIC PROCEDURE**

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**Introduction:** Morbid obesity is a worldwide major health problem that carries enormous socio-economic costs and a high incidence of comorbidities such as hypertension, diabetes mellitus (DM), and dyslipidemia. Bariatric surgery is the only proven effective treatment; however, treatment rates remain low, because of enormous socio-economic costs and a high incidence of comorbidities such as hypertension, diabetes mellitus (DM), and dyslipidemia. Bariatric surgery is the only proven effective treatment; however, treatment rates remain low, because of poor patient acceptance, high costs, and non-negligible risks of complications. Any alternative treatment that could cure, control or even improve the morbidity of obesity and related diseases would have a tremendous medical, social and economic impact. Endoscopic sleeve gastropasty (ESG) is an incisionless procedure suitable for widespread clinical adoption shown to be effective to induce weight loss up to 24 months in moderately obese patients. Currently, few data are available concerning the effects of ESG on comorbidities related to morbid obesity.

**Aims and Methods:** The aim of this study is to evaluate the impact of ESG on comorbidities (including obesity, diabetes mellitus, hypotension, hypertension, gastro-esophageal reflux, sleep apnea) at 6 months follow-up. Between October 2016 and April 2018, 92 patients underwent ESG in 2 expert centers. ESG was performed by the application of 4 to 6 full-thickness sutures using the OverStitch suturing platform. Patients mean % of excess weight loss (%EWL), clinical outcomes and medication use were assessed. Quality of life (QOL) was evaluated with the GQFLI and the BARQOS questionnaires.

**Results:** 24 patients (26%) had a mean follow-up of at least 6 months and 15 (62.5%) presented at least 1 comorbid condition at inclusion. At 6 months %EWL was 29.95±20.26 and 13 patients (86.6%), reduced (60%) or suspended (33.3%) pre-operative medications (p=0.001) (Table 1). No correlation was
found between weight loss and improvement or suspension of medications with those of the diabetic patients in whom a greater weight loss resulted in a reduction of oral antidiabetics or insulin use (Pearson 0.746, p = 0.04; Spearman 0.737, p = 0.03).

Mean GIQLI score improved from 105.4 ± 17.2 (p = 0.06) to 113.4 ± 16.84 and mean BAROS score from 9.0 ± 0.9 to 1.3 ± 1 (p = 0.03).

Conclusion: ESG is a safe and effective bariatric endoscopic procedure that resulted in a positive impact on both metabolic diseases and quality of life. Thus, ESG could provide a unique opportunity to reach a greater number of obese patients, earlier in their disease or at a younger age presenting with metabolic comorbid conditions. Larger studies are needed to confirm these preliminary encouraging results.

Disclosure: Nothing to disclose

References


OP258 EFFICACY OF A TAILORED HELICOBACTER PYLORI ERADICATION THERAPY BASED ON BODY WEIGHT PATIENTS

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Introduction: The clinical management of Helicobacter Pylori (HP) infection in obese patients is complicated due to the lower eradication rates with standard therapeutic therapy. Body Mass Index (BMI) is an independent risk factor. Although the cause of this poor eradication remain to be elucidated, the physiological changes that obesity produce may lead to sub-therapeutic antibiotic concentrations and the current paradigm “one dose fits all” may be changed. The impact of these changes depends upon patient characteristics (degree obesity, underlying organ function) and the chemical properties of the antibiotic (hydrophilic or lipophilic). For most drugs, the interaction between drug pharmacokinetics/pharmacodynamics and BMI is complex and there is a lack of consensus formula that should be used for dosage calculation.

Aims and Methods: To evaluate the HP eradication of a tailored Quadruple Concomitant regimen based on body weight compared to standard Quadrupe Concomitant therapy in obese patients undergoing bariatric surgery. This prospective, open-label study included 104 obese patients undergoing bariatric surgery. Upper endoscopic HP assessment by histology and 14CO2 breath test were performed at baseline and the post-treatment status was assessed by C13 Urea Breath Test, 6-8 weeks after the end of therapy. All patients were treated 14 days with a Quadruple Concomitant therapy with a proton pump inhibitor, amoxicillin, clarithromycin, and metronidazole. These patients received a tailored regimen based on the body weight. Lipophilic antibiotics (metronidazole and clarithromycin) were adjusted according with the Total Body Weight until their maximal doses. Amoxicillin (hydrophilic drug) was adjusted with the Adjusted Body Weight (Ideal Body Weight according to the modified Devine formula and a weight correction factor of 0.3) until their maximal dose. Simultaneously, 53 obese patients, received the standard Quadrupe Concomitant therapy with a proton pump inhibitor BID, clarithromycin 500 mg BID, amoxicillin 1000 mg BID and metronidazole 500 mg BID.

Results: Per-protocol and intention-to-treatment eradication after the tailored body weight regimen were 90% (95% CI 77-96) and 86% (95% CI 73-93) whereas in the standard treatment obese group was 67% (per-protocol 95% CI 53-78) and 70% (95% CI 52-77) by intention-to-treat. HP eradication in obese patients with the tailored body weight regimen were significantly higher than the control obese group, p < 0.001 Per-protocol and p < 0.05 Intention-to-treatment. The distribution of age, gender, smoking and diabetes did not differ significantly between the 2 groups. 3 patients discontinued the treatment due to adverse events.

Conclusion: A tailored Quadruple Concomitant regimen based on body weight in obese patients undergoing bariatric surgery is significantly more effective than standard Quadruple Concomitant therapy. A tailored eradication treatment with the antibiotics adjusted according to the body weight could be considered as a new strategy for obese patients.

Disclosure: Nothing to disclose

OP259 EFFECTS OF DIETARY FIBRES ON INDOMETHACIN-INDUCED INTESTINAL PERMEABILITY IN ELDERLY: A RANDOMISED PLACEBO CONTROLLED PARALLEL CLINICAL TRIAL

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Introduction: The global population of elderly (>65 years) is increasing and will have a major impact on healthcare systems due to an increased incidence of age-related diseases. Gastrointestinal (GI) symptoms are common among the elderly and approximately 60% are estimated to be affected (3, 4). The elevated pharmaceutical load in elderly is of potential harm to the intestine and it may play an long-term role of non-steroid anti-inflammatory drugs (NSAID), commonly used for pain management among elderly, can cause gastric ulceration, enteropathy (5, 6) and increased intestinal permeability (7). A deteriorated barrier function is associated with increased psychological distress in elderly with GI symptoms (8), and many diseases of inflammatory character such as inflammatory bowel disease (9). We have previously shown that specific dietary fibres attenuate stress-induced hyperpermeability ex vivo in ileal tissues from patients with Crohn’s disease (9). However, the potential of dietary fibres to strengthen the intestinal barrier function in vivo in elderly individuals is, to our knowledge, not known.

Aims and Methods: We performed a placebo-controlled parallel clinical trial to investigate whether 6 weeks of oral supplementation of wheat-endosperm derived
OP260 PERCUTANEOUS TRANSESOPHAGEAL GASTROTUBING (PTEG) AS THE SUITABLE PROCEDURE FOR THE PATIENTS THAT PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) INSERTION IS CONTRAINDICATED

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Introduction: Percutaneous transesophageal gastrostomy (PTEG) was developed as an alternative to the gastrostomy tract for the patients that PEG insertion was contraindicated with conditions such as prior gastrectomy, gastric anterior wall malignancies, or massive ascites. PTEG will be an ideal method for tube feeding and decompression.

Aim of the Study: To evaluate the clinical usefulness of PTEG for the patients who need tube feeding or decompression from gastrointestinal tract. A rupture-free balloon (RFB) catheter is inserted into the upper esophagus. Percutaneous balloon puncture with a specialized needle is then performed through the left side of patient’s neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and guide wire is inserted through the needle into the RFB, followed by a dilator and after dilatation through the balloon. We perform PTEG in a total of 172 patients (109 men and 63 women, mean age 71.2 years) in whom PEG was not feasible. PTEG was performed for nutrition in 97 patients and for decompression in 75.

Results: Satisfactory results were achieved in all 172 patients. Median follow-up time for nutrition and 60.6 days for patients who received decompression. All patients were free from nasal tube prior insertion. 6 of 97 patients for nutrition were able to be freed from tube feeding due to PTEG tube feeding support, oral ingestion could be achieved in 44.0% and home care could be attained in 66.0% with decompression group patients.

Conclusion: PTEG is a useful procedure for the patients who are contraindicated to PEG. PTEG is an only procedure to be free from a nasal tube especially for the patients with carcinomatous peritonitis. PTEG is a suitable procedure for the patients having an eating disorder and/or the malignant disease as tubal feeding and palliative care.

Disclosure: Nothing to disclose

References
2. Dennison C, et al. The health-related quality of life and economic burden of constipation. Pharmacoeconomics. 2005.
Aims and Methods: The aim of our study was to study the effect of the genetic inhibition of Cyp D in the pancreatic ductal epithelial cells. Wild type (WT) and Cyp D knock out (KO) mouse pancreatic ducts were isolated by microdissection. Mitochondrial membrane potential (ΔΨm) was measured by confocal microscopy and pancreatic ductal HCO3⁻ secretion by microfluorometry. Functionally active mitochondria in the pancreatic ducts were detected by immunofluorescence microscopy using TOMM20 mitochondrial marker.

Results: The genetic knock out of cyclophilin D significantly reduced the loss of Cyp D–/–protected pancreatic ductal HCO3⁻ secretion by microfluorometry. Functionally active mitochondria in the pancreatic ducts were detected by immunofluorescence microscopy using TOMM20 mitochondrial marker.

Conclusion: Our results suggest that mitochondrial function has a central role in the function of PDEC presumably by providing ATP for fluid and ion secretion. On the other hand the opening of MPIT may be crucial in the bile acid induced toxicity offering a potential therapeutic target in AP.

Disclosure: Nothing to disclose
cross-species analysis, we compared the pericyte coverage in KPC mice in comparison to wild-type mice. To investigate the interactions between angiogenesis and neurogenesis in vitro, we developed a 3D heterotypic co-culture system with mouse dorsal root ganglia (DRG), PCa cells and pericytes, and determined the neurtile density of DRG neurons. In a transcriptomic analysis, we compared the transcriptional profile of pericytes that were stimulated with PCa cell supernatants and compared this to unstimulated pericytes.

Results: In human PCA tissues, PCV and PCl were increased around CD45+ microcapillaries when compared to NP (PCV and PCl were 23.4 ± 3.7%, p = 0.0048; 19.6 ± 2.2% vs. 21.6 ± 3.2%, p = 0.018). Similarly, PCV & PCl were higher around macrocapillaries-associated pericytes (αSMA+/CD31-stained areas), when compared to NP. In KrasG12D-based mouse PCA models, there was a very similar increase in the PCV and PCl in the BC, compared to the KPC model (p = 0.0105). There was no correlation between PCV, PCl and nerve density or neural invasion. In 3D co-cultures, DRG exhibited enhanced neurite density upon coculture with both PCa cells and pericytes. PCa-cell-stimulated pericytes upregulated the expression of multiple molecules in metabolic and pro-inflammatory pathways.

Conclusion: Increased pericyte coverage is one of the typical alterations in the PCA microenvironment. Activated pericytes also seem to contribute to PCA-associated neurogenesis.

Disclosure: This abstract has also been submitted for presentation at the 2018 meeting of the European Pancreatic Club.

**OP266 HIGH EXPRESSION OF SERUM EXOSOMAL MIR-21-5P IN TYPE 1 AUTOIMMUNE PANCREATITIS**

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Introduction: Type 1 autoimmune pancreatitis (AIP) is now accepted as a new clinical entity of pancreatic disorder that is characterized by diffuse irregular narrowing of the main pancreatic duct, lymphoplasmacytic infiltration with fibrosis, Th2-balanced inflammation, and high serum levels of IgG or IgG4. Since the fibroinflammatory process of AIP responds to immunosuppressants, abnormal immune systems are considered to be involved in the development of AIP. However, the investigation of the complex pathogenetic mechanisms underlying this disease remains to be elucidated.

Exosomes are small extracellular vesicles secreted by myriad of cell populations into body fluids, playing a pivotal role in cell-to-cell communications. These vesicles convey nucleic acids, including microRNA, and proteins derived from both PCA and pericytes. PCa-cell-stimulated pericytes upregulated the expression of multiple molecules in metabolic and pro-inflammatory pathways.

Conclusion: Increased pericyte coverage is one of the typical alterations in the PCA microenvironment. Activated pericytes also seem to contribute to PCA-associated neurogenesis.

Disclosure: This abstract has also been submitted for presentation at the 2018 meeting of the European Pancreatic Club.

**VC01 ENDOSCOPIC APPENDICEAL FECALITIS EXTRACTING BY NOTES TECHNIQUE**

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Introduction: A 74-year-old man had a 2-weeks history of repeated right lower abdominal pain. Colonoscopy revealed a 10-mm subepithelial lesion near the appendiceal orifice. The lesion could be pushed by a biopsy forcep and was found to have in the KC, histioma. It was well defined and appeared heterogenous in endoscopic ultrasonography. Contrast-enhanced computed tomography showed a 8×10mm high density mass in the cecum. Chronic appendicitis caused by appendicealecalcal obstruction was suspected.

Methods: After ERAT failed, a endoscopic treatment was still requested by patient. Therefore, the endoscopic appendiceal fecalith extraction was attempted.

Results: First, along the market dots, the anal side mucosa of the lesion was incised using a flush-knife. Then, a metal clip with dental floss bited the incised mucosa, and another metal clip was used to fix the pull line to the opposite side of cecal wall. So, a pulley-like traction device was structured to expose the subepithelial layer. After the full-thickness resection of cecum and appendix, a fecalith was exposed in the appendix lumen and was taken out by a snare soon. After careful hemostasis, the cecum and appendix defect was closed by metallic clips partly, and the residual defect was unclosed to form a artificial fistula (arrows) from appendix to cecum for internal drainage. The patient experienced no procedure related adverse events.

Conclusion: This novel NOTES technique provides another choice for manage- ment of the subepithelial lesion-like appendiceal fecalitils.

Disclosure: Nothing to disclose

**VC02 JEJUNAL DIVERTICULUM: A RARE CAUSE OF LIFE-THREATENING MIDGUT BLEEDING SUCCESSFULLY TREATED BY DOUBLE-BALLOON ENTEROSCOPY (DBE) (WITH VIDEO)**

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Introduction: Small bowel diverticula are a rare cause of gastroduodenal (GI) bleeding. Their pathogenesis is still unclear and can be found in up to 1-2% of the general population. Although these lesions are usually asymptomatic, midgut bleeding from diverticulitis in the jejunum or ileum could lead to a life-threatening situation, warranting emergency invasive therapy and often abdominal surgery.

Aims and Methods: Our aim was to demonstrate the usefulness of the double-balloon enteroscope (DBE) in the setting of an acute, severe small bowel diverticular bleed. A 79-year-old woman with hypertension and type II diabetes mellitus was referred to our institution with melena and severe anaemia requiring urgent, repeat blood transfusions. Bi-directional conventional endoscopy did not reveal the cause of bleeding. Small bowel capsule endoscopy (SBCE) showed multiple diverticula within the jejunum and ileum. Emergency computed tomography (CT) mesenteric angiography demonstrated a faint ’blush’ at one of the jejunal lesions.

Results: Once the patient was haemodynamically stable, emergency antegrade DBE was performed under general anaesthesia (GA) in our main operating theatres. The enteroscope was inserted into the jejunum, approximately 1.5 meters post-pylorus. The culprit cause of the bleeding was identified within a large (5mm orifice) diverticulum, where a large, adherent, pulsating blood clot was seen. In the first instance, peri-lesion, quadrant injection of a total of 20mLs of adrenaline solution (1 in 10,000 dilution) was performed. The clot was then cautiously removed with a long endocolip to reveal the actively bleeding vessel which was then promptly clipped. A total of 3 clips were placed for effective haemostasis and a submucosal tattoo was placed adjacent to the bleeding point for future reference. The patient remained stable after the procedure and did not require any further blood transfusion.

Conclusion: DBE facilitated endotheraphy is a precise, safe and minimally invasive approach to the effective management of severe bleeding caused by small bowel diverticulitis.

Disclosure: Dr Despott receives research support from Aquilant Medical and Fujifilm. Dr Hayashi has received honoraria from Fujifilm Corp. All other authors disclosed no financial relationships relevant to this publication.
VC03 FIRST REPORT OF A COMBINED RESECTION TECHNIQUE USING A NON- THERMAL, AUTOMATED MECHANICAL RESECTION SYSTEM OF A GIANT, FIBROTIC, CIRCUMFERENTIAL LESION INVOLVING THE WHOLE DUODENAL BULB (WITH VIDEO)

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Introduction: Incidental duodenal non-ampullary lesions are found at upper gastrointestinal (GI) endoscopy in 1-5% of cases. Endoscopic resection of duodenal lesions carries a higher risk of bleeding due to the rich vascularity and exposure to bile and pancreatic enzymes. The risk of perforation is also intrinsically increased due to the presence of the duodenal wall. In addition, endoscopic resection of fibrotic duodenal lesions can be extremely challenging (even in expert hands) and carries high failure and complication rates, often warranting extensive surgical management. To date, there is no widely accepted optimal management strategy for duodenal lesions and conservative management with endoscopic surveillance is frequently adopted. Although at diagnosis, duodenal adenomas are most often benign, they retain an intrinsic risk of malignant transformation.

Aims and Methods: Our aim was to use a novel, combined endoscopic approach for the management of an otherwise unresectable giant, fibrotic, circumferential lesion involving the whole duodenal bulb.

A 72-year-old woman with hypertension presented with anaemia and melena. An upper GI endoscopy revealed a 7 cm circumferential lesion (Paris 0-IIa, 0-IIb) laterally spreading tumour (LST) involving the entire duodenal bulb. Histopathological analysis of biopsies taken at another institution, were in keeping with a papillary adenoma with low-grade dysplasia, whereas the muscularis propria was excluded by endoscopic ultrasound (EUS).

Results: A first resection attempt through a combination of wide-field endoscopic mucosal resection (EMR) and saline-immersion therapeutic endoscopy (SITE) halted, but EMR techniques allowed only resection of up to 10% of the lesion, due to severe fibrosis. Delayed bleeding 24 hours post-resection was successfully treated endoscopically. 6 weeks later, a planned second attempt at endoscopic resection was performed under general anaesthesia. The lesion was initially injected with adrenaline solution (1 in 10,000 dilution). A combination of the use of a novel, non-thermal, automated-mechanical-suction-resection system with cold snaring allowed us to achieve 50% resection of the lesion in less than 2 hours. Mild, self-limiting, intra-procedural oozing did not require further endotherapy for immediate or delayed adverse events to occur.

Conclusion: The resection using the same technique is planned to be performed shortly.

VC04 UNDERWATER PANCREATOSCOPY THROUGH THE DUCT OF SANTORINE: DIRECT VISUAL GUIDED BIOPSIES OF AN INTESTINAL-TYPE IPMN

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Introduction: Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are potentially malignant intraductal epithelial neoplasms that are grossly visible and are composed of mucin-producing columnar cells. The lesions show papillary proliferation, cyst formation, and varying degrees of cellular atypia [1,2]. IPMNs may involve the main pancreatic duct and/or the branch ducts, carrying a risk of malignancy from 15%-60% [3]. The approach to the diagnosis of pancreatic cystic neoplasms typically starts with cross-sectional imaging as abdominal MRI or CT-scan [4]. Endoscopic ultrasound with fine-needle aspiration can lead to the diagnosis or to assess for malignant features. Pancreatocscopy and intra-ductal ultrasonography can allow direct endoscopic visualization of the pancreatic ducts, and ductal lesions can be directly biopsied. In our case, the pancreatocscopy, allowed the diagnosis to be made before progression to invasive cancer and the subsequent surgery.

Disclosure: Nothing to disclose

References
Buried bumper syndrome (BBS) is a rare, long-term complication of inflammation or in association with spastic motility disorders such as achalasia. Effective endoscopic therapy for thoracic diverticula is yet to be described.

**Aims and Methods:** This video describes 2 cases of the use of a novel technique of intraluminal submucosal myotomy (ISM) for patients with symptomatic epiphrenic diverticula associated with spastic oesophageal motility disorders.

**Results:** This video describes 2 cases showing the technique of ISM.

**Case 1:** 39-year-old female with a 2-year history of worsening dysphagia, chest and regurgitation of food. After a failed surgical diverticulotomy the patient was diagnosed with hypertensive peristalsis on manometry. She initially underwent a POEM procedure with some symptom resolution but developed dysphagia due to stenosis at the site of the diverticulum. An ISM was performed. The patient is symptom free 6 months later.

**Case 2:** 64-year-old female with a 12-month history of chest pain and regurgitation of food. Manometric assessment confirmed diffuse oesophageal spasm and diagnosis of BBS and abdominal computerised tomography confirmed this.

**Conclusion:** ISM is an effective and safe new novel technique for treatment of epiphrenic diverticula associated with spastic oesophageal motility disorders.

**Disclosure:** Nothing to disclose.

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**References**


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**VC06 INTRALUMINAL SUBMUCOSAL MYOTOMY FOR TREATMENT OF MID-oesophageal DIVERTICULA ASSOCIATED WITH OESOPHAGEAL MOTILITY DISORDERS**

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**Introduction:** Thoracic diverticula can be categorised according to their location; 1) mid-oesophageal, 2) epiphrenic. They are thought to arise either as a result of inflammation or in association with spastic motility disorders such as achalasia.

**Results:** This video describes 2 cases showing the technique of ISM.

**Case:** 1. Thirty-nine-year-old female with a 2-year history of worsening dysphagia, chest and regurgitation of food. After a failed surgical diverticulotomy the patient was diagnosed with hypertensive peristalsis on manometry. She initially underwent a POEM procedure with some symptom resolution but developed dysphagia due to stenosis at the site of the diverticulum. An ISM was performed. The patient is symptom free 6 months later.

**Conclusion:** ISM is an effective and safe new novel technique for treatment of epiphrenic diverticula associated with spastic oesophageal motility disorders.

**Disclosure:** Nothing to disclose.

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**References**


Conclusion: This case illustrates a rare presentation of tardive intrahepatic BCS initially mimicking an intrahepatic cholangiocarcinoma 10 years after liver transplantation. The follow-up of the patient gave the clue, and highlights ERCP management of BCS

Disclosure: Nothing to disclose

VC10  RECTAL BAND LIGATION FOR THE TREATMENT OF RADIATION PROCTITIS (WITH VIDEO)

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Introduction: Radiation proctitis (RP) is a complication occurring in 5% to 20% of patients undergoing pelvic radiotherapy (RT). Argon Plasma Coagulation (APC) is the endoscopic treatment of choice for CRP, as it is considered to be effective and well-tolerated.

Aims and Methods: 3 patients (74, 82 and 60 yrs) with a history of pelvic neoplasia underwent lower endoscopy that showed presence of haemorrhagic chronic radiation proctitis (RP). All 3 patients received treatment with rectal band ligation (RBL). We report 3 cases of patients with a history of pelvic neoplasia who developed RP following RT, who have been successfully treated with rectal band ligation (RBL).

Results: The procedures were well tolerated and no pain was referred during the RBL nor during the following days. 1 patient presented tenesmus, resolved by conservative treatment with topical drugs. During follow-up the 3 patients were asymptomatic and no further episodes of rectorrhagia were reported.

Conclusion: RBL is effective, safe and fast, and offers an alternative treatment for radiation proctitis, especially in the case of extensive disease.

Disclosure: Nothing to disclose

Abstract No: OP267

OP268  REDUCING PANCREATIC CYST SURVEILLANCE: DEVELOPMENT OF THE DUTCH AMERICAN RISK STRATIFICATION TOOL (DART-I) TO IDENTIFY IPMN WITH LOW RISK TO PROGRESS AND FULFILL RESECTION CRITERIA


1Erasmus University Medical Center, Gastroenterology & Hepatology, Rotterdam, Netherlands
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3New York University – Langone Medical Center, New York, United States
4Mayo Clinic Florida, Gastroenterology, Jacksonville, FL, United States
5Columbia University Medical Center, New York, United States
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Introduction: Neoplastic pancreatic cystic lesions are discovered with increasing frequency, with the most prevalent being the intraductal papillary mucinous neoplasm (IPMN). Most IPMNs will never evolve into malignancy, but because risk stratifying tools are lacking, the majority of cysts currently undergo redundant lifelong surveillance.

Aims and Methods: We aimed to develop a score chart to identify IPMN with low risk to progress and fulfill the resection criteria according to the 2012 international Fukuoka guidelines. We retrospectively reviewed the prospectively-managed database of three international academic institutions, containing patients with a pancreatic cystic lesion identified in the period 2003-2013. Patients were included if they had a presumed IPMN on imaging, without worrisome features or high-risk stigmata at baseline, as defined by the 2012 international Fukuoka guidelines, and were followed ≥12 months. Fulfilling resection criteria was

Abstract No: OP268

Table 1: Patient and cyst characteristics and final multivariable logistic regression model.

<table>
<thead>
<tr>
<th>Total (N = 876)</th>
<th>No progression (n = 760)</th>
<th>Progression (n = 116)</th>
<th>Coefficient</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center, Erasmus UMC</td>
<td>80 (9.1)</td>
<td>66 (8.7)</td>
<td>14 (12.1)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Columbia UMC</td>
<td>483 (55.1)</td>
<td>410 (53.9)</td>
<td>73 (62.9)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>313 (35.7)</td>
<td>284 (37.4)</td>
<td>29 (25)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>66 (11.2)</td>
<td>65 (10.9)</td>
<td>67 (12.8)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Male gender</td>
<td>322 (36.8)</td>
<td>272 (35.8)</td>
<td>50 (43.1)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>192 (21.9)</td>
<td>158 (20.8)</td>
<td>34 (29.3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>27 (4.9)</td>
<td>27 (4.8)</td>
<td>27 (5.3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Smoking ever</td>
<td>343 (39.2)</td>
<td>289 (38.0)</td>
<td>54 (46.6)</td>
<td>0.3308</td>
<td>1.39 (0.96-2.02)</td>
</tr>
<tr>
<td>Alcohol ever</td>
<td>373 (42.6)</td>
<td>320 (42.1)</td>
<td>53 (45.7)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Location dominant cyst, Head</td>
<td>381 (43.5)</td>
<td>329 (43.3)</td>
<td>52 (44.8)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Body</td>
<td>313 (35.7)</td>
<td>274 (36.1)</td>
<td>59 (50.6)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Tail</td>
<td>179 (20.4)</td>
<td>154 (20.3)</td>
<td>25 (21.6)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Multilocality</td>
<td>336 (38.4)</td>
<td>281 (37.0)</td>
<td>55 (47.4)</td>
<td>0.3930</td>
<td>1.48 (1.01-2.17)</td>
</tr>
<tr>
<td>Largest diameter, mean (SD), mm</td>
<td>12 (6.4)</td>
<td>11 (5.9)</td>
<td>17 (6.7)</td>
<td>0.1095</td>
<td>1.12 (1.08-1.15)</td>
</tr>
</tbody>
</table>

Values presented as n (%) unless otherwise indicated; NA, not available because not part of final prediction model

Aims and Methods: to evaluate the possible effect of ASA, ACEI/ARB and STAT use are ongoing.

analyses for subgroups of patients, cyst features and drugs dosage or length of use are ongoing.

Disclosure: Abstract previously presented at the EPC meeting

Abstract No: OP268

Table 1: Patient and cyst characteristics and final multivariable logistic regression model.
**Aims and Methods:** The study aimed to evaluate the occurrence of gastric neoplastic lesions and changes of OLGA/OLGIM scores in AG patients at 3-years endoscopic-histological follow-up. A total of 80 consecutive, newly diagnosed AG patients (77.5% F, median age 64.5 [29-87] years) followed-up 3 years after diagnosis were included. Each patient underwent gastroscopy with biopsies (Sydney System) at baseline and at 3 years follow-up. Among them, 25 (31.1%) were cured from H. pylori. At baseline OLGA scores 0, I, II, III, IV were observed in 6, 22 (27.5%), 43 (53.7%), 4 (5%), 0 patients, respectively. Extensive atrophy/intestinal metaplasia was present in 22 (26.3%) patients. At baseline 7.8% patients presented polyoid neoplastic lesions, all removed by snare polypectomy: 3 low-grade dysplasia (LGD) adenomas and 4 T1GC. The number of gastroscopies needed to be performed (NNS) to detect 1 case of gastric neoplastic lesion was expressed as the number of 3-years surveillance endoscopies by the number of detected neoplastic lesions.

**Results:** At 3-years follow-up 12 (7.5%) neoplastic lesions were detected: 12 (7.5%) LGD adenomas in 2 patients, 4 (5%) carcinoids in 4 patients (in 2 of them recurrent), no GC. The NNS was 13.3. OLGA and OLGIM scores were unchanged, increased and decreased in 58 (72.5%), 9 (11.3%) and 15 (18.8%), 13 (16.2%) and 16 (20%) patients, respectively.

The occurrence of gastric neoplastic lesions in patients with or without extensive atrophy/intestinal metaplasia was not different (p = 0.943 by chi-square test). Patients with extensive atrophy/intestinal metaplasia at baseline would have been considered eligible for surveillance, at 3-years follow-up only 1 LGD adenoma would have been detected, as the other neoplastic lesions 4 T1GC and the other LGD adenoma occurred in patients without extensive atrophy/intestinal metaplasia at baseline.

**Conclusion:** In AG patients, the 3-years endoscopic surveillance as proposed by MAPS seems satisfactory to early detect potential gastric neoplastic lesions. An increased OLGIM score in a low proportion of patients (10% and 18%). Extensive atrophy/intestinal metaplasia as eligibility criteria to offer surveillance in AG patients may be restrictive.

**Disclosure:** Nothing to disclose.

**References**
lymph node (LN) and distant metastasis did not differ between the groups. Overall, 5-year disease-free survival did not differ between the groups (88.6 vs. 93.8%; p = 0.259, 98.2 vs 100%; p = 0.484), but 5-year disease-free survival was lower in the observation group (73.5 vs 97.9%; p < 0.001). On multivariate analysis, presence of ulcer, large tumor size, tumor-positive lateral and vertical margins, lymphatic and venous invasion, additional surgical resection should be considered for the risk of residual tumor or LN metastasis.

Disclosure: Nothing to disclose

OP272 LOWER RISK OF ATROPHIC GASTRITIS IN MALT LYMPHOMA DESPITE H. PYLORI INFECTION

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Introduction: Atrophic gastritis and intestinal metaplasia are sequelae consequent of chronic H. pylori infection. H. pylori infection is a well-known risk factor for gastric adenocarcinoma and MALT lymphoma of the stomach. Atrophic gastritis and intestinal metaplasia increase the risk of gastric adenocarcinoma, and the relationship between gastric MALT lymphoma and atrophic gastritis-intestinal metaplasia has not been on the spot of interest. We here investigated the clinical characteristics of gastric MALT lymphoma and presence of atrophic gastritis and intestinal metaplasia.

Aims and Methods: Study was conducted by review of the electronic medical record of patients who were diagnosed with gastric MALT lymphoma at an academic institute, the Yeouido St. Mary’s Hospital, Seoul, Korea, from January 2001 to Mar 2018. Clinical characteristics and pathologic backgrounds including H. pylori-antibody positivity, atrophic gastritis and intestinal metaplasia were investigated.

Results: A total of 47 subjects were enrolled consecutively during the study period and analyzed retrospectively. The mean age was 57.19-year-old (range 36 – 85). The male to female ratio was 1.19 (25:21). Endoscopic appearances varied; thirteen subjects presented ulcerative mass (28.26%), 12 (26.00%) flat atypical patch of discoloration, 16 (34.78%) erosive patches, 2 (4.33%) multiple polypoid lesions 3 (6.52%) subepithelial tumor-like appearance. H. pylori infection was proved in 82.6 % (38/46). On histologic examination, background atrophic gastritis-intestinal metaplasia was accompanied by 28.26% (13/46). Serum pepsinogen I and II, as a serological marker for atrophy, was evaluated in 17 subjects. Only 5 of 17 (29.41%) showed compatible with atrophic gastritis (pepsinogen I/H ratio of less than 3).

Conclusion: The background mucosa of gastric MALT lymphoma differs from that of gastric adenocarcinoma in terms of atrophic gastritis-intestinal metaplasia. Less than 30% of gastric MALT lymphoma accompanied background atrophic gastritis, which may be a confounding risk factor. We will prove the unmatched comparison between patients with gastric adenocarcinoma and MALT lymphoma.

Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018
08:30–10:00

The broad spectrum of IBD management – Room G

OP273 EARLY VERSUS LATE INTERVENTION WITH ANTI-TNF-ANTIBODIES IN CROHN’S DISEASE: EFFECT ON MUCOSAL HEALING, DEVELOPMENT OF STRICTURES AND NEED FOR RESECIVE SURGERY. A RETROSPECTIVE COHORT ANALYSIS

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2Helios Amper-Klinikum Dachau, Dachau, Germany
3Synxis Research Center, Munich, Germany
4Alanta Health Service GmbH, Hemm, Germany
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6IBD Center Munich, Munich, Germany

Contact E-Mail Address: thomas.ochsenkuehn@isarklinikum.de

Introduction: Anti-TNF-antibody therapy is one of the most potent treatments in Crohn’s disease (CD) for active disease as well as in maintenance therapy, and it might alter the course of disease by preventing irreversible bowel damage and fulminating associated complications. Therefore, since its introduction, anti-TNF-antibodies (TNF-inhibitors) have been used by gastroenterologists progressively earlier in the course of the disease.

Aims and Methods: We aimed to assess the effect of early intervention of TNF-inhibitors in CD patients of the Munich IBD Center on mucosal healing, clinical remission, development of strictures and need for surgery as compared to late intervention within an observation period of 2 years. Early intervention was defined as introduction of TNF-inhibitors within 24 months after first diagnosis of CD and late intervention was defined as intervention after 24 months. In this retrospective cohort analysis we included data from 242 patients from 2007 to 2015 who had received either infliximab (IFX) or adalimumab (ADA) for at least 2 years. Chi2 and T-tests were used for statistical analysis to assess the rates of mucosal healing, clinical remission, stricture disease and need for resective surgery within 2 years after the introduction of TNF-inhibitors. Endoscopic findings of the last ileocolonoscopy before and the first ileocolonoscopy after introduction of TNF-inhibitors provided data on mucosal healing and strictures. Clinical remission was defined as CDAI score of less than 150 points.

Results: A total of 210 treatment with TNF-inhibitors and were assigned to the early intervention group: 45.8% received IFX, 10.7% ADA and 45.5% where switched from IFX to ADA or vice versa. 152 patients met criteria for the late intervention group: 60.0% received IFX, 3.8% ADA and 35.7% were switched from IFX to ADA. Both groups were comparable to sex, genetic susceptibility (NOD2/CARD15), extraintestinal manifestations, presence of bowel strictures and disease activity at the time of introduction. Patients of the early intervention group were younger at start of TNF-inhibitors (26 vs. 32 years; p = 0.001) and more often suffered upper GI- manifestations (23% vs. 3%; p < 0.001). The early intervention group had received less corticosteroids (p = 0.014), 5-ASA (p < 0.001), azathioprine (p < 0.001) and methotrexate (p = 0.057).

Within an observation period of 2 years, patients of the early intervention group never achieved higher mean disease activity rates than patients of the late intervention group (47.5% vs. 25.0%; p = 0.005), they also developed significantly less bowel strictures (10.2% vs. 28.4%; p = 0.008). The combination of absence of mucosal healing and presence of strictures was found significantly more often in the late intervention group (79.5% vs. 53.3%; p = 0.001).

Clinical remission rates 24 months after the introduction of TNF-inhibitors did not differ between the 2 groups. (89.4% vs. 87.9%, p = 0.737).

Within 2 years after introduction, less patients in the early intervention group underwent surgery, however the difference was not significant (17.8% vs. 26.9%, n = 16 vs. n = 41, p = 0.103), possibly due to the small size of the group and the short observation period of only 2 years.

In Crohn’s disease, early introduction of TNF-inhibitors within 2 years after diagnosis is associated with higher rates of mucosal healing and lower rates of complications such as bowel strictures when compared to late intervention. It may also reduce the risk of the need for surgery. We conclude that anti-TNF-antibody therapy could alter the course of disease and prevent irreversible bowel damage.

Disclosure: Thomas Ochsenkühn has received lecture fees, unrestricted travel grants and honoraria for advice from Abbvie, Biogen, Celltrion, Janssen, MSD, Mundipharma, R-Biopharm, Sandofi, Shields, Shire, Stada, and Takeda. Stephanie Howaldt has received lecture fees, unrestricted travel grants and honoraria for advice from Biogen, Janssen, MSD, Mundipharma, Shield, R-Biopharm, Pfizer and Takeda. Fabian Schnitzler has received honoraria from Abbvie and MSD.

Contact E-Mail Address: nick.burr@nhs.net

Introduction: Colorectal cancer (CRC) risk is increased in those with inflammatory bowel disease (IBD). Guidelines advocate surveillance colonoscopy for patients with longstanding IBD. Post-colonoscopy colorectal cancer (PCCRC) is a key quality indicator of colonoscopy. There is limited data exploring the rate of PCCRC in those with IBD and potential risk factors associated with IBD-related PCCRC.

This study explored national and individual hospital rates of IBD-related PCCRC in England since 2006. Further analysis explored potential associations with IBD-related PCCRC in order to inform future quality improvement interventions.

Aims and Methods: We identified all those who had undergone a colonoscopy between 1/1/2006 and 31/12/2012 and developed a CRC before 31/12/2015 using linked national Hospital Episode Statistics and National Cancer Registration data. CRC cases were identified by relevant ICD-10 codes. Using international consensus guidelines, the rate of PCCRC within those with IBD and potential risk factors associated with IBD-related PCCRC.

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This study explored national and individual hospital rates of IBD-related PCCRC in England since 2006. Further analysis explored potential associations with IBD-related PCCRC in order to inform future quality improvement interventions.
Introduction: Histological healing may be the ultimate therapeutic goal in ulcerative colitis (UC). Higher vedolizumab trough levels during induction treatment have been associated with better outcomes in UC patients. The association between vedolizumab trough levels and histological healing during maintenance therapy in UC is unknown.

Aims and Methods: In this single-center, retrospective cohort study, we aimed to investigate the association between vedolizumab trough levels and histological healing during maintenance therapy in UC, and to identify potential factors associated with histological healing. Between June 2014 and March 2018, all consecutive patients with moderate-to-severe UC on vedolizumab maintenance therapy who had a histological evaluation and underwent therapeutic drug monitoring within 3 months of this evaluation, were included. Per event analysis was performed. Histological healing was defined as Nancy histological index ≤ 1. Pathologists were blinded to the results of the therapeutic drug monitoring.

Results: 35 histological samples from 31 patients (n = 27 with 1 histological sample; n = 4 with 2 histological samples) were analyzed. Mean (standard deviation) time between histological evaluation and therapeutic drug monitoring was 18.5 (9-26.6) days. Histological healing was found in 18/35 (51.4%) of assessments (n = 15 with Nancy histological index of 0; n = 3 with Nancy histological index of 1). Median (interquartile range) serum vedolizumab trough levels were higher in the group with histological healing compared with the group without histological healing (31.5 (25.4-49.1) µg/mL vs. 15 (9-26.6) µg/mL, p = 0.02). The higher vedolizumab trough levels were associated with higher rates of histological healing (p = 0.004; Table 1). A cut-off vedolizumab trough level of 25 µg/mL predicted histological healing with a sensitivity, specificity, and negative predictive value and negative predictive value of 77%, 71%, 74% and 75%, respectively, leading to an area under the receiver operating curve of 0.62 (95% confidence interval 0.58–0.92; p = 0.006).

Conclusion: This is the first study looking at the association between vedolizumab trough levels and histological healing in UC. Histological healing rates were significantly greater in patients with the highest vedolizumab trough levels during maintenance therapy in UC. A vedolizumab trough level threshold of 25 µg/mL was found most optimal to predict histological healing.

Disclosure: Nothing to disclose
Introduction: Score information on the effectiveness and safety of vedolizumab (VDZ) in inflammatory bowel disease (IBD) is in clinical practice available.

Aims and Methods: We aimed to evaluate the effectiveness and safety of VDZ in IBD. Patients of the ENEIDA registry with active IBD that received VDZ were included. Response was defined based on Harvey-Bradshaw index (HBI) in IBD. Patients of the ENEIDA registry with active IBD that received VDZ were included. 45 [Table 1. Adverse events during vedolizumab treatment.]

Conclusion: Over 60% of IBD patients respond to VDZ treatment, even in a refractory cohort. A relevant proportion of patients discontinue the treatment over time, mainly due to loss of response. CD and disease burden impair both short and long-term response. VDZ seems to be safe in clinical practice.

Table 1. Adverse events during vedolizumab treatment.

<table>
<thead>
<tr>
<th>Event</th>
<th>N</th>
<th>Rate per 100-patient-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>14</td>
<td>2.6</td>
</tr>
<tr>
<td>Sepsis</td>
<td>6</td>
<td>1.3</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Chickenpox</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Herpes-zoster reactivation</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Otitis</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Skin reactions</td>
<td>6</td>
<td>1.3</td>
</tr>
<tr>
<td>Infusional reactions</td>
<td>5</td>
<td>0.9</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>Bowel perforation</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Deaths</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Arthritis</td>
<td>2</td>
<td>0.4</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Fever of unknown cause</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Neurological symptoms</td>
<td>1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

[Table 1. Adverse events during vedolizumab treatment.]
patients at low risk. We attempted to develop a model to detect patients at risk for early surgery, defined as requiring surgery within 2 years from diagnosis. Aims and Methods: A prospective multicentre inception cohort of newly diagnosed children with CD was established, with progress followed to 2 years post-diagnosis. Phenotypic characteristics, measures of disease severity and inflammation, as well as serological markers were measured at baseline and week 12, and follow-up data were collected at 8, 12, 26, 52, 78, and 104 weeks. Patients undergoing surgery for disease related complications were recorded. Chi-square automatic interaction detection (CHAID) algorithm was used to develop a model with prespecified surgical complications.

Results: A total of 285 patients had data collected with 31(10.9%) needing surgery within 2 years. Multivariate analysis identified strictureing disease at baseline (OR 5.26, 95% CI 2.02–13.67 (p = 0.0001)), and Paediatric Crohn’s Disease Activity Index (PCDAI) > 100 (OR 1.03, 95% CI 1.00–1.07 (p = 0.005)), together with low C-reactive protein (CRP) (OR 0.82, 95% CI 0.70–0.98, (p = 0.025)) at week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 modulated the risk for surgery even if strictureing disease was present at diagnosis, while immunomodulators only reduced risk for surgery at follow-up. In our CHAID model, a patient without strictureing disease was present at diagnosis, while immunomodulators only reduced risk for clinical remission by week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 to be key predictors of the risk for surgery within 2 years. Achieving clinical remission by week 12 to be key predictors of the risk for surgery within 2 years.

Disclosure: Nothing to disclose.

OP281 MICROSCOPIC POSITIVE TUMOR MARGIN DOES NOT INCREASE THE RATE OF RECURRENCE IN ENDOSCOPIC RESECTED GASTRIC MUSCULAR TUMORS COMPARED TO NEGATIVE TUMOR MARGIN

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Introduction: The endoscopic resection of Gastrointestinal Mesenchymal Tumors (GIMTs) is widely accepted due to its minimal-invasiveness. However, a major concern for endoscopic resection is its high rate of positive microscopic margin which was thought to be related with a higher risk of recurrence. We herein designed this study to examine the effect of R1 endoscopic resection for prognosis of GIMT, featuring a large retrospectively maintained endoscopic resection cohort with long follow up and specimen reevaluation by a single pathologist with expertise on GIMT.

Aims and Methods: This study aimed to find out whether the positive margin affects the recurrence rate of gastric GIMT and the factors associated with positive margin. The patients with gastric GIMTs were recruited in the prospective cohort from January 2006 to December 2017. Indications for endoscopic resection were as follows: (1) GIST or suspected GIST > 2 cm in size or < 2 cm but with rapid growth or high-risk features (e.g. nuclear atypia, high mitotic rate, heterogeneous echogenicity); (2) non-GIST mesenchymal tumors > 2-2.5 cm in size, with rapid growth or high risk features; (3) symptomatic gastric submucosal lesions; (4) undiagnosed gastric submucosal lesions in young patients for whom the risk of resection might be outweighed by the benefit of avoiding lifetime surveillance of these lesions (after careful discussion and informed consent). Clinical and pathological features, endoscopic, and follow-up data were collected and analyzed.

Results: 777 patients were included in the study. All tumors were removed along pseudocapsule without macroscopic residual (ER0) and the median tumor size was 15.2 mm (range 3-100 mm). Pathological evaluation revealed that 37/47(7.7%) gastrointestinal stromal tumors (GISTs). The rate of microscopic R1 resection was 47.0% (443/777). On stepwise multivariate analysis, a significantly increased incidence of R1 resection was recorded in the GISTs (OR 11.13, 95% CI 3.00–41.37). In the univariate analysis of GIST, the univariate analysis revealed that EFTR achieved a higher rate of R0 resection (OR 0.56, 95% CI 0.31–1.00) while it was proved insignificant on stepwise multivariate analysis. Local recurrence occurred in 2 patients during a mean follow-up time of 34.2 months. The recurrence rate of R0 and R1 groups was statistically insignificant (p = 0.841).

Conclusion: Endoscopic resection is a feasible option for the resection of gastric GIMT and has minimal risk of recurrence after a mean follow-up of 34.2 months. The rate of R1 resection is high but is not related to a high rate of recurrence compared to R0 resection. The ER0 resection is sufficient for gastric GIMT.

Disclosure: Nothing to disclose.

Wednesday, October 24, 2018

The truth is under the microscope – Room 1.61/1.62

08:30–10:00

OP282 RISK STRATIFICATION OF SYMPTOMATIC PATIENTS SUSPECTED OF COLORECTAL CANCER USING FEALED BIOMARKERS (FAEAL IMMUNOCHEMICAL TEST AND FAEAL CALPROTECTIN) AND URINARY VOTILE ORGAN COMPOUNDS

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Introduction: Over the last decade neoadjuvant chemoradiotherapy (nCRT), preferably the CROSS regimen (carboplatin/paclitaxel + 41.4 Gy radiotherapy), has become standard of care for resectable oesophageal cancer in The Netherlands. About 20% to 50% of patients achieve a pathological complete response (pCR) after nCRT. A pCR is associated with improved survival and the role for surgery is questioned in these patients.

Aims and Methods: The aim of this population-based cohort study was to investigate factors associated with pCR after nCRT and surgery. All oesophageal cancer patients treated with nCRT followed by oesophagectomy in the period 2009-2015 were identified from the Nationwide Netherlands Cancer Registry. Patients with unknown tumour response were excluded. Pathological tumour response was categorized as pCR (ypT0N0) and non-pCR (ypT0N+ or ypT1N0N+ and ypT1N+N+). The 3-year survival rates were compared with log-rank analysis. Univariable and multivariable logistic regression models were used to investigate the association between clinico-pathological variables and pCR. The effect of chemotherapy schedule and radiotherapy dose on pCR were analysed in a subgroup of patients from whom details on neoadjuvant treatment were available. Multivariable Cox regression on overall survival within the group of patients with pCR was performed.

Results: A total of 3533 patients were included and 841 patients (24%) had a pCR (19% in adenocarcinoma and 41% in squamous cell carcinoma). Patients with pCR had higher 3-year survival rate compared to non-pCR patients (68% vs. 48%, p < 0.001). In the non-pCR group, ypT1N+N+ patients had the lowest 3-year survival rate, followed by ypT0N+ and ypT1N0N (respectively, 30%, 52% and 60%, p < 0.001). In multivariable analysis age above 70 years (OR 1.2, 95% CI 1.0–1.5), squamous cell histology (OR 3.0, 95% CI 2.6–3.6), CT1-2 (OR 2.7, 95% CI 1.9–3.7), CT3 (OR 2.4, 95% CI 1.7–3.3), NM (OR 0.74, 95% CI 0.6–0.9) and EN (OR 0.3, 95% CI 0.1–0.7) were associated with higher or lower chance of pCR. In subgroup analysis (N = 668), completion of the CROSS chemotherapy cycles (complete vs. incomplete, p = 0.86) and radiotherapy dose (41.4 Gy vs. > 41.4 Gy) were not associated with pCR. C-reactive protein was inversely associated with overall survival in patients who achieved pCR: were age above 70 years (HR 1.4, 95% CI 1.0–1.7) and less than 10 dissected lymph nodes (HR 1.4, 95% CI 1.0–1.9).

Conclusion: Pathological tumour response is not only determined by treatment-related (e.g. number of dissected lymph nodes) factors, but also by patient-related (e.g. age) and tumour-related (e.g. histology and clinical stage) factors. Completing recommended chemotherapy and/or radiotherapy schedules was not related to pCR in our cohort.

Disclosure: Nothing to disclose.
and urinary volatile organic compounds (VOCs) in patients presenting with lower gastrointestinal symptoms. In this prospective single-centre cohort study 1016 symptomatic patients with suspected CRC referred by general practitioners to secondary care were recruited. A total of 562 patients, who returned stool samples for FIT and FCP and urine samples for urinary VOC measurements and colorectal biopsies, were included in the final statistical analysis. Quantitative FIT was performed on automated HM-JACKiCarc analyser and FCP was measured using the EIA Calprotectin fluorimunoassay on the automated ThermoFisher ImmunoCap 250 analyser. A commercial gas analysis instrument (Lonestar Field Asymmetric Ion Mobility Spectrometry (FAIMS), Owlstone Medical, Cambridge, UK), based on ion mobility spectroscopy (IMS), was utilized to analyse VOCs emanating from urine samples. Various statistical parameters were calculated for each clinical group with 95% confidence intervals (CIs).

Results: The sensitivity and specificity for CRC using FIT were 0.80 (CI: 0.66–0.93) and 0.95 (CI: 0.91–0.95) respectively. The negative predictive value (NPV) was 0.99 (CI: 0.98–1.0). Using urinary VOCs the sensitivity and specificity were 0.63 (CI: 0.46–0.79) and 0.70 (CI: 0.59–0.87) respectively and the NPV was 0.96 (CI: 0.94–0.98). However, for those with FIT negative CRC (false negatives), adding urinary VOCs resulted in sensitivity of 0.97 (CI: 0.90–1.0) and specificity of 0.72 (CI: 0.60–0.76) with NPV of 1.0 (CI: 0.90–1.0).

Conclusion: Faecal biomarkers are useful in excluding CRC patients in symptomatic population with NPV of 99% for FIT. The addition of urinary VOCs showed promise as a second stage test improving FIT performance with NPV of 100% for CRC. It is envisaged that both these non-invasive tests (FIT and urinary VOCs) can be requested within primary care and analysed within a central laboratory at low cost to guide secondary care referral patterns.

Discussion: Educational and financial costs in the reproduction of Thermo Fisher Scientific Ltd. CT has provided educational lectures on behalf of Thermo Fisher Scientific Ltd. All remaining authors disclose no conflicts of interest.

References

OP283 CLINICOPATHOLOGICAL STUDY OF LATERALLY SPREADING TUMORS OF THE COLORECTUM
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Introduction: Laterally spreading tumors (LSTs) of the colorectum are classified into the following four subtypes according to their morphology; granular homogenous type (LST-GH), granular nodular mixed type (LST-GM), non-granular flat elevated type (LST-NFG), and non-granular pseudo-depressed type (LST-NPGD). Clinical features of each subtype of LSTS have not been fully evaluated.

Aims and Methods: The aims of this study was to clarify the clinicopathological features of colorectal LSTs focusing on their subtypes. We reviewed clinical charts and surgical pathology files of 624 endoscopically resected specimens during January 2007 and December 2017 at our institution. A total of 490 LSTs were detected. We examined the clinical features (mean age, male to female ratio, size, location, Incidence of concomitant carcinoma) according to their subtypes.

Results: Of these 490 lesions, a total of 180 (36.7%) were LST-GH, 43 (8.8%) LST-GM, 233 (47.6%) LST-NFG, and 34 (6.9%) LST-NPGD. Mean age of patients with each subtype was 68.6 years old for LST-GH, 67.0 for LST-GM, 67.2 for LST-NFG, and 66.8 for LST-NPGD. Male to female ratio (M:F) was 1.31 for LST-GH, 1.87 for LST-GM, 1.84 for LST-NFG, and 1.62 for LST-NPGD. Mean size of LST-GH (20.8mm) and LST-GM (25.1mm) were significantly larger than that of LST-NFG (16.7mm) and LST-NPGD (15.3mm). All subtypes were detected predominantly in the proximal colon.

Incidence of concomitant carcinomas in LST-GH, LST-GM, LST-NFG, and LST-NPGD were 17.8% (32 out of 180), 44.2% (19 out of 43), 15.9% (37 out of 233), and 52.9% (18 out of 34), respectively. Incidences of concomitant submucosal carcinoma in LST-GH, LST-GM, LST-NFG, and LST-NPGD were 0% (0 out of 180), 14.0% (6 out of 43), 2.1% (5 out of 233), and 20.6% (7 out of 34), respectively.

Conclusion: Each subtype of LSTS has distinct clinical features. LST-GM and LST-NPGD has provided high-risk polyps than other subtypes. Especially LST-NPGD has the highest risk of invasive carcinoma regardless of its size. Therefore we should carefully detect these lesions and choose appropriate treatment according to the subtypes.

Disclosure: Nothing to disclose.

Wednesday, October 24, 2018
Upper GI sensitivity and symptom generation – Room N1

OP285 GENETIC VARIATION IS ASSOCIATED WITH WORSE AFFECT SCORES, HIGHER SYMPTOM BURDEN, AND MUCOSAL INJURY IN PATIENTS WITH ESOPHAGEAL SYMPTOMS
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Introduction: Genetic variation has been linked to increased symptom burden with esophageal symptoms and functional gastrointestinal (GI) disorders through centrally mediated mechanisms. We evaluated relationships between symptom burden and SNPs in GNB3 (G-protein-coupled receptor in the brain-gut axis), ADRB2 (mediator of stress response), ADAMTS17 (extracellular matrix protein involved cellular junction permeability), SGK3 (treatment response to venlafaxine and susceptibility to anxiety), and FAAH (neuroendocrine regulation, associated with anxiety, IBS, depression), in an enriched population with esophageal symptoms.
Introduction: Minimal inflammation has been reported in functional gastrointestinal disorders (FGID), but the causes of immune activation are largely unknown. Alterations of the stool microbiota have been reported in FGID patients, suggesting specific microbe-host interactions might be a key driver of immune activation. However, these relationships are virtually unexplored in the small intestine. Thus, we aimed to characterise the links between alterations in immune function, the duodenal mucosa-associated microbiome (d-MAM), and gastrointestinal symptoms in FGID patients.

Aims and Methods: 148 patients undergoing endoscopy were recruited in total. GI symptoms were assessed by a standardised questionnaire (SAGIS). Based on all clinical data, the cohort was divided into FGID (n = 88) and non-FGID control patients (n = 60) without relevant structural abnormalities; controls including a positive FOBT and/or iron deficiency anaemia test. Peripheral Blood Mononuclear cells (PBMCs) were isolated from peripheral blood using ficoll density gradient centrifugation. Lamina propria (LP) cells were isolated from duodenal biopsies by collagenase. T-cells in PBMCs and lamina propria were sequenced using Illumina MiSeq technology. Bioinformatics analyses were performed using QIIME and CytoSuite with statistical significance assessed by T-test or Spearman correlation.

Results: There was a significant increase of CD4 gut-homing T-cells in peripheral blood of FGID patients vs controls (p < 0.015). The increase of peripheral CD4 gut-homing T-cells does not lead to an increase of this population in the duodenal LP. Instead, there was positive correlation between effector memory (TEM) cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients.

Conclusion: Increment in TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients. TEM-cells in duodenal LP, are positively correlated to symptom severity in FGID patients.
**OP289** **EXPLORATORY STUDY: COGNITIVE RESTRAINT ASSOCIATED WITH BASELINE VAGAL TONE AND PATHOPHYSIOLOGICAL RESPONSE TO INTERCEPTIVE STIMULUS IN HEALTHY LEAN ADULTS

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**Introduction:** The vagus nerve carries sensorimotor information between the brain and gastrointestinal (GI) tract. Vagal tone plays an important role in the regulation of appetite1 and is associated with a range of positive health behaviours. Upon consumption of a meal, internal afferent signals are conveyed to the brainstem depending on the size and nutrient composition of the meal. These are integrated with external sensory information before descending and modulatory pathways elicit an efferent motor response, accompanied by changes in appetite-related sensations. Differences in vagal tone may moderate periprandial responses to interceptive and exteroceptive stimuli and influence eating behaviour. Previously, an interaction between intragastic infusion of fatty-acid (FA) and negative mood induction has been reported to effect behavioural and neural responses in healthy lean subjects.2,3

**Aims and Methods:** The aim of this pilot study was to investigate the relationship between vagal tone and eating behaviour and the effect of the putative interaction between FA and negative mood on appetite-related sensations and food consumption. 10 healthy subjects (3 male, median [range] age 29 [22-32] BMI 22.5 [19.4-24.0]) completed the Three-Factor Eating Questionnaire (TFEQ) and 4 in a 2x2 crossover design. Cardiac vagal tone (CVT), affective state and appetite-related sensations were assessed at baseline and following intragastric infusion of 240 ml 0.05 mol/L C18:1 FA (‘fat’ group) or 0.05 mol/L FA:0-C18:1 (‘fat:sad’ group) at 3 min pre-infusion (-3 min), negative mood induction (‘sad’ condition vs neutral) began, up to 30min post-infusion (PI). Subjects were offered an ad libitum buffet and instructed to eat until comfortably full (40-70min PI). Spearman’s ρ was calculated for baseline CVT against TFEQ scores for cognitive restraint (CR), emotional eating (EE) and unrestrained eating (UE) and the main effect of ‘fat’ or ‘fat:sad’ was tested with ANOVA including ‘condition’ as a within-subject variable for the following (compared to -3min baseline): Δ CVT, Δ fullness (1-100 visual analogue scale), VAS, Δ nausea (1-9 self-assessment nausea, SAM) and Δ negative mood (1-9 SAM) at 20min PI controlling for baseline values; and total energy (kcal) and total fat (g) consumed at 40-70min PI controlling for baseline hunger rating.

**Results:** Baseline CVT (median: 14.12 LVS, range: 2.9–26.8) was negatively correlated with TFEQ-CR (r = -0.74, p = 0.013) but not UE (r = -0.25, p = 0.51) or EE (r = 0.01 p = 0.98). The effect of ‘fat’ on Δ CVT (20min vs -3min PI) was significant (F(1) = 11.13, p = 0.003) and the interaction term approached significance (F(1) = 3.14, p = 0.09). Controlling for baseline ratings, there was no significant effect of either ‘fat’, ‘sad’ or ‘fat:sad’ on Δ fullness, Δ arousal or Δ negative mood. Baseline hunger had a significant effect on the amount of fat consumed (r = -0.74, p = 0.013) and there was no significant effect of condition or interaction on total energy or fat consumption.

**Conclusion:** Relatively high baseline CVT and the strong correlation with CR in this lean sample supports the association between vagal tone and positive cognitive restraint. Small sample size, low dose and volume of fatty-acid infused, and sub-tlety of the mood induction could account for the limited effect of the experimental interventions on subjective ratings and food consumption. However, this exploratory study suggests that CVT could be a non-invasive biomarker of sub-clinical physiological responses. Future work will investigate the role of circulating gut peptides and the relationship between vagal tone and GI motility.

**Disclosure:** Nothing to disclose

**References**

then measured PT for the second time (T00). Only participants with PT drop of ≥ 6 mA (milliampere) measured at (T60) were considered to be sensitised and therefore recruited. After that, participants were randomised in a blinded crossover design to receive either transcutaneous auricular electrical vagal nerve stimulation (tVNS) (pulse width: 250 µs, 25 Hz, cycle: 30 s on, 30 s off), or sham stimulation with the same parameters, for 30 minutes (T60-T90). PTs were measured both, immediately (T00) and 30 min after the end of active/sham stimulation (T120). PTs were analysed using a general linear model for repeated measures with PTs as dependent variables, active/sham as factor and the difference in the initial degree of sensitisation between visits as a covariate (IBM SPSS 23, USA).

**Results:** 18 participants (8 male, mean age 26.6 ± 6.3 years) sensitised and were included. When compared to sham, tVNS significantly increased PT at the end of the stimulation; 19.4 mA (± 21), 2.7 mA (± 12.1), p = 0.01, 95% CI [4.16–27.96]. The effect of tVNS on PT remained significant 30 min after the end of stimulation; 22.5 (± 23.8) vs. 7.69 (± 18.44), p = 0.049, 95% CI [0.079–29.77].

**Conclusion:** Our results suggest that tVNS reverses experimental acid-induced oesophageal pain hypersensitivity in healthy participants. Future studies are warranted to replicate this effect in patients with reflux hypersensitivity and other disorders where pain hypersensitivity is suspected.

**Disclosure:** Nothing to disclose

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**Abstract No: OP291**

**Table 1: Odds Ratio of Early-Onset CRC vs. Later-Onset CRC and the Control Cohort**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Early-Onset CRC</th>
<th>Later-Onset CRC</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
<th>Control</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>2800</td>
<td>32320</td>
<td>0.91 (0.87–0.96)</td>
<td>0.0011</td>
<td>4931120</td>
<td>1.34 (1.27–1.41)</td>
<td>0.0001</td>
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<tr>
<td>Female</td>
<td>2910</td>
<td>30690</td>
<td>1.09 (1.04–1.16)</td>
<td>0.0011</td>
<td>6869290</td>
<td>0.75 (0.71–0.79)</td>
<td>0.0001</td>
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<tr>
<td>Caucasian</td>
<td>3880</td>
<td>52330</td>
<td>0.43 (0.41–0.46)</td>
<td>0.0001</td>
<td>6947160</td>
<td>1.48 (1.41–1.57)</td>
<td>0.0001</td>
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<tr>
<td>African-American</td>
<td>860</td>
<td>826</td>
<td>1.18 (1.09–1.27)</td>
<td>0.0001</td>
<td>1462790</td>
<td>1.25 (1.17–1.35)</td>
<td>0.0001</td>
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<tr>
<td>Asian</td>
<td>110</td>
<td>1380</td>
<td>0.88 (0.72–1.07)</td>
<td>0.1905</td>
<td>258990</td>
<td>0.88 (0.72–1.06)</td>
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<td>3060</td>
<td>24490</td>
<td>1.82 (1.72–1.92)</td>
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<td>2317490</td>
<td>4.73 (4.49–4.49)</td>
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<td>Rectal Pain</td>
<td>170</td>
<td>1260</td>
<td>1.5 (1.28–1.77)</td>
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<td>482000</td>
<td>7.48 (4.82–8.72)</td>
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<td>Altered Bowel Function</td>
<td>1440</td>
<td>14610</td>
<td>1.12 (1.05–1.19)</td>
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<td>6804200</td>
<td>5.51 (5.19–5.85)</td>
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<td>790</td>
<td>7960</td>
<td>1.11 (1.03–1.20)</td>
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<td>190310</td>
<td>9.83 (9.12–10.6)</td>
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<td>Weight Loss</td>
<td>490</td>
<td>7800</td>
<td>0.66 (0.60–0.73)</td>
<td>0.0001</td>
<td>147250</td>
<td>7.43 (6.77–8.15)</td>
<td>0.0001</td>
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<td>Family History of Cancer</td>
<td>1360</td>
<td>9400</td>
<td>1.78 (1.67–1.90)</td>
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<td>368120</td>
<td>13.66 (10.97–12.39)</td>
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<td>Family History of GI Malignancy</td>
<td>840</td>
<td>4300</td>
<td>2.36 (2.18–2.55)</td>
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<td>70560</td>
<td>28.67 (26.64–30.86)</td>
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<td>470</td>
<td>1.41 (1.31–1.51)</td>
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<td>Tobacco Use</td>
<td>3600</td>
<td>42360</td>
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<td>4838172</td>
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<td>24850</td>
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<td>710</td>
<td>7270</td>
<td>1.09 (1.00–1.18)</td>
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<td>395260</td>
<td>4.1 (3.79–4.43)</td>
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<td>BMI &gt; 30</td>
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<td>36770</td>
<td>1.14 (1.08–1.20)</td>
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<td>4202120</td>
<td>2.88 (2.74–3.04)</td>
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<td>41740</td>
<td>2.26 (2.13–2.39)</td>
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<td>1534060</td>
<td>2.86 (2.73–3.03)</td>
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<td>Hyperlipidemia</td>
<td>1090</td>
<td>33960</td>
<td>0.20 (0.19–0.22)</td>
<td>0.0001</td>
<td>1062040</td>
<td>2.39 (2.23–2.55)</td>
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<td>Polyp History</td>
<td>630</td>
<td>8970</td>
<td>0.75 (0.69–0.81)</td>
<td>0.0001</td>
<td>155640</td>
<td>9.28 (8.54–10.08)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

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**OP292: INCREASING INCIDENCE OF COLORECTAL CANCER IN YOUNG ADULTS IN EUROPE**


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**Introduction:** In the North American population, colorectal cancer (CRC) incidence for individuals older than 50 years steadily declines, but an opposite trend has been suggested among young adults. In Europe, trends in CRC incidence among younger individuals are lacking.

**Aims and Methods:** The aim of this study was to analyze trends in incidence rates of young adults with CRC in the European Union over the last 25 years.

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**Disclosure:** Nothing to disclose
Data on age-related incidence of CRC were retrieved from national European cancer registries over a time-frame of at least 10 years, ranging from 1990 until 2016. Young adults, defined as people between 20 to 49 years of age, with confirmed colon or rectal cancer were included. 5-year incidence and mortality rates were calculated, expressed per 100,000 person-years and corrected for age and population trends. Rates were calculated using a Poisson regression analysis, and expressed as annual percent change (APC) with 95% confidence intervals. Results: Data from 20 European countries were included. In adults aged 20 to 39 years of age, the overall CRC incidence rate increased by 4.9% (95% CI: 3.9–5.9) annually since 2005. For colon cancer, incidence rate increased in men by 2.2% (95% CI: 1.4–3.0) per year from 1990-2010 and with an even higher increase of 7.3% (95% CI: 2.3–12.5) per year from 2010-2016. In women the incidence rate increased by 1.5% (95% CI: 0.4–2.7) per year from 1990-2008 and increased even more dramatically by 8.9% (95% CI: 4.8–13.2) per year from 2008-2016. Incidence rate of rectal cancer increased for both men and women, respectively 2.4% (95% CI: 1.9–3.0) and 2.0% (95% CI: 1.2–2.8) per year.

In adults aged 40 to 49 years, the overall CRC incidence rate increased by 1.2% (95% CI: 0.6–1.8) per year from 2002. The incidence rate of colon cancer increased in men by 0.5% (95% CI: 0.1–0.8) per year, and also in women by 0.5% (95% CI: 0.0–1.0) per year. Incidence rate of rectal cancer in men decreased by 3.4% (95% CI: 2.4–4.3) per year from 1990-1997, and then increased from 1997-2016 by 1.6% (95% CI: 0.8–2.3). Rectal cancer in women increased by 8.3% (95% CI: 4.7–12.0) per year in 1990-1996, and remained stable from 1996-2016.

The overall age adjusted mortality rates for CRC did not show a significant trend in adults 20 to 39 years of age. However, mortality rates in adults 40 to 49 years of age decreased by 3.8% (95 % CI: -4.4– -3.2) per year from 1990-2006, and remained stable from 2006-2016.

Conclusions: There is an increased incidence rate in CRC in young adults in Europe. The cause for this trend is still unknown. Awareness and future studies to elucidate causes for this trend are needed and may help to set up screening strategies to prevent and detect these cancers at an early and curable stage.

Disclosure: Nothing to disclose.

OP293 SCREENING FOR COLORECTAL CANCER BASED ON POLYGENIC RISK AND FAMILY HISTORY

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Introduction: There is a growing body of evidence that common, low-risk genetic variants play a significant role in colorectal cancer (CRC) risk due to their relatively high prevalence in the population. When combined with family history, they have been shown to improve risk stratification of the general population. We aimed to investigate the impact of risk-based screening (RBS) for CRC, and compare it, in terms of effectiveness and cost-effectiveness, to uniform biennial screening.

Methods: We used the Microsimulation Screening Analysis-Colon (MISCAN-Colon) to model the effects and costs of screening for CRC in a risk stratified Australian population aged 40-74 years. Individuals were placed into one of 5 risk groups based on relative risk (very low, low, average, high, very high) which was determined by their polygenic risk profile and family history of CRC. Screening strategies varied by start age (40, 46, 50, 54 or 50 years), test (no screening, faecal immunochemical test (FIT) and colonoscopy (COL)) and interval (annual, biennial or triennial FIT, and 5- or 10-year COL). Within simulating scenarios of biennial FIT screening for individuals aged 50-74 years and 4 RBS scenarios (R1-4). RBS scenarios increased in complexity: in R1 we modified screening start age, while in R2 we also modified start age and interval and in R3 and R4 we also modified screening intervals. Screening stop age was 74 years for all scenarios. In a sensitivity analysis we included costs for obtaining risk profile which included polygenic testing.

Results: Without screening, 7.8 CRC cases per 1,000 40-year olds were clinically detected over the 50-year follow-up period. This scenario resulted in 26.6 CRC deaths, yielded 23,723 QALYs and cost AUD$2.14 million. Compared to no screening, uniform screening resulted in lower CRC incidence (66.8 cases) and mortality (19.6) and an increased yield in QALYs (23,755 QALYs) and costs (AUD$2.8 million). The RBS strategies resulted in similar CRC incidence and mortality to uniform screening, with the most intensive strategy (R4) having the lowest incidence and mortality. QALYs and costs increased slightly in the RBS scenarios with R4 having the highest yield and costs.

The average cost-effectiveness ratio (ACER) of uniform screening compared to no screening was $1,249 per QALY gained. However, when we considered all strategies, R2, where screening start age and interval were modified, demonstrated cost-effectiveness with an ACER of $1,546 per QALY gained compared to screening start age and interval were modified, and those at highest risk were offered 5-yearly COL, was also cost-effective with an ICER of $10,989 compared to R2. When costs for obtaining risk profile were included, only uniform screening was deemed to be cost-effective.

Conclusion: Our results indicate that RBS determined by common genetic variants and family history is cost-effective, however, overall the gains are small. If, in addition to an earlier start age of screening, individuals at highest risk are offered 5-yearly COL instead of FIT (R4), benefits are expected to be largest. Including costs for obtaining risk profile significantly alters the results, with only uniform screening being cost-effective. The benefits of RBS may alter as new variants are discovered.

Disclosure: Nothing to disclose.

OP294 YIELD OF LYNCH SYNDROME SURVEILLANCE FOR INDIVIDUAL MMM GENES

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Introduction: Lynch syndrome (LS) is the most common hereditary cause of colorectal cancer (CRC) and is caused by germline mutations in the MMM genes MLH1, MSH2, MSH6 or PMS2. Although different genes may result in different CRC risk, all LS patients are currently offered the same surveillance interval regardless of the gene involved. Therefore, we aimed to assess the yield of LS surveillance for each individual MMM gene carrier group.

Aims and Methods: All patients diagnosed with LS in our center and participating in LS surveillance were included. Patients who had developed CRC before the identification of a MMM mutation were excluded. Data on age, gender, MMM gene involved, number of colonoscopies performed, interval between colonoscopies, and findings at each examination including histopathology were collected. A total of 314 LS carriers were included. Colonoscopy data were available for 264 (84%) patients from 113 different families (38% male, median age at time of first colonoscopy was 44 years (IQR 35-56 years, range 20-80 years). Of these patients, 55 had a MLH1, 44 a MSH2, 143 a MSH6 and 22 a PMS2 mutation. Median follow-up time was 6 years (IQR 2-10 years). At first colonoscopy, adenomas were found in 70 (27%), advanced adenomas in 33 (13%) and CRC in 8 patients (range 46-69 years, 3 MLH1, 1 MSH2 and 4 MSH6 mutation carriers). A total of 916 follow-up colonoscopies were performed in 220 patients. CRC was found in 9 patients, 4 in MLH1 mutation carriers and 5 in MSH2 mutation carriers. No CRC was found in MSH6 or PMS2 mutation carriers. There were no significant differences in the number of colonoscopies with adenomas or advanced adenomas between the different gene mutation carrier groups. In total, 264 adenomas were diagnosed in 101 LS different patients (47% of the patients). Mean number of adenomas per procedure (MAP) was 0.28. Mean number of adenomas per positive procedure (MAP+) was 1.38. There were also no significant differences in time to development of an adenoma or advanced adenoma between the groups adjusted for age and gender. In MLH1 and MSH2 mutation carriers advanced neoplasia (advanced adenoma or colorectal carcinoma) was found in shorter follow-up time than in MSH6 mutation carriers, 6 patients died during LS surveillance. Only 1 patient died from CRC, which was diagnosed at the first colonoscopy. In total 3.6 patients died from pancreatic cancer (1 MSH6 and 2 MSH2 mutation carriers).

Conclusion: Since no CRC was found during follow-up in MSH6 and PMS2 mutation carriers and advanced neoplasia was found in shorter follow-up time in MLH1 and MSH2 mutation carriers, the colonoscopy interval in MSH6 and PMS2 mutation carriers might be less stringent than for MLH1 and MSH2 mutation carriers.

Disclosure: Nothing to disclose.
Results:

122 subjects in each group were required to demonstrate non-inferiority of WLE versus CE for detection of adenomas in patients with LS. We conducted a multicenter randomized study with endoscopists prospectively randomized 1:1 to WLE or CE. The main outcome was the adenoma detection rate (ADR). The ADR for WLE versus CE were as follow: adenomas 1.04 (1.37) versus 0.95 (1.20) (p = 0.015), proximal serrated lesions 10.2% (6.0%-16.6%) versus 7.8% (4.3%-13.7%) (p = 0.183) respectively. The mean (±standard deviation) of lesions per patient for WLE versus CE were as follow: total polyps 50% (41.5%–58.5%) versus 58.7% (58.6%–74.7%) (p = 0.281), sessile serrated lesions 5.5% (2.4%-10.8%) versus 3.9% (1.6%-6.3%) (p = 0.554) and advanced adenomas 7.8% (4.3%-13.7%) versus 3.9% (1.6%-6.3%) (p = 0.183) respectively. The mean (±standard deviation) of lesions per patient for WLE versus CE were as follow: adenomas 1.04 (1.37) versus 0.86 (1.04) (p = 0.069), sessile polyps 2.36 (1.77) versus 2.67 (2.29) (p = 0.004), serrated lesions 0.67 (0.37) versus 0.426 (0.25) (p = 0.01) respectively. The previous colonoscopy was performed with standard definition white-light with adequate bowel preparation. The total procedural time and withdrawal time (mean ± standard deviation; in minutes) were superior in the CE arm: 22.42 ± 4.82 versus 30.67 ± 12.84 (p < 0.001) and 13.5 ± 6.53 versus 18.37 ± 7.57 (p = 0.001) respectively.

Conclusion: In a scenario with expert endoscopists, high-definition WLE is an optimal and efficient endoscopic technique for surveillance of Lynch syndrome patients. CE prolonged the procedural time without increasing detection of relevant lesions.

Disclosure: Nothing to disclose

Reference


OP295 RESULTS OF THE DANISH POLYPOSIS REGISTRY – FOCUS ON COLORECTAL CANCER IN THE 20TH CENTURY

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Introduction: Familial adenomatous polyposis (FAP) is an autosomal dominant disorder that predisposes to colorectal cancer (CRC). It is recommended that patients with FAP are monitored in national databases. The Danish Polypsis Registry is a nationwide, complete registry of FAP patients established in 1977. The aims of this study were to assess the current incidence and prevalence of colorectal cancer in FAP patients, the course of surgical treatment, and finally to compare the course of disease for probands and call-up patients.

Aims and Methods: The annual incidence rate was calculated by dividing number of newly diagnosed cases with the mean population for that year (Statistics Denmark), while the prevalence was calculated by dividing the number of FAP patients with the total population by end of the year (Statistics Denmark).

The complete number of CRC was extracted from Nordcan. Probandes were defined as patients diagnosed due to bowel symptoms and without any knowledge of a secondary malignant disease. Call-up patients were defined as screen detected patients diagnosed at prophylactic examination due to FAP diagnosis in first degree relatives.

Results: By the end of 2017, the Danish Polypsis Registry comprised 221 families with 722 affected individuals, including 610 with histologically verified FAP (309 probands and 311 call-ups). The annual incidence of FAP was 0.13/100,000, while the prevalence by the end of 2017 was 6.04/100,000. During 1999-2017, the proportion of FAP related CRC (n = 34), constituted only 0.05% of the all CRC (n = 72.238) in Denmark. 198 (32%) patients had CRC when diagnosed with FAP. The rate of CRC at the time of the FAP diagnosis was significantly higher in probands compared to call-ups (62% vs 2%, p < 0.0001). Of 610 patients with complete follow-up, 198 (32%) had CRC. Dukes classification was known in 154 patients: 26 (17%) were stage A, 42 (27%) stage B, and 86 (56%) stage C. Colectomy was the preferred surgical modality in 78%, rising from 52% before 1975, to 89% since 2002. The use of colectomy was significantly higher in call-ups (249/249) compared to probands (188/260) (100% vs. 73%, p < 0.0001). Of 295 patients with a known cause of death, 195 (66%) died of CRC, 37 from another malignant disease (13%), while 65 (22%) died from a non-malignant disease.

Conclusion: The Danish Polypsis Registry enables close monitoring of the rate of CRC and quality measurements as the rate of colectomy.

Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 08:30-10:00
From microbiota to immune mechanisms in CRC carcinogenesis – Room L8

OP297 PROFILES OF BACTERIA-DERIVED EXTRACELLULAR VESICLES IN STOOL, SERUM AND URINE IN PATIENTS WITH COLON CANCER: A PRELIMINARY STUDY

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Introduction: Alternations of gut microbiota is well-known in colorectal carcinoma. Gut microbiota-derived extracellular vesicles (EVs) are widely distributed throughout the body including the blood and urine. In this study, we investigated profiles of bacteria-derived EVs in stool, blood and urine, and evaluated whether they can be a useful marker for the metagenomic analysis of colorectal cancer (CRC).

Aims and Methods: This study incorporated 50 healthy controls and 14 patients with CRC. Information on anthropometric variables, location of tumor, cancer stage, and smoking and drinking habits were collected in patients with CRC. Additionally, we analyzed and compared the bacteria-derived EVs of the stool subjects by using 16S ribosomal RNA gene sequencing of their stool, blood and urine samples, which allowed us to identify over 3,200 operational taxonomic units corresponding to gut microbiota reported in previous studies.
RESULTS: In stool, non-EV bacterial microbiome, microbial diversity was significantly different between CRC patients and controls (Shannon index, p = 0.006); relative abundance of phylum Proteobacteria was decreased (FDR q = 0.003) and abundance of family Bacteroidaceae was increased (q = 0.002).

CONCLUSION: In stool, EV-derived microbiome shows a distinct profile compared to non-EV bacterial microbiome. These results suggest that some of the bacteria-derived EVs such as Comamonadaceae in stool, blood or urine may play a role in colorectal carcinogenesis and might be surrogate markers for the diagnosis of CRC. Further studies are necessary to clarify this issue.

Disclosure: Nothing to disclose.

OP298 FUSOBACTERIUM NUCLEATUM PROMOTE METASTASIS OF COLORECTAL CANCER

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Introduction: Fusobacterium nucleatum (F. nucleatum) is one of the most prevalent bacterial species in colorectal cancer (CRC) tissues and play an important role in colorectal carcinogenesis [1, 2]. A recent study reported Fusobacterium strains were consistently detected in primary tumors and paired metastases, suggesting that Fusobacterium might travels with the primary tumor cells to distant sites, as part of metastatic tissue colonization [3]. However, whether F. nucleatum could drive the metastasis of colorectal cancer is remained to be clarified. We aimed to clarified the role of F. nucleatum in metastasis of colorectal cancer.

Aims and Methods: The abundance of F. nucleatum in fecal samples from CRC patients and healthy people were detected by quantitative real-time PCR. Colorectal cancer cell lines were incubated with F. nucleatum or phosphate buffer saline (PBS control) and analyzed migration and invasion by transwell and wound healing assays. Cells were incubated with F. nucleatum or PBS and injected into tail vein of nude mice and metastasized nodules in the lungs were counted. The relative expression of matrix metalloproteinases (MMPs) were analyzed by quantitative real-time PCR and western blot.

RESULTS: The relative abundance of F. nucleatum was increased in fecal samples of colorectal cancer patients compared with healthy people (N = 30, T = 37). Furthermore, the abundance of F. nucleatum in fecal samples from CRC patients with lymph nodes metastasis was more than patients without metastasis. F. nucleatum co-culture promote CRC cells migration and invasion in vitro. Similarly, injection of CRC cells infected with F. nucleatum. We found MMPs (MMP-1, MMP-3, MMP-9, MMP-12) were significantly upregulated in CRC cells incubated with F. nucleatum versus PBS.

CONCLUSION: Our research firstly provided novel evidence that F. nucleatum promote metastasis of colorectal cancer, suggesting tumor microbiota are essential components of the cancer micro-environment.

Disclosure: Nothing to disclose.

References
(19%) women in the control group. We found a significant increase of IL-2, IL-4, IL-6, IL-17A and IL-23 in the serum of patients with polyposis compared to controls (p = 0.001, p = 0.001, p = 0.01, p = 0.001, 0.001 respectively). We did not detect significant differences of IL-11 and IL-10 between both groups (p = 0.16, p = 0.4). A significant increase of CRP was found in the group of patients with polyposis, where the HOMA index did not present significant differences. We found a significantly higher number of smokers in the group of patients with polyposis than the control group (67% vs 16%, p = 0.001) respectively. Also, a significantly higher percentage of cases had DM (11% vs. 5%, p = 0.06) and 24% of individuals with polyposis developed CC.

Conclusion: The high concentration of CRP and presence of high levels of IL-2, IL-4, IL-6, IL-23 and IL-17A in the group of patients with polyposis indicates the presence of an inflammatory response in these patients. Signaling by IL-23/IL-17A axis along with other cytokines and other factors such as tobacco consumption and DM may be playing an important role in the development of polyposis in these patients.

Disclosure: Nothing to disclose

OP301 COMBINED LOW DENSITIES OF FOXP3+ AND CD3+ TUMOR-INFILTRATING LYMPHOCYTES FOR THE INTRA-STAGE II IDENTIFICATION OF COLON CANCELS WITH THE HIGHEST RISK OF PROGRESSION

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Introduction: The densities of CD3+ and CD8+ tumor-infiltrating lymphocytes (TILs) and tumor necrosis factor (TNM) are currently key prognostic markers of non-metastatic colorectal cancer (CRC), potentially leading to an innovative Immunoscore forecasting system. FoxP3+TILs, not included in the immunoscore, may as well impact on CRC prognosis. Implementing the immunoscore classification of CRC, we compared the prognostic weight of CD3+ and FoxP3+ TILs, and TNM classifiers for predicting the outcome of patients with stage II and III CRC.

Aims and Methods: The surface covered by FoxP3+ and CD3+ TILs at the invasive front of 413 stage II-III CRC and TNM first classifiers were first challenged by classification and regression tree analysis (CART) by recursive partitioning to identify independent prognostic factors. Significant prognostic factors and their interactions were then re-assessed by logistic regression and Cox modeling, also in a validation set of 215 stage II CRCs.

Results: In the trial set, recursive partitioning recognized an influence of TILs on recurrence risk only within the decisional tree of stage II. Low-FoxP3+ TIL densities (≤0.10 TIL/mm²) were associated with significantly reduced risk of recurrence (HR 0.4) and progression (HR 0.71 for CD3+ TILs). In pooled stage II and III patients with concomitant low TILs the poorest survival, irrespective of allocation to adjuvant therapy (43.5%) or to surveillance (45.5%; p = 1.0).

Conclusion: Combined assessment of independent FoxP3+ and CD3+ TILs accurately forecasted the stage outcome in two independent HL microsatellite-stable CRC patients, eventually outplayed by nodal invasion. By contributing to improved stratification of the recurrence risk, TIL assessment may clarify what patients would benefit from adjuvant chemotherapy in stage II CRC. Conclusions of the measurements of two independent TIL populations can be inspected for determining refined thresholds at which their prognostic (and predictive) value is maximized. The foetalling power of TILs warrants refinement using data from randomized controlled trials, to establish interactions with TNM and the with post-surgical treatments.

Disclosure: Nothing to disclose

OP302 RNASEH2-GUIDED RIBONUCLEOTIDE EXCISION REPAIR PREVENTS INTESTINAL TUMORIGENESIS

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Introduction: Insufficient repair of DNA lesions results in the acquisition of somatic mutations and displays the driving force in carcinogenesis. Ribonucleotide incorporation by eukaryotic DNA polymerases occurs during every round of genome duplication and represents by far the most frequent type of naturally occurring DNA lesions. RNAse H2 removes misincorporated ribonucleotides from genomic DNA in a process termed ribonucleotide excision repair (REB). Whether intestinal epithelial proliferation requires REB and whether abrogation of REB is involved in the etiology of carcinogenesis at all is unknown.

Aims and Methods: Mice with an epithelial specific deletion of RNAse H2 subunit b (H2bΔNtC) and co-deletion of the tumor suppressor p53 (H2b/p53ΔNtC) were generated and phenotyped at young and old age. RNA sequencing was performed in isolated epithelial cells and intestinal organs. Mutational signature of spontaneous tumors from H2b/p53ΔNtC mice were characterized using exome sequencing. Association of tumor RNA H2 expression and patient survival was assessed in transcriptome data from 467 CRC patients.

Results: H2bΔNtC mice display chronic epithelial DNA damage and develop a p53-dependent proliferative exhaustion of the intestinal stem cell compartment. H2b/p53ΔNtC mice have restored epithelial proliferation and spontaneously develop small intestinal carcinomas. Resulting tumors display a distinct mutational signature characterized by T > G base substitutions at CpG islands.

Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018 10:30-12:00 IBD clinical trials II – Room E2

OP303 EFFICACY AND SAFETY OF MIRIKIZUMAB (LY3074828) IN PATIENTS WITH MODERATE-TO-SEVERE ULCERATIVE COLITIS IN A PHASE 2 STUDY


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Introduction: The cytokine IL-23 is involved in inflammatory bowel disease pathogenesis. A Phase 2, multi-centre, randomised, double-blind, placebo (pbo)-controlled trial (NCT02589665) of mirikizumab (mri; IL-23p19 antibody) was conducted to evaluate mri’s efficacy and safety in patients with moderate-to-severe ulcerative colitis (UC). The primary objective was to evaluate superiority of mri to pbo in inducing clinical remission at wk 12. Other objectives included clinical response, safety, and adjunctive inflammatory markers (faecal calprotectin (FC), serum C-reactive protein (CRP)). The ongoing study’s completed induction phase results are reported here (presented at DDW 2018).

Disclosure: Nothing to disclose

Aims and Methods: The cytokine IL-23 is involved in inflammatory bowel disease pathogenesis. A Phase 2, multi-centre, randomised, double-blind, placebo (pbo)-controlled trial (NCT02589665) of mirikizumab (mri; IL-23p19 antibody) was conducted to evaluate mri’s efficacy and safety in patients with moderate-to-severe ulcerative colitis (UC). The primary objective was to evaluate superiority of mri to pbo in inducing clinical remission at wk 12. Other objectives included clinical response, safety, and adjunctive inflammatory markers (faecal calprotectin (FC), serum C-reactive protein (CRP)). The ongoing study’s completed induction phase results are reported here (presented at DDW 2018).

Disclosure: Nothing to disclose
Aims and Methods: Patients with moderate-to-severe UC (Mayo score of 6 to 12; endoscopic subscore ≥2) were randomized at equal ratios to receive pbo (N = 63), miri 50 mg (N = 63) or 200 mg (N = 62) with possibility of exposure-based increases (2-12-fold or 1.5–3-fold, respectively, up to a 600 mg dose), or a fixed miri 600 mg (N = 61) dose intravenously at wks. 0, 4, and 8. Patients could receive oral 5-ASA or corticosteroids (<20 mg/d prednisone equivalent), thiopurines, must have failed a conventional UC therapy, and could be naive to or had prior exposure to biologics. Endoscopic videos were read centrally by experts blinded to treatment allocation and time point. Comparisons of rates of clinical remission3, primary outcome and clinical response2 were made using logistic regression analysis.

Results: Baseline characteristics were similar among treatment groups, although mean fCLP and CRP levels were higher in the miri 600 mg group. Most patients (63%) had been previously exposed to or failed biologic therapy, with 85% and 11.3% in the pbo and pooled miri (Miri all) groups receiving ≥ 3 biologics, respectively. At wk 12, clinical remission rates were greater (p < 0.01) in patients treated with miri 200 mg, but not miri 50 mg or miri 600 mg, versus pbo-treated patients. Clinical response rates at wk 12 were greater (p < 0.05) for all miri groups, compared to pbo group. At wk 12, fCLP and CRP levels were reduced (p < 0.05 and < 0.01, respectively) in the Miri All group versus pbo. There were similar rates of serious adverse events and treatment-emergent adverse events (TEAEs) across treatment groups.

Conclusion: Miri demonstrated efficacy in the induction treatment for patients with moderate-to-severe UC, as assessed by multiple measures. Miri treatment reduced faecal calprotectin and CRP levels across all doses compared to baseline. Overall adverse event frequencies were similar for miri and pbo-treated patients. These are the first data evaluating the efficacy of an IL-23p19 antibody in patients with moderate-to-severe UC. 20

Disclosure: Drs. Sandborn, Ferrante, Bhandari, D’Haens, Berliba, and Feagan report consulting fees and/or research grants from and/or have participated in speaker’s bureau for and/or have participated on a scientific advisory boards for commercial interests including Eli Lilly and Company, and/or are on the board of directors of various organizations. J Laskowski is an employee of Eli Lilly and Company. Mercer University School of Medicine, Macon, United States

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Introduction: Corticosteroids have been widely used for their anti-inflammatory effects in the treatment of inflammatory bowel disease (IBD). However, corticosteroids have several side effects, such as increased risk of infection, osteoporosis, and Cushing’s syndrome. Therefore, there is a need for alternatives to corticosteroids in the treatment of IBD.

Aims and Methods: In the phase 2 CELEST study of UPA in patients with CD, the new anti-inflammatory agent UPA was shown to be effective in reducing inflammation and improving endoscopic scores in patients with CD. The purpose of this study is to evaluate the efficacy and safety of UPA in the treatment of patients with CD.

Results: In the phase 2 CELEST study, 177 patients with CD were enrolled and treated with UPA. The primary endpoint of the study was the reduction in endoscopic scores at 16 weeks compared to baseline.

Conclusion: The results of this study show that UPA is effective in reducing inflammation and improving endoscopic scores in patients with CD. This study provides evidence for the use of UPA in the treatment of CD and highlights the potential benefits of this new anti-inflammatory agent.

Disclosure: Drs. Sandborn, Ferrante, Bhandari, D’Haens, Berliba, and Feagan report consulting fees and/or research grants from and/or have participated in speaker’s bureau for and/or have participated on a scientific advisory boards for commercial interests including Eli Lilly and Company, and/or are on the board of directors of various organizations. J Laskowski is an employee of Eli Lilly and Company. Mercer University School of Medicine, Macon, United States

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Introduction: Corticosteroids have been widely used for their anti-inflammatory effects in the treatment of inflammatory bowel disease (IBD). However, corticosteroids have several side effects, such as increased risk of infection, osteoporosis, and Cushing’s syndrome. Therefore, there is a need for alternatives to corticosteroids in the treatment of IBD.

Aims and Methods: In the phase 2 CELEST study of UPA in patients with CD, the new anti-inflammatory agent UPA was shown to be effective in reducing inflammation and improving endoscopic scores in patients with CD. The purpose of this study is to evaluate the efficacy and safety of UPA in the treatment of patients with CD.

Results: In the phase 2 CELEST study, 177 patients with CD were enrolled and treated with UPA. The primary endpoint of the study was the reduction in endoscopic scores at 16 weeks compared to baseline.

Conclusion: The results of this study show that UPA is effective in reducing inflammation and improving endoscopic scores in patients with CD. This study provides evidence for the use of UPA in the treatment of CD and highlights the potential benefits of this new anti-inflammatory agent.

Disclosure: Drs. Sandborn, Ferrante, Bhandari, D’Haens, Berliba, and Feagan report consulting fees and/or research grants from and/or have participated in speaker’s bureau for and/or have participated on a scientific advisory boards for commercial interests including Eli Lilly and Company, and/or are on the board of directors of various organizations. J Laskowski is an employee of Eli Lilly and Company. Mercer University School of Medicine, Macon, United States

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Table. Baseline demographics and disease characteristics, summary of efficacy and safety, and time to treatment failure for the tofacitinib treatment interruption population in OCTAVE Sustain

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>IBDDQ ≥170</th>
<th>IBDDQ &lt;170</th>
<th>Polychoric correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
</tbody>
</table>

OP305 TIME TO LOSS OF EFFICACY FOLLOWING TOFACITINIB INTERRUPTION IN PATIENTS WITH UCULERATIVE COLITIS: RESULTS FROM OCTAVE SUSTAIN

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Introduction: Patients with adequately controlled ulcerative colitis (UC) may have a need to stop pharmacological treatment for a range of reasons, including adverse events, to accommodate surgery or transition of care. Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for UC. This analysis included patients with clinical response to 8 weeks of tofacitinib treatment in OCTAVE Induction 1 & 2 (NCT01465763 & NCT01458951), who were subsequently randomised to receive placebo in the 52-week OCTAVE Sustain maintenance study (NCT014558574), to be a surrogate for treatment interruption.

Aims and Methods: We aimed to evaluate time to treatment failure following treatment interruption for clinical responders to tofacitinib as induction therapy. Treatment failure was defined, based on total Mayo score, as increase ≥3 points from OCTAVE Sustain baseline total Mayo score, plus increase in rectal bleeding subscore and endoscopic subscore ≥1 point and absolute endoscopic subscore ≥2 points. Patients with treatment failure after ≥8 weeks in OCTAVE Sustain were required to discontinue the study. Dropouts due to insufficient clinical response were treated as treatment failures. Event rates for treatment failure and quartile event times were estimated based on the Kaplan-Meier method.

Results: This analysis included 174 patients who had tofacitinib induction therapy and were randomised to placebo in OCTAVE Sustain. Baseline demographics and disease characteristics were consistent with the overall study population (Table): 52 patients (29.9%) were in remission at OCTAVE graphics and disease characteristics were consistent with the overall study. Dr. Van Assche has received consultant fees from AbbVie and other commercial entities. Dr. Reimish has served as speaker and consultant for AbbVie and other commercial entities and received research funding from AbbVie and other commercial entities. Dr. Yacyshyn has research support from MSD. Dr. Sedghi has no conflicts of interest. Drs. Goteti, Lee, and Lacerda are full-time employees of AbbVie and may own AbbVie stock or stock options. AbbVie funded the study, contributed to its design, and was involved in the collection, analysis, and interpretation of the data, and in the writing, review, and approval of the publication. Medical writing support was provided by Maria Hovenden, PhD, Complete Publication Solutions, LLC (North Wales, PA) and was funded by AbbVie.

References

OP306 EFFICACY AND SAFETY OF USTEKINUMAB FOR CROHN'S DISEASE: RESULTS FROM IM-UNITI LONG-TERM EXTENSION THROUGH 3 YEARS


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3Janssen Research & Development, LLC, Spring House, United States
4Janssen Scientific Affairs, LLC, Horsham, United States
5Icahn School of Medicine at Mount Sinai, New York, United States
6Northwestern University Feinberg School of Medicine, Chicago, United States

Table. Baseline demographics and disease characteristics, summary of efficacy and safety, and time to treatment failure for the ustekinumab treatment interruption population in IM-UNITI Sustain

<table>
<thead>
<tr>
<th>Baseline demographics and disease characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>OCTAVE Sustain baseline Mayo score, mean (SD)</td>
</tr>
</tbody>
</table>

| Efficacy at baseline of OCTAVE Sustain, n (%)      |
| Remission                                        |
| Mucosal healing                                  |
| Clinical response                                |

| Effect at Week 52 of OCTAVE Sustain, n (%)        |
| Remission                                        |
| Mucosal healing                                  |
| Clinical response                                |

| Summary of safety in OCTAVE Sustain, n (%)        |
| AEs                                              |
| SAEs                                            |
| Discontinued due to AE                           |
| Discontinued due to insufficient clinical response |

Estimated cumulative event rate at OCTAVE Sustain time point

<table>
<thead>
<tr>
<th>Treatment failure, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Week 4</td>
</tr>
<tr>
<td>Week 8</td>
</tr>
<tr>
<td>Week 16</td>
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<tr>
<td>Week 24</td>
</tr>
<tr>
<td>Week 32</td>
</tr>
<tr>
<td>Week 40</td>
</tr>
<tr>
<td>Week 52</td>
</tr>
</tbody>
</table>

Time to event, days

First quartile 65
Second quartile 135
Third quartile 371

*Patients with clinical response to 8 weeks of tofacitinib induction therapy and randomised to placebo in OCTAVE Sustain; 1Based on N=169 evaluable patients. AE, adverse event; N, number of evaluable patients; n, number of patients with event; SAE, serious adverse event; SD, standard deviation; UC, ulcerative colitis.

Disclosure: MC Dubinsky has received consultancy fees from AbbVie, BMS, Celgene, Gilead, Janssen, Pfizer Inc, Takeda; K Clarke has received speaker fees from AbbVie, Janssen, Takeda; and been on advisory boards for Pfizer Inc; JG Kraus has received speaker fees from AbbVie, Dr Falk, MSD, Takeda, and is on advisory boards for MSD, Takeda; Y Bouhnik has received consulting fees from AbbVie, Biogaran, Boehringer Ingelheim, Ferring, Hospira, Janssen MSD, Norgine, Pfizer Inc, Roche, Sandimmune, Takeda, UCB; and research support from Pfizer Inc, Takeda; A Sooanasta, AJ Thorpe, H Zhang, GS Friedman, DA Woodworth, N Lawendy, C Su are Pfizer Inc employees and shareholders.
OP307 LONG-TERM SAFETY AND EFFICACY OF RISANKIZUMAB TREATMENT IN PATIENTS WITH CROHN’S DISEASE: INTERIM RESULTS OF THE ONGOING PHASE 2 OPEN-LABEL EXTENSION STUDY


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5Boehringer Ingelheim Deutschland GmbH & Co. KG, Ludwigshafen, Germany
6AbbVie Inc., North Chicago, United States
7AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany
8A122

Disclosure: This study was funded by Janssen Research & Development, Inc.

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Introduction: Risankizumab (RZB), an IL-23 inhibitor, as induction and maintenance treatment in patients (pts) with moderate-to-severe Crohn’s disease (CD) have been previously described. Pts whose clinical response or remission to RZB in the Ph2 induction and maintenance study could enrol in an open-label extension (OLE) study. Interim efficacy and safety of RZB maintenance treatment up to 2 years, are reported from the ongoing OLE.

Aims and Methods: Pts who showed clinical response (decrease from baseline [BL] in CD Activity Index [CDAI] ≥100) without remission (CDAI <150) after 2 period (Week 26) or clinical response and/or remission after Period 3 (Week 52) of the preceding study1 were enrolled to receive open-label 180 mg s.c. RZB every 8 weeks for up to 4 years. LTE where pts with missing data or who terminated study participation prior to completion of the preceding study were re-induced with open-label 600 mg i.v. RZB infusions at weeks 0, 4, 8. Pts could only receive subsequent 180 mg s.c. RZB maintenance treatment if they achieved response or remission following re-induction treatment. Hepocellular carcinomas were performed at yearly visits. Treatment-emergent adverse events (AEs) were collected throughout the study participation for up to 15 weeks after the last dose of study drug or up to the data cut-off date of March 31, 2018. Efficacy data (clinical remission and endoscopic remission CDAI 280/200/C20, CDEIS 240/150) for pts with initial isolated ileitis are reported up to week 48, when all pts enrolled in the OLE had the opportunity to reach the visit date before the interim cut-off date. Non-response imputation (NRI) was used for missing data.

Results: A total of 65 pts with CD were enrolled, including 4 pts who were re-induced. At BL of preceding study, median (range) age 34 (19-67) years and median disease duration 10 (2-38) years; 60 pts (92.3%) were previously exposed to TNF-antagonists; 13 pts (23.5%) had previous corticosteroid and immunomodulators treatment, respectively at BL of preceding study. The mean (SD) exposure to RZB was 657.2 (190.73) days (Median: 689; Range: 164-900). As of the data cut-off date, 14 (21.5%) pts prematurely discontinued from the study. At Week 0 of the current study, 48/65 (73.9%) pts were in clinical remission and 28/65 (43.1%) pts had endoscopic remission. Clinical response rates were maintained up to week 48 (Table). The proportion of pts with endoscopic remission increased from BL to week 48 (Table). AEs were reported for 58/65 pts (89.2%) (42.7%) of randomized patients (21.5%) for cytokiniemia (2 pts). No events of tuberculosis, malignancies, or deaths occurred in the study.

Conclusion: SC UST maintained clinical response and remission through 3 years in a substantial proportion of patients, particularly those who were naïve to TNF antagonists. UST was well-tolerated through 3 years, with no new safety signals observed.

Disclosure: M. Ferrante: Research grant: Jansen, Takeda; Consultancy: AbbVie, Boehringer Ingelheim, Ferring, Janssen, MSD, Pfizer; Speakers fee: AbbVie, Boehringer Ingelheim, Chiesi, Ferring, Jansen, Lamepro, Mitsubishi Tanabe, MSD, Pfizer, Tramedico, Toltillo, Zeria G D’Haens; consulting and/or lecture fees from AbbVie, ActoGeniological, AIM, Boehringer Ingelheim GmbH, Centocor, Chemo Centrux, Cosmo Technologies, Eli Lilly, Pharmaceuticals, Ferring, Galapagos, Giuliani SpA, Given Imaging, GlaxoSmithKline, Janssen Biologics, MSD, Neovacs, Nordisk, Otsuka, PDL BioPharma, Pfizer, Receptos, Salix, SetPoint, Shire Pharmaceuticals, Schering-Plough, Takeda, Tiltio, UCB Pharma, Versant, and Vifor Pharma; research grants from AbbVie Jansen, Given Imaging, MSD, Dr Farkh Pharma, and PhotoPill; and speaking honoraria from AbbVie, Tiltio, Tramedico, Ferring, MSD, UCB Pharma, Norgine, and Shire Pharmaceuticals: consulting fees from AbbVie, Arena Pharmaceuticals, Boehringer Ingelheim, Celltrion, Ferring, Genentech, Janssen, MSD, Oppilan, Pfizer, Robarts, Roche, Second Genome, Takeda, Theravance, Tigenix, Topivert; and speaker’s fees from AbbVie, Ferrering, Jansen, MSD, Shire Pharmaceuticals, Takeda and Tramedico and research and teaching fees from MSD. M. Ferrante has received research grants from AbbVie, Chiesi, Ipsen, MSD, Roche, speakers and consultancy fees from AbbVie, Ferrering, Jansen, MSD, Shire Pharmaceuticals, Takeda and Tramedico, and research grants from AstraZeneca, Centocor, Ferring, Millenium, Schering-Plough, and UCB, and has received research grants from AstraZeneca, and Schering Plough A Kaser has received consulting fees from Boehringer Ingelheim, Ferrering, Genentech, GlaxoSmithKline, Hospira, Janssen, Pfizer and VHSquared. D. Hall, WO Bocher, I Herichova: are Boehringer Ingelheim employees. J. Kalabí, X. Liao, D. Gustafson are AbbVie employees; may own AbbVie stock and/or options.
**Reference**


**WEDNESDAY, OCTOBER 24, 2018**

10:30–12:00

**An upper GI melange – Room K**

**OP309**

**A 3-BIOMARKER PANEL ON BIOPSY TISSUE TARGETED BY ADVANCED ENDOCOMIC IMAGING CAN PREDICT RESPONSE TO DYSPLASIA IN PATIENTS WITH BARRETT’S OESOPHAGUS**


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2. Academic Medical Centre – Gastroenterology & Hepatology, Academic Medical Centre; Amsterdam/NL, Gastroenterology & Hepatology, Amsterdam, Netherlands
3. Queen's Medical Centre campus Nottingham University Hospitals, Nottingham Digestive Diseases Centre, Nottingham, United Kingdom

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**Introduction:** The aim of endoscopic surveillance of Barrett’s oesophagus (BO) is prevention of invasive adenocarcinoma by detection of early neoplasia. However, in the absence of histologic dysplasia it is difficult to assess the risk of progression. Molecular biomarkers could aid risk stratification. The aim of this study was to assess the utility of a panel of biomarkers on a small number of biopsies in predicting neoplastic progression of BO.

**Aims and Methods:** In a previous prospective study in three European centres we tested 18 and 19 strongly or weakly dysplastic biopsies targeted by autofluorescence imaging for diagnosis of dysplasia. The biomarker panel included p53 and cyclinA immunohistochemistry (IHC), aneuploidy and G2/tetraploidy, hypermethylation of p16, RUNX3 and HPP1, and loss of heterozygosity at 9p and 17p loci. Gorelick et al. found that patients with endoscopic high grade dysplasia (HG) or invasive carcinoma (IMC) were followed up endoscopically. Logistic regression by stepwise selection approach and LASSO regularization was used to select the most predictive biomarkers to form a small panel. Feger’s exact test was used to calculate odds ratios (OR). Means and medians were compared with Mann-Whitney and Student t-test. The primary endpoint was any histologic progression (progression from non-dysplastic BO to any grade of dysplasia or progression from low-grade (LGD) to HGD/IMC). Secondary endpoints included any progression to HGD/IMC and time to progression.

**Results:** Out of 203 patients with BO in the original cohort, 78 were excluded due to HGD/IMC at baseline endoscopy (n=29). LGD treated with RFA at follow-up.

**References**

up (n = 8) and lack of follow up (n = 41). The characteristics of the 125 patients included in the analysis are shown in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total patient population (n = 125)</th>
<th>Progressors (n = 42)</th>
<th>Non-progressors vs non-progressors comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>M:F (ratio)</td>
<td>106:19 (5.58:1)</td>
<td>36:6 (6:1)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>Mean age (Range)</td>
<td>64.9 (35.0–83.6)</td>
<td>63.98 (44.16–83.35)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>Mean BO length</td>
<td>7.13 (2.17–17)</td>
<td>7.00 (3.14–17)</td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td>Median follow-up in years (IQR)</td>
<td>3.85 (1.37–3.31)</td>
<td>1.22 (0.59–3.30)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>Baseline histology</td>
<td>NDBO/Indefinite dysplasia/LGD</td>
<td>96/10/19</td>
<td>24/41/14</td>
</tr>
</tbody>
</table>

[Table 1. Baseline demographic, endoscopic and histopathological characteristics of patients included in the study]

Logistic regression analysis revealed that p53 and aneuploidy were the only covariates which independently predicted progression to dysplasia (Regression coefficient: 0.91 +/− 0.46 and 1.39 +/− 0.67, respectively). p53 had an OR for any neoplastic progression of 2.94 (CI 1.30–6.66, p < 0.01), while aneuploidy had an OR of 5.37 (CI 1.54–18.76, p < 0.01). Of the remaining biomarkers, cyclinA was a weak predictor but missed statistical significance (p = 0.08). The ORs for progression to HGD/IMC for p53 and aneuploidy were 3.77 (CI 1.53–9.29, p < 0.01) and 6.17 (CI 1.65–23.11, p < 0.01), respectively. When combined into a 2-biomarker panel with a cut-off of 1 positive biomarker, p53 and aneuploidy had OR of 3.66 (CI 1.59–8.45, p < 0.01) for any progression and 4.83 (CI 1.90–12.14, p < 0.001) for progression to HGD/IMC. Moreover, we tested whether the addition of cyclinA improved risk stratification. The 3-biomarker panel with a cut-off of 2 positive markers predicted any neoplastic progression with an OR of 7.57 (CI 1.36–30.81, p < 0.001), and progression to HGD/IMC with an OR of 12.50 (CI 3.43–45.60, p < 0.0001) for progression to HGD/IMC. Finally, among progressors, those with positive biomarker panel had significantly shorter time-to-progression compared to patients with negative biomarker panel (Median 0.42 vs 1.47 yrs, p < 0.01).

Conclusion: In conclusion, we found that a small 3-biomarker panel, comprising of p53, aneuploidy and cyclinA, on biopsies targeted by advanced imaging, is a strong predictor of neoplastic progression in patients with BO and could inform endoscopic management.

Disclosure: Prof K. Ragunath has received research support, consultancy and educational grants from Olympus.

OP310 PATIENT-DERIVED ORGANOID-BASED PREDICTION OF CONCURRENT CHEMO-RADIOThERAPY RESPONSE IN ESOPHAGEAL CANCER

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Introduction: Prediction for factors determinants of concurrent chemoradiotherapy (CCRT) response has been limited. Patients derived organoid have advantages in providing more physiologically relevant and predictive data for clinical use. We established organoid biobanks with an OR of 12.50 (CI 3.43–45.60, p < 0.01).

Aims and Methods: Patient-derived organoid culture was performed using tumor tissues acquired from esophageal cancer before 1st CCRT start. After 7 days cultured, same sized organoids were collected and were treated with 5-FU and S4 chemotherapy was provided. After 6 days, primary cultured cells were stained and fluorescent images were captured. Clinical response was assessed after 4th cycle CCRT. Clinical response was classified as complete remission (CR), partial remission (PR), and disease progression (PD).

Results: A total of 27 esophageal cancer patients were enrolled. Final success rate of patient-derived organoid culture was 78% (21/27). CCRT response in patient-derived organoids were evaluated in 21 cases. A total of 16 persons were followed up more than 4 cycles of CCRT and were analyzed. Clinical CR was observed in 10 persons and 2 persons showed clinical PR (n = 4) or PD (n = 2). Live activity was noted in less than 10% of organoids in all patients with clinical CR and was observed in 30–40% of organoids in all patients with clinical PD. Live activity was noted in less than 20%–30% of organoids in all patients with clinical PR. Conclusion: It takes 2 weeks to evaluate the CCRT response in organoids from tissue acquirement. High agreement between clinical response and response in organoids was observed. The evaluation of CCRT response in organoids will provide a good predictor of clinical CCRT response and precision medicine.

Disclosure: Nothing to disclose

OP311 THE GUT MICROBIOME INFLUENCES PROGRESSION FROM METAPLASIA TO DYSPLASIA IN THE IL-1β MOUSE MODEL OF BARRETT OESOPHAGUS

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2Columbia University Medical Center, Division of Digestive and Liver Diseases, Herbert Irving Comprehensive Cancer Center, New York, United States
3Technical University of Munich, Lehrstuhl für Ernährung und Immunologie, Freising, Germany
4Uniklinik RWTH Aachen, Institut für Medizinische Mikrobiologie, Aachen, Germany
5Massachusetts Institute of Technology, Division of Comparative Medicine, Cambridge, United States

Introduction: The incidence of Oesophageal Adenocarcinoma (OAC) is increasing, with the only known significant risk factor being Barrett’s Oesophagus (BO). Even though there is an association of BO and OAC with obesity and diet, little is known about the responsible mechanisms. Confounding environmental or dietary factors that are prevalent in obese patients might also influence the risk of BO progression. Changes in diet lead to alterations in the gut microbiome and such alterations can have an effect on the susceptibility to gastrointestinal neoplasia. A possible link of microbiome changes in BO and OAC needs to be analyzed in order to understand the role of the microbiome in carcinogenesis or cancer prevention and surveillance strategies.

Aims and Methods: To investigate whether the gut microbiota influences inflammation and tumor development in our mouse model, we used the first time re-derived germ-free (GF) IL-1β mice (IL-1β). We further utilized changes in the diet and housing, specifically a specific-pathogen-free (SPF) and an open cage facility. Using histology and immunohistochemistry the phenotype of the mice was characterized. The microbiota was analyzed using high-throughput DNA sequencing followed by sequence analysis using QIIME and mothur followed by LEfSe. The PICRUSt pipeline was then used for in silico pathway analysis.

Results: IL-1β mice fed with a high-fat diet (HFD) with 48% fat compared to regular lab chow, or HFD matched control diet (Ctrl) showed a more severe phenotype with increased dysplasia. The HFD phenotype could be reproduced in the open cage facility, where we additionally observed an increased phenotype with HFD leading to a further acceleration compared to the SPF. Elimination of the microbiota led to a marked reduction of inflammation, metaplasia and most important dysplasia in the BE mouse model. This correlated with a reduced influx of neutrophils and immature myeloid cells into the esophagus of germ-free IL-1β mice, directly linking the gut microbiome to the inflammatory phenotype. A summary of the increase of the phenotype could be observed with decreasing hygiene level. Since the lower GI tract harbors the majority of the intestinal microbiota, we analyzed the intestinal microbiota by 16S rRNA gene amplicon sequencing of fecal samples. While only a modest reduction in microbial diversity could be observed, analysis of microbial β-diversity showed separate clustering of HFD fed IL-1β mice in comparison to all other groups, due to a unique taxonomic profile. We further observed an altered Firmicutes to Bacteroidetes ratio, correlating with similar alterations of this ratio in patients. Changes in community structure in microbiota from HFD fed IL-1β mice pointed to unique functions. PICRUSt analysis of 16S data generated a predictive metagenome with different clustering of the KEGG data in the IL-1β mice with HFD compared to Chow and IL-1β, suggesting a functional microbial high-fat associated component contributing to disease acceleration. One of the most significantly regulated pathways in the predictive KEGG analysis of the community profile was bacterial polysaccharide biosynthesis,

Conclusion: Our results demonstrate an influence of the gut microbiome on oesophageal carcinogenesis. While the mechanisms responsible for these differences need to be investigated, studies in patients should be performed. Changes in the microbiome of BO patients could be used to identify patients at risk for progression to OAC or the microbiome could be changed by dietary or drug interventions for a more favorable outcome.

Disclosure: Nothing to disclose

OP312 LONG-TERM EFFICACY AND SAFETY OF RPC4046, AN ANTI-INTERLEUKIN-13 MONOClonAL ANTIBODY, IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS: RESULTS FROM THE OPEN-LABEL EXTENSION OF THE HEROES STUDY

E.S. Dellon1, M.H. Collins1, Y. Assouline-Dayan2, L. Evans4, S. Gupta2, J.R. Calvert1, E. Spéder1, A. Straumann1, E. Safroneeva1, A. Olson9, E.S. Dellon1, M.H. Collins2, Y. Assouline-Dayan3, L. Evans4, S. Gupta5, G.J. Opieck1, R. Aranda1, I. Hirano10
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2Cincinnati Children’s Hospital Medical Center, Cincinnati, United States
3St. Luke’s Riverside College of Medicine, Jacksonville, United States
4Grand Teton Research Group, Idaho Falls, United States
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7Swiss EsE Clinic, Olten, Switzerland
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References: This project was funded by the National Research Foundation, Republic of Korea (NRF-2015R1D1A1A01059219).

Disclosure: Nothing to disclose
**Introduction:** HEROES was a 16-wk double-blind (DB), placebo-controlled, phase 2, multicenter trial followed by a 52-wk open-label extension (OLE) in adults with active eosinophilic esophagitis (EoE) that demonstrated a statistically significant reduction in esophageal eosinophil count and improvements in EoE Endoscopic Reference Score (EERS), EoE Histology Grade, Stage Score (EoEHS), and perception of esophageal severity and symptoms. The objective of OLE was to characterize the effects of RPC4046 for up to 52 wks.

**Aims and Methods:** Patients who completed the 16-wk DB, placebo-controlled period entered OLE and received weekly doses of RPC4046 360 mg subcutaneously and clinical assessments occurred at OLE wks 12, 24, and 52. Outcomes included assessment of mean and peak eosinophil count, EoEHS, EREFS, symptoms (EoE Activity Index [EAI]), and safety. Eosinophilic eosinophil counts and histology scores were determined by a central pathologist. OLE analysis was performed according to the original DB treatment assignment.

**Results:** In the DB period, 99 patients were randomized 1:1:1 to RPC4046 360 mg (n = 33), 180 mg (n = 32), or placebo (n = 34). 90 patients completed the 16-wk DB period, 86 entered OLE, and 66 completed the additional 52 wks of therapy. Mean eosinophilic eosinophil counts (cells/hpf) in OLE remained stable in patients on RPC4046 360 mg or 180 mg prior to OLE but improved rapidly in patients on placebo prior to OLE. Similar effects by treatment group before OLE and received 360 mg in OLE had sustained clinical and histologic improvement of EoE disease activity through 52 wks. Patients who received placebo during the DB period and then received RPC4046 360 mg in OLE showed improvement by wk 12 that was maintained through wk 52. Generally, the overall incidence and types of AEs remained consistent with longer duration of exposure.

**OP313 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): INTERIM ANALYSIS OF 16,600 FIRST-LINE TREATMENTS**


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**Disclosure:** ESD: Adare, Alivio, Allakos, Banner, Celgene Corporation/Receptos, Enumeral, GSK, Regeneron, and Shire – consultant; Adare, Banner, Celgene Corporation/Receptos, Meritage, Miraca, Nutricia, Regeneron, and Shire – research support; MHC: Celgene Corporation/Receptos, Regeneron, and Shire – consultant and grant/research support. YA-D and LE: Nothing to disclose. SG: Shire – grant/research support; AbbVie, Allakos, Celgene Corporation/Receptos, and QOL – consultant. AS: Adare, Celgene Corporation/Receptos, Merck Sharp & Dohme, and Regeneron – research support; AbbVie, Adare, Celgene Corporation/Receptos, Falk, Merck Sharp & Dohme, and Regeneron – research support; AV: Adare, Celgene Corporation/Receptos, Falk, Merck Sharp & Dohme, Regeneron, and Shire – consultant; Celgene Corporation/Receptos – grant/research support. ES: Apaltis Pharma, Celgene Corporation, Novartis, and Regeneron – consultant. AW and RA: Celgene Corporation/Receptos (now a wholly owned subsidiary of Celgene Corporation) – employment. AO and GCO: Celgene Corporation – employment. HH: HH has served as a consultant for Adare, Allakos, Celgene Corporation/Receptos, Regeneron, and Shire – grant/research support.

**Introduction:** The best approach for Helicobacter pylori management remains unclear. An audit process is essential to ensure that clinical practice is aligned with the latest recommendations and guidelines.

**Aims and Methods:** Our aim was to evaluate the efficacy of most common first-line treatments. International multicenter prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes of H. pylori management by European gastroenterologists. National coordinators from each country to identify a representative group of recruiters. All infected adult patients were systematically registered at an e-CRF by AEG-REDCap. Variables included Patient demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data.
Results: So far, 21,300 patients from 27 European countries have been evaluated. Average age was 49 years, 60% were women, and 18% had peptic ulcer. The majority of cases (78%, 16,614 patients) were naive to H. pylori treatment. Pre-treatment resistance rates were 24% to clarithromycin, 34% to metronidazole, and 14% to both. Drug prescription and efficacy is shown in the table. Triple therapy with amoxicillin and clarithromycin was the most commonly prescribed (45%), achieving overall < 80% eradication rate. Over 90% eradication was obtained with 10-day bismuth quadruple therapies or 14-day concomitant treatment. Longer treatment duration, higher acid inhibition and compliance were associated with higher eradication rates in the multivariate analysis.

Conclusion: Management of H. pylori infection by European gastroenterologists is heterogeneous, suboptimal and frequently discrepant with current recommendations. Only quadruple therapies lasting at least 10 days are able to achieve over 90% eradication rates.

Introduction: H. pylori eradication is a critical step in the management of gastric ulcer, pylori-related gastritis and other gastric conditions. No medication can be prescribed for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has

Aims and Methods: The aim of this study was to explore the potential effects of statin use on the risk of gastric cancer, the results are largely confounded by the presence of other variables (age, sex, comorbidities and the follow-up was censored at GC diagnosis, death or study end date). The observation period commenced from the date of HP therapy initiated in 2 patients with CTLA-4 mutations and in 1 patient with and LRBA (n = 1), TNFAIP (n = 1) and NFKB1 (n = 1). Targeted therapy was initiated in 2 patients with CTLA-4 mutations and in 1 patient with and STAT-3 mutation.

Conclusion: Genetic study of adult patients with non-celiac severe enteropathy with villosity avulsion reveals monogenic disorder in half of cases.

Disclosure: Nothing to disclose

[Table 1]

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayoly.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>% Use</th>
<th>ITT (95% CI)</th>
<th>PP (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPI + C + A</td>
<td>6,998</td>
<td>41.4%</td>
<td>70.7% (74.6-76.7)</td>
<td>77.9% (76.9-78.8)</td>
</tr>
<tr>
<td>PPI + C + A + M</td>
<td>5,285</td>
<td>19.8%</td>
<td>87.3% (86.0-88.3)</td>
<td>89.4% (88.3-90.4)</td>
</tr>
<tr>
<td>PPI + C + M</td>
<td>980</td>
<td>5.8%</td>
<td>74.6% (71.3-79.6)</td>
<td>81.4% (78.8-83.9)</td>
</tr>
<tr>
<td>PPI + C + A + T seq</td>
<td>795</td>
<td>5.2%</td>
<td>80.0% (78.6-82.5)</td>
<td>93.3% (91.5-95.0)</td>
</tr>
<tr>
<td>PPI + C + A + B</td>
<td>898</td>
<td>5.4%</td>
<td>86.1% (83.3-88.9)</td>
<td>87.7% (85.3-90.0)</td>
</tr>
<tr>
<td>PPI + C + A + M seq</td>
<td>626</td>
<td>4.0%</td>
<td>75.2% (72.9-78.2)</td>
<td>82.4% (79.4-85.3)</td>
</tr>
<tr>
<td>PPI + A</td>
<td>311</td>
<td>5.1%</td>
<td>70.7% (67.9-74.8)</td>
<td>82.4% (79.0-85.7)</td>
</tr>
<tr>
<td>PPI + A + L</td>
<td>378</td>
<td>2.3%</td>
<td>78.0% (73.6-82.1)</td>
<td>79.5% (75.3-83.6)</td>
</tr>
<tr>
<td>PPI + M + Tc+B c.s.</td>
<td>422</td>
<td>2.6%</td>
<td>89.2% (85.8-92.3)</td>
<td>95.3% (92.6-97.9)</td>
</tr>
<tr>
<td>PPI + C + A + T</td>
<td>149</td>
<td>0.9%</td>
<td>82.6% (81.2-91.1)</td>
<td>94.4% (90.6-98.1)</td>
</tr>
<tr>
<td>PPI + M + Tc+B</td>
<td>179</td>
<td>1.1%</td>
<td>77.1% (73.1-80.0)</td>
<td>90.8% (86.0-95.5)</td>
</tr>
</tbody>
</table>


OPI314 STATIN USE AND GASTRIC CANCER RISK IN H. PYLORI-ERADICATED SUBJECTS: A TERRITORY-WIDE COHORT STUDY WITH PROPENSITY SCORE ADJUSTMENT

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Introduction: Despite successful H. pylori (HP) eradication, some individuals can still progress to gastric cancer (GC). Although statin has been shown to reduce the risk of gastric cancer, the results are largely confounded by the presence of other variables (age, sex, comorbidities and the follow-up was censored at GC diagnosis, death or study end date). The observation period commenced from the date of HP therapy initiated in 2 patients with CTLA-4 mutations and in 1 patient with LRBA (n = 1), TNFAIP (n = 1) and NFKB1 (n = 1). Targeted therapy was initiated in 2 patients with CTLA-4 mutations and in 1 patient with and STAT-3 mutation.

Conclusion: Genetic study of adult patients with non-celiac severe enteropathy with villosity avulsion reveals monogenic disorder in half of cases with possibility of targeted therapy.

Disclosure: Nothing to disclose

OPI316 EXTERNAL VALIDATION OF THE INTERNATIONAL BLEEDING RISK SCORE IN BOTH UPPER AND LOWER GI BLEEDING: AN INTERNATIONAL MULTICENTRE STUDY

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3Yale School of Medicine, New Haven, United States
4Huinek Medical Center, Gastroenterology, Afula, Israel
5Hospital Carto, Polia (Salerno), Italy
6Hospital Virgen de las Nieves, Digestive Diseases, Granada, Spain
7Royal Cornwall Hospital Truro, Endoscopy, Cornwall, United Kingdom
8Chrischush Hospital, Chirschush, Singapore
9University of Otago Dept. of Medicine, Dunedin, New Zealand
10Ramban Health Care Campus Dept. of Gastroenterology, Gastroenterology,.
Pathology was frequent among the 8 participants (age 46 ± 12 years). In the washout period of sampling 21 ± 5 months, the plastic wrapping was consumed and daily 740 ± 580 mL of water were drank from plastic bottles (11% furry drinks). None was vegetarian and sea fish was consumed by 6 participants (2.6 ± 1.2 kg per month). 5/8 samples have been analyzed so far. The analytical screening identified polystyrene (PS) and polyurethane (PU) plastics in 2 of 5 samples, while in the other samples no definite results are yet obtainable due to high residual cellulose and fat content masking the presence of microplastic.

Conclusion: Increased plastic pollution can cause plastic contamination of foods, which may affect the GI-tract. We are the first to detect presence of polystyrene and polyurethane microparticles in human stool samples. Currently, we are optimizing the stool-sample separation technique of clearing non-plastic particles to further improve quantification and characterization of microplastic load by FT-IR micro-spectroscopy.

Disclosure: Nothing to disclose
Disclosure: Nothing to disclose

OP319 CHANGING TREND IN EUS-GUIDED TISSUE ACQUISITION: IN MEMORIAM – FNA, BIRTH – FNB
J.Y. Bang, S. Kirtane, K. Kralj, U. Navaneethan, M. Hasan, R. Hawes, S. Varadarajulu
Florida Hospital, Center for Interventional Endoscopy, Orlando, United States

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Introduction: Fine needle aspiration cytology (FNA) has been the preferred method of specimen evaluation for the past 25 years. Recently, fine needle biopsy (FNB) has become increasingly popular to procure histological core tissue. Although several studies have compared both methods, the impact of FNB on clinical practice is unclear.

Aims and Methods: We aimed to evaluate the impact of FNB on EUS-guided sampling of solid masses over a 4-year period. EUS-FNA using a 22 or 25G needle was the preferred technique for sampling solid mass lesions from 2014-2015 and EUS-FNB using a 22G needle from 2016-2017. Suction was not applied, stylet was not used after the first pass and fanning maneuver was adopted. Per unit policy, after establishing an onsite diagnostic adequacy by rapid evaluation (ROSE), 2 dedicated passes were performed for offsite assessment by cell block preparation. The main outcome measures were 1) Compare the median number of passes required to achieve diagnostic adequacy at ROSE, 2) Compare diagnostic yield at offsite assessment by cell block, which was defined as presence of histological tissue conducive for interpretation.

Results: Of 2020 patients who underwent EUS-guided sampling of solid masses, 2082 (68.9%) underwent FNA and 938 (31.1%) underwent FNB. Lesions were pancreatic 2154 (71.3%), subepithelial 218 (7.2%), lymph nodes 352 (11.7%) or metastatic 152 (4.9%). CCA vs. controls, respectively, MITF (AUC = 0.947) and XRK6 (AUC = 0.936) in controls, LOC441376 (AUC = 0.937) and PHEA1 (AUC = 0.927) in UC vs. controls, CMIP (AUC = 1.000), CCHNB1IP1 (AUC = 1.000) in CCA vs. PSC, and SFRS17A (AUC = 0.991), MTD3 (AUC = 0.980) in CCA vs. controls, respectively.

Conclusion: Aims and Methods: The study’s aim was to evaluate the potential value of serum and urine extracellular vesicles (EVs) as carriers of mRNA biomarkers for various gastrointestinal malignancies. Recent advances in the field of extracellular vesicle research indicate their potential as diagnostic tools.

Disclosure: Nothing to disclose

OP320 PREDICTIVE VALUE OF PAGE-B SCORE IN TUNISIAN PATIENTS WITH CHRONIC HEPATITIS B UNDER ENTECAVIR
B. Nawel1, R. Ennaifer2, B. Bouchabou2, Z. Rania3, H. Ben Romdhane4
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2Mongi Slim Hospital University Of Tunis El Manar, Hepatology, Marsa, Tunisia
3Hospital Silion Ville Nabeul, Gastroenterology, Ariana, Tunisia
4Mongi Slim Hospital, Gastroenterology, Marsa, Tunisia

Contact E-Mail Address: bennawel@gmail.com

Introduction: Nucleos(t)ide analogues appear to reduce the risk of hepatocellular carcinoma (HCC) compared to untreated patients due to viro-suppression. However, HCC continues to occur in treated patients with virologic remission. The most important challenge is to identify patients requiring close monitoring of HCC undergoing treatment. For this, many scores were used but appear to have good predictability.

Aims and Methods: The study’s aim was to assess the accuracy of the PAGE-B score and to compare it with other validated scores of other conventional HCC risk prediction models such as REACH B score.

Disclosure: Nothing to disclose

References:
1. Mongi Slim Hospital, Gastroenterology, Marsa, Tunisia
2. Hospital Silion Ville Nabeul, Gastroenterology, Ariana, Tunisia
3. Mongi Slim Hospital, Gastroenterology, Marsa, Tunisia
4. La Marsa, Mongi Slim, Tunis, Tunisia

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Disclosure: Nothing to disclose

WEDNESDAY, OCTOBER 24, 2018
10:30-12:00
Primary liver cancer – Room N2

OP320 SERUM AND URINE EXTRACELLULAR VESICLES CONTAIN mRNA BIOMARKERS FOR PRIMARY SCLEROSES CHOLANGITIS (PSC) AND CHOLANGIOCARCINOMA (CCA)
J.M. Ban˜ales5,6,13, P. Perez4,5,6, A.M. Aransay4,5, L. Bujanda Ferna´ ndez de Pierola1,5, A. Arbelaiz1, A. Lapitz1, M. Krawczyk2,3, J.L. Lavı´n4, M. Marzioni10, R.I.R. Macias5,11, J.J. Marin5,11, T.H. Karlsen12, J. Falcon-Carlos III National Institute of Health, Centro de Investigacio ´n Biome´dica en Red de Enfermedades Hepa´ticas y Digestivas” (CIBERehd), Madrid, Spain

Introduction: Fine needle aspiration cytology (FNA) has been the preferred method of specimen evaluation for the past 25 years. Recently, fine needle biopsy (FNB) has become increasingly popular to procure histological core tissue. Although several studies have compared both methods, the impact of FNB on clinical practice is unclear.

Aims and Methods: We aimed to evaluate the impact of FNB on EUS-guided sampling of solid masses over a 4-year period. EUS-FNA using a 22 or 25G needle was the preferred technique for sampling solid mass lesions from 2014-2015 and EUS-FNB using a 22G needle from 2016-2017. Suction was not applied, stylet was not used after the first pass and fanning maneuver was adopted. Per unit policy, after establishing an onsite diagnostic adequacy by rapid evaluation (ROSE), 2 dedicated passes were performed for offsite assessment by cell block preparation. The main outcome measures were 1) Compare the median number of passes required to achieve diagnostic adequacy at ROSE, 2) Compare diagnostic yield at offsite assessment by cell block, which was defined as presence of histological tissue conducive for interpretation.

Results: Of 2020 patients who underwent EUS-guided sampling of solid masses, 2082 (68.9%) underwent FNA and 938 (31.1%) underwent FNB. Lesions were pancreatic 2154 (71.3%), subepithelial 218 (7.2%), lymph nodes 352 (11.7%) or metastatic 152 (4.9%). CCA vs. controls, respectively, MITF (AUC = 0.947) and XRK6 (AUC = 0.936) in controls, LOC441376 (AUC = 0.937) and PHEA1 (AUC = 0.927) in UC vs. controls, CMIP (AUC = 1.000), CCHNB1IP1 (AUC = 1.000) in CCA vs. PSC, and SFRS17A (AUC = 0.991), MTD3 (AUC = 0.980) in CCA vs. controls, respectively.

Conclusion: Aims and Methods: The study’s aim was to assess the accuracy of the PAGE-B score and to compare it with other validated scores of other conventional HCC risk prediction models such as REACH B score.

Disclosure: Nothing to disclose

References:
1. Mongi Slim Hospital, Gastroenterology, Marsa, Tunisia
2. Hospital Silion Ville Nabeul, Gastroenterology, Ariana, Tunisia
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4. La Marsa, Mongi Slim, Tunis, Tunisia

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Disclosure: Nothing to disclose
OP322  DOUBLECORTIN-LIKE KINASE 1 (DCLK1) EXPRESSION CHARACTERIZES SPECIFIC SUBPOPULATIONS OF CANCER STEM CELLS (CSCs) IN HUMAN CHOLANGIOCARCINOMA (CCA) AND ITS INHIBITION EXERTS ANTI-CANCER EFFECTS

L. Nevì¹, S. Di Matteo¹, G. Carpino², V. Cardinale³, I. Zizzari³, V. Ambrosino¹, D. Costantini¹, S. Safarki¹, E. Manzi³, V. De Pippo³, A.M. De Rose⁶, F. Melandrino⁶, M. Bragazzi⁶, G. Grazi⁶, P.B. Berloco⁶, F. Giuliani⁶, E. Al Ayyoubi⁶

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⁶University of Roma La Sapienza, Department of Anatomical, Histological, Forensic Medicine and Orthopedics Sciences, Rome, Italy

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Introduction: Cholangiocarcinoma (CCA) is a very aggressive cancer with a minimal responsiveness to chemotherapies. We have previously demonstrated that CCA is enriched of Cancer Stem Cells (CSCs); these features being associated with aggressiveness and drug resistance. In different solid tumours, DCLK1 has been associated to be a dynamic score that can be calculated during treatment. We have shown that Tunisian patients without cirrhosis with PAGE-B score < 10 had a very low risk of developing HCC within 5 years after treatment and therefore, do not require close monitoring.

Discussion: Nothing to disclose.

References

OP323  DIAGNOSTIC AND PROGNOSTIC VALUES OF BOTH S100A4 AND GPC3 IN THE TUMORS OF HEPATOCELLULAR CARCINOMA IN EGYPTIAN CIRRHOTIC HCV PATIENTS: A TISSUE MICROARRAY-BASED STUDY

M. El-Bendary¹, K. Farid³, A. El-Mesery³, T. Abdullah³, M. Arafa³, W. El-Kashef³

¹Mansoura Faculty of Medicine- Mansoura University, Tropical Medicine and Hepatology, Mansoura, Egypt
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³Mansoura Faculty of Medicine- Mansoura University, Pathology Department, Mansoura, Egypt

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Introduction: S100 calcium binding protein A4 (S100A4) which is related to epithelial mesenchymal transition (EMT) is mainly involved in metastasis. Glypican-3 (GPC3) which is mainly expressed during pregnancy in fetal organs regulating morphogenesis has been known to be engaged in HCC development. This study evaluated both S100A4 and GPC3 expression in primary HCC in relation to tumor aggressiveness and diagnosis.

Aims and Methods: Tissues of 70 patients that met the inclusion criteria for hepatocytectomy out of 404 cases of HCC in Egyptian cirrhotic HCV patients were evaluated by immunohistochemistry (IHC) using antibodies against SA100A4 and GPC3 on the slides of tissue microarrays (TMAs) and compared with tumor-adjacent tissue (controls). All patients were followed up for survival, local recurrence and metastasis over a period of at least 6 months.

Results: GPC3 was more expressed in HCC than S100A4 when both were compared to control (79% and 21%), (p < 0.001 and p < 0.0001) respectively while no significant association with GPC3 expression with all three parameters (p > 0.05). GPC3 expression was associated with time of HCC recurrence (p = 0.02) while not with S100A4 (p > 0.05). The mean value of AFP was higher in both positive cases for S100A4 (p = 0.004) and GPC3 (p = 0.04). But in both S100A4 and GPC3 positive cases the overall survival time was affected (p > 0.05). A significant relation was found between overall survival and both S100A4 and GPC3 (p > 0.05). The median overall survival was shorter in decompensated patients and in higher grade tumors (p = 0.012 and p = 0.046 respectively). After univariate regression analysis, the only significant independent predictor for recurrence was decompensation (OR 3.037) and the following independent predictors for metastasis were significant; S100A4 positive staining (OR 9.63) and necrosis (OR 8.33). After multivariate regression analysis, the most significant predictor for metastasis was S100A4 positive staining (OR 8.4). Conclusion: S100A4 could be considered as a prognostic marker for HCC progression as it is related to tumor metastasis, grading and vascular invasion while GPC3 is a reliable marker of HCC diagnosis.

Disclosure: Nothing to disclose.

References
is important to research into safe and practical approaches in management of these patients. In this study we performed an open-label randomized controlled trial with the combined percutaneous injection of ethanol and mitoxantrone (cytotoxic drug with very high affinity to liver cells), has been found to be superior to the injection of ethanol alone in the treatment of Hepatocellular Carcinoma (HCC).

Aims and Methods: Our work is aimed at comparing percutaneous combined local injection of ethanol and mitoxantrone and percutaneous radiofrequency ablation in the treatment of hepatocellular carcinoma. This study excluded patients with more than 1 focal lesion and lesions larger than 4cm. There were 124 patients, 60 were randomized into Group I who were treated with ethanol plus mitoxantrone, while 60 were randomized into Group II who were treated with radiofrequency ablation. Clinical assessment, laboratory evaluation and CT studies were performed to all patients at baseline and at 1, 3, 6, and 12 months post treatment. The primary endpoint was complete ablation of the focal lesion. Data were checked, entered and analysed using SPSS 14 for Windows.

Results: Complete ablation has been achieved in 81.3%, 81.3%, 76.6% and 71.9% of patients in group I at 1, 3, 6 and 12 months respectively, whereas in group II the complete ablation was 88.3%, 88.3%, 85.5% and 81.7% at 1, 3, 6 and 12 months with no statistical significant difference between the two groups. Percentage of complete ablation in small tumours (<2.5cm) is higher than large tumours in both groups. Side effects and complications are significantly higher in group II.

Conclusion: Combined injection of ethanol and mitoxantrone is comparable to radiofrequency ablation with less frequent complications. Ethanol when combined with mitoxantrone can provide a safe, effective and cheaper option for the treatment of HCC especially for small tumours.

Disclosure: Nothing to disclose.

WEDNESDAY, OCTOBER 24, 2018
10:30-12:00
Diarrhea and bloating in functional bowel disorders – Room L7

OP326 EFFICACY OF PHARMACOLOGICAL THERAPIES FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS
P. Luthra1, N. Buri2, D.M. Brenner3, A.C. Ford4,5
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2Leeds Institute of Biomedical & Clinical Sciences, Leeds, United Kingdom
3Division of Gastroenterology and Hepatology, Northwestern University, Chicago, Illinois, United States

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Introduction: Opioids are increasingly prescribed in the West, and have deleterious gastrointestinal consequences. Pharmacological therapies to treat opioid-induced constipation (OIC) are available, but their relative efficacy is unclear. We performed a systematic review and network meta-analysis to address this deficit in current knowledge.

Aims and Methods: We searched MEDLINE, EMBASE, EMBASE Classic, and the Cochrane central register of controlled trials through to December 2017 to identify randomised controlled trials (RCTs) of pharmacological therapies in the treatment of OIC. RCTs that reported a dichotomous assessment of overall response to therapy, and were published using a random effects model. Efficacy and safety of pharmacological therapies was reported as a pooled relative risk (RR) with 95% confidence intervals (CIs) to summarise the effect of each comparator, and ranked treatments according to their p-score.

Results: 27 eligible RCTs of pharmacological therapies, containing 9149 patients, were identified. In our primary analysis, using failure to achieve an average of ≥3 bowel movements (BMs) per week with an increase of ≥1 BM per week over baseline, or an average of ≥3 BMs per week, to define non-response the network meta-analysis detected during colonoscopy. The endoscopic classification called “DICA” (Diverticular Inflammation and Complication Assessment) has been recently introduced. Retrospective study found a significant relationship between severity of DICA score and clinical and demographic characteristics of people having diverticulosis/diverticular disease.

Aims and Methods: Aim of this study was to assess the clinical characteristics of patients according to DICA classification and enrolled in a multicentre, international, prospective study.

2215 prospective patients at the first diagnosis of diverticular disease were enrolled after exclusion of radiological signs of acute diverticulitis; inflammatory bowel diseases; ischemic colitis; prior colon resection; patients with severe liver failure (Child-Pugh C) or severe kidney failure; pregnant women; patients who are currently using or who have received any laxative agents or mesalamine or probiotics or antibiotics < 2 weeks prior to the enrollment; inability to comply with study protocol and to give informed consent to the procedure; patients with or history of cancer, of any origin, within 5 years before enrollment; history of alcohol, drug, or chemical abuse. All patients were classified according to DICA classification.

Results: 1377 (62.15%) patients were classified as DICA 1, 599 (27.04%) as DICA 2, and 239 (10.80%) as DICA 3. Table 1 described clinical and demographic characteristics of the enrolled population. We found that the DICA 3 patients, were older, were more frequently females and smokers, had more frequently appendectomy and showed a more than 1 co-morbidity than DICA 1 and DICA 2 patients. Abdominal pain and meteorism were the most frequent symptoms in those people, but DICA 3 patients were more somatic and with more severe expression of symptoms than DICA 1 and DICA 2 people.

Moreover, local calprotectin showed higher levels in DICA 3 than in DICA 1 and DICA 2 patients (p < 0.0001).

No scheduled therapy was generally adopted for DICA 1 patients (53.7%), while it was adopted in only 26.4% and 10.9% of DICA 2 and DICA 3 patients

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6Federal University of Goiás, Dr., Goiânia, Brazil
7Sofar Osp. Clinica Gastro Universita, Perugia, Italy
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14SOFAR, Viterbo, Italy
15Utsa 4 Alcorvencion, Endoscopic Unit – Department Of Surgery, Santander, Italy
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Introduction: Diverticulosis of the colon is the most frequent anatomical alteration detected during colonoscopy. The endoscopic classification called “DICA” (Diverticular Inflammation and Complication Assessment) has been recently developed in order to have an objective endoscopic description of the colon harbouring diverticula. Retrospective study found a significant relationship between severity of DICA score and clinical and demographic characteristics of people having diverticulosis/diverticular disease.

Aims and Methods: Aim of this study was to assess the clinical characteristics of patients according to DICA classification and enrolled in a multicentre, international, prospective study.

2215 prospective patients at the first diagnosis of diverticular disease were enrolled after exclusion of radiological signs of acute diverticulitis; inflammatory bowel diseases; ischemic colitis; prior colon resection; patients with severe liver failure (Child-Pugh C) or severe kidney failure; pregnant women; patients who are currently using or who have received any laxative agents or mesalamine or probiotics or antibiotics < 2 weeks prior to the enrollment; inability to comply with study protocol and to give informed consent to the procedure; patients with or history of cancer, of any origin, within 5 years before enrollment; history of alcohol, drug, or chemical abuse. All patients were classified according to DICA classification.

Results: 1377 (62.15%) patients were classified as DICA 1, 599 (27.04%) as DICA 2, and 239 (10.80%) as DICA 3. Table 1 described clinical and demographic characteristics of the enrolled population. We found that the DICA 3 patients, were older, were more frequently females and smokers, had more frequently appendectomy and showed a more than 1 co-morbidity than DICA 1 and DICA 2 patients. Abdominal pain and meteorism were the most frequent symptoms in those people, but DICA 3 patients were more somatic and with more severe expression of symptoms than DICA 1 and DICA 2 people.

Moreover, local calprotectin showed higher levels in DICA 3 than in DICA 1 and DICA 2 patients (p < 0.0001).

No scheduled therapy was generally adopted for DICA 1 patients (53.7%), while it was adopted in only 26.4% and 10.9% of DICA 2 and DICA 3 patients
OP328 OUTLET DYSFUNCTION IS PREVALENT IN SEVERE FUNCTIONAL BLOATING: A PROSPECTIVE, MULTICENTER, ITALIAN STUDY

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Introduction: Bloating and abdominal distension are bothersome symptoms frequently complained about by patients with functional gastrointestinal disorders (FGID). Etiology is unclear in many cases. However, recent studies provided evidence of impaired handling of gas as mechanism potentially relevant to the symptom. Few data are available on defecation behavior in these patients (1). Aims and Methods: Our aim was to study the relationship between the defecation pattern, the severity of bloating and the abdominal girth changes in FGID patients consulting for bloating as prevalent complaint poorly responsive to controlled diet advice. We performed a prospective, multi-center study of patients with severe abdominal bloating (VAS score ≥ 24 on a 100-mm scale) as prevalent complaint with visible abdominal distension. Patients were recruited at 4 gastroenterology outpatient clinics in Italy. Comorbid FGID were grouped according to Rome III criteria. All patients were prescribed a lactose-free diet augmented by NICE dietary advice for irritable bowel syndrome (IBS) for 2 weeks. A belt around the abdomen at standardized sites provided assessment of abdominal girth 2 hours after a meal. All patients reporting inadequate relief of bloating at the end of the run-in underwent a standardized balloon expulsion test (BET) scored as either successful or failed if the balloon could not be evacuated within 2 minutes (2). A straining questionnaire was also administered.

Results: 134 patients (112 female, 39.8 ± 11.9 mean age, 10 IBS-D, 14 IBS-M, 45 IBS-C, 13 IBS-U, 7 Functional Constipation, 36 Functional Bloating, 7 Functional Dyspepsia) completed the 2-week run-in period. Patients completed a daily diary log including abdominal bloating score (100-mm VAS), Bristol Stool Form and stool frequency. At randomization visit, all patients filled in a questionnaire on subjective improvement of bloating on a 5-point Likert scale (true to major improvement) and a further abdominal bloating 100-mm VAS. A belt around the abdomen at standardized sites provided assessment of abdominal girth 2 hours after a meal. All patients reporting inadequate relief of bloating at the end of the run-in underwent a standardized balloon expulsion test (BET) scored as either successful or failed if the balloon could not be evacuated within 2 minutes (2). A straining questionnaire was also administered.

Conclusion: In this prospective, multicenter trial modified NICE diet advice was of clinical benefit in approximately 30% of FGID patients consulting for severe abdominal bloating. Disordered defecation was prevalent in the non-responders and correlated with subjective bloating perception. A biofeedback trial to improve defecation effort is ongoing to investigate the relevance of outlet dysfunction as contributing etiology to functional bloating.

Disclosure: Nothing to disclose.

References

OP330 PREDICTORS OF, AND PREDICTORS OF, A POSITIVE SEHCAT SCAN FOR BILE ACID DIARRHOEA IN GASTROENTEROLOGY OUTPATIENTS: A FOLLOW-UP STUDY

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Introduction: Despite recommendations from national guidelines, many clinicians do not perform 23-seleno-25-homo-tauro-cholic acid (SeHCAT) scanning to rule out bile acid diarrhoea (BAD) in patients with chronic diarrhoea [1]. Our previous study auditing the use of SeHCAT scan in our centre showed a yield of 51% in this patient group and identified that patients with terminal ileal (TI) Crohn’s disease or TI resection were highly likely to have an abnormal SeHCAT scan [2]. As a result, we asked clinicians to use a therapeutic trial of a bile acid sequestrant in these patient groups instead of referring them for scanning, hence conserving nuclear medicine resources.

Aims and Methods: In light of changes to the referral criteria, we re-evaluated the yield of SeHCAT scanning in chronic diarrhoea patients, and examined factors predicting an abnormal retention. We retrospectively identified consecutive patients with chronic diarrhoea undergoing SeHCAT scanning at Leeds Teaching Hospitals Trust over a 5-year period from 2012 to 2016. We reviewed electronic patient records to obtain information on presenting gastrointestinal symptoms and any proposed risk factors for BAD. Patients were classified as having irritable bowel syndrome with diarrhoea (IBS-D) if they also reported abdominal pain or discomfort. BAD was categorized into 3 different subtypes (types I, II, and III), and severity (mild: 10–14.9% retention, moderate: 5–9.9%, severe: < 5%). We used a Pearson χ² test to assess the association between a positive SeHCAT scan and any risk factors for BAD.

Results: Between 2012 and 2016, 1071 patients were referred for SeHCAT scanning. As expected, indications for scanning changed between 2012 and 2016, with a significant reduction in referral of patients with TI Crohn’s disease or TI resection year on year (χ² for trend, p < 0.001). Despite this, 457 (42.7%) patients had BAD and there was no downward trend in yield of SeHCAT scanning during the 5-year study period (χ² for trend from 2012–2016, p = 0.39). This remained the case when data were compared with the previous 7-year study.
period from 2005 to 2011 (χ² for trend from 2005-2016, p = 0.28). The proportion of patients with type II and III BAD increased from 2012 to 2016 (χ² for trend, p < 0.001). Overall, 51.6% had type II BAD, 36.1% type III, and 12.3% type I. BAD was mild in 31.7%, moderate in 34.4%, and severe in 33.9%. Of the 453 patients with IBS-D symptoms, 154 (33.7%) had a positive SeHCAT (Table 1), indicating type II (idiopathic) BAD. In total, 653 (61.0%) patients had no known risk factor for BAD, other than chronic diarrhoea, but 233 (35.7%) of these individuals had BAD, with 143 (61.4%) of them having moderate or severe BAD.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Groups</th>
<th>Mean (SD)</th>
<th>(n = 1071)</th>
<th>P value</th>
<th>(n = 614)</th>
<th>Sens./Spec.</th>
<th>PPV/NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BAD (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td></td>
<td>710 (66.3)</td>
<td>414 (67.4)</td>
<td>0.36</td>
<td>296 (65.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No known risk factor for</td>
<td></td>
<td>633 (61.0)</td>
<td>420 (68.4)</td>
<td>0.001</td>
<td>233 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAD (%)</td>
<td></td>
<td>356 (33.4)</td>
<td>208 (34.0)</td>
<td>0.59</td>
<td>148 (32.5)</td>
<td></td>
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</tr>
<tr>
<td><strong>IBS-D (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Abdominal pain or discom-</td>
<td></td>
<td>738 (69.2)</td>
<td>442 (72.3)</td>
<td>0.01</td>
<td>296 (65.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>fort (%)</td>
<td></td>
<td>453 (42.3)</td>
<td>299 (48.7)</td>
<td>0.001</td>
<td>154 (33.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P value for Pearson χ² for comparison of categorical data, and one-way analysis of variance for comparison of age, across the three groups*

### Table 2

<table>
<thead>
<tr>
<th>SeHCAT ≥ 10%</th>
<th>ROC analysis</th>
<th>Cutoff values for positive test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting C4</td>
<td>Area under the curve (95% CI)</td>
<td>Sens./Spec. (%)</td>
</tr>
<tr>
<td>34 (16–65)**</td>
<td>0.83 (0.72–0.93)**</td>
<td>66/54</td>
</tr>
<tr>
<td>34 ≥ 154</td>
<td>65/85</td>
<td></td>
</tr>
<tr>
<td>34 ≥ 45.1</td>
<td>83/71</td>
<td></td>
</tr>
</tbody>
</table>

### References

3. Jørgensen P, Bouchelouche D, Rainteau S, Layani-Moreno L, Munck L. The prevalence of Bile Acid Diarrhoea (BAD) is 1% in the general population and up to 32% in patients with diarrhoea-predominant irritable bowel syndrome (1). Availability of the diagnostic scintigraphic SeHCAT retention test is limited. 7α-hydroxy-4-cholesten-3-one (C4) is a proposed diagnostic alternative to SeHCAT (2, 3). Compared with SeHCAT, fasting Fibroblast Growth Factor-19 (FGF19) has an average diagnostic strength (4) but our pilot study suggested that the FGF19 response to a meal plus chenodeoxycholic acid (CDCA) stimulation may have diagnostic strength comparable with that of C4 (5).

### Aims and Methods:

We aimed to validate the biochemical tests C4 and the response in FGF19 to a meal plus CDCA with the SeHCAT test (NCT03059537). We prospectively recruited patients referred for SeHCAT at four Danish centres to compare SeHCAT, C4, and stimulated FGF19. Exclusion criteria included cirrhosis, ileal resection, active IBD, and use of laxatives or anti-diarrhoeal drugs 1 week before SeHCAT visit 1 and during the study. At SeHCAT visit 1 patients started a 6-day Bristol Stool Form (BSF) diary. At SeHCAT visit 2 we sampled fasting blood, subjects ingested 1250 mg CDCA and a solid meal (2 boiled eggs, 2 slices of toast bread, and 500 mL water). Plasma was sampled after 90, 120, and 150 minutes. We analysed FGF19 by enzyme-linked immunosorbent assay and C4 by high-performance liquid chromatography-tandem mass spectrometry. SeHCAT ≤ 10% defined BAD and SeHCAT > 10% defined idiopathic diarrhoea. Data are presented as median and interquartile ranges. Continuous variables are compared with the Mann-Whitney U-test.

### Results:

Of 71 subjects, 26 (9 male) had BAD and 45 (27 male) had idiopathic diarrhoea. Median age was 45 years (34-49) vs. 55 years (45-64); p < 0.01. Average stools per day was 3.9 (3.0-5.3) vs. 3.0 (2.0-4.0); p = 0.01. Average BSV was 5.9 (5.5-6.3) vs. 5.6 (5.0-6.2); p = 0.17. After the CDCA ingestion, the plasma C4 values peaked at 90 minutes and FGF19 peaked at 150 minutes, with no significant difference in values between patients with BAD or idiopathic diarrhoea except for FGF19 at fasting; p < 0.01. Table 1 shows biochemical results and the receiver operating characteristics (ROC) analysis with predefined and proposed cut-off values. With C4 < 15.4 ng/mL as the cut-off for a definite negative test, 40 of 71 subjects were C4-negative; 34 of these 40 (85%) were true negative. With C4 > 45.1 ng/mL as the cut-off for a definite positive test 12 of 71 subjects were C4-positive, and 10 of these 12 (83%) were true positive. This diagnostic algorithm left 19 of 71 subjects with an inconclusive C4-test, of which 10 had SeHCAT ≤ 10%. A similar algorithm for fasting FGF19 with the cut-off values shown in Table 1 left 33 subjects with an inconclusive FGF19 test.

### Conclusion:

Stimulation with a meal plus CDCA does not increase the diagnostic yield of FGF19 for diagnosing BAD. In our population, C4 is the superior biochemical test and qualifies for a screening test. This needs further validation with the treatment response in a controlled trial.

### Disclosure:

Sigma-tau Rare Disease Ltd. provided CDCA (Xenbilox) without restrictions as an independent grant.

### References


OP332 EXPOSURE TO MICROBIOTA EARLY IN LIFE DETERMINES COLITIS SEVERITY IN ADULT MICE

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Introduction: The etiology of inflammatory bowel diseases (IBD) remains complex. Increasing evidence supports the view that perturbation of the immune system may interact with the intestinal microbiota via an increased susceptibility to IBD in adulthood. However, how perturbations in host-microbial symbiosis and immunity in childhood impact the intestinal immunity later during adulthood remains enigmatic.

Aims and Methods: In this study, we explored the early time window, and the underlying mechanisms, during which microbiota impacts the IBD susceptibility later in life. Germ-free mice were colonized with microbiota before or after weaning and their susceptibility to develop colitis induced experimentally by dextran sulfate sodium was assessed at adult age. Immune responses, microbial metabolites and microbiota composition were determined during weaning and/or before colitis induction at adult age.

Results: We identified weaning as a window of opportunity during which exposure to microbiota determines the severity of experimental colitis in adult mice. We showed that exposure to microbiota during weaning, but not later, induces an immune response that contributes to regulate the severity of colitis in adult mice. RNA-seq analysis in the colon before colitis induction of GF mice exposed to microbiota before or after weaning revealed immune abnormalities associated with different type of cells. The underlying mechanisms involve microbial metabolites, such as short chain fatty acids (SCFAs), the administration of which downregulates pre-weaning colitis severity in adult age. This protective effect of SCFAs early in life is dependent on the cross-talk between intestinal epithelial cells and regulatory T cells expressing the transcription factor RORγt (Retinoic-Acid Receptor-related Orphan Receptor gamma t).

Conclusion: These results validate how host-microbial symbiosis during a specific time window of opportunity early in life determines long-term susceptibility to inflammatory pathology.

Disclosure: Nothing to disclose

OP333 ULCERATIVE COLITIS PATIENTS IN LONG-TERM STABLE REMISSION RECOVER EUBIOTIC CHARACTERISTICS OF THEIR MICROBIOTA

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Introduction: Ulcerative colitis (UC) and Crohn’s disease (CD) are inflammatory bowel diseases characterized by an aggressive immune response thought to be propagated by microbial metabolites. There are limited data concerning microbiota in UC patients with long-term remission. We determined whether patients with UC in long-term remission have microbiota that is similar to healthy controls. UC patients

Aims and Methods: To evaluate the microbiota in UC patients in long-term remission. A cross-sectional study was performed in 4 groups of subjects: 1) UC-L: UC patients in long-term remission (≥5 years of flare-free disease, with clinical, endoscopic and histological remission at time of study); 2) UC-S: UC patients in short-term remission and high relapse rate (3 months in clinical remission at time of study and previously more than 1 relapse per year); 3) UC-F: UC patients with active disease (SCCAI > 4 at time of study) and 4) HC: healthy unrelated controls. We obtained 2 frozen stool samples from all subjects, except from the UC-F group from which we obtained 1 frozen stool sample at the beginning of the flare. Total bacteria, F. prausnitzii, A. muciniphila, E. coli and F. nucleatum were measured by quantitative Real Time PCR (qPCR, copies/g stool).

Results: 112 subjects were included, 29 in UC-L group, 20 in UC-S, 39 in UC-F and 24 HC. Median age of UC patients was 39 years and in HC was 34 years, women comprised 52% of all UC and 58% of HC. F. prausnitzii abundance was significantly higher in UC-L and UC-F compared to the UC-L group (median 7.67E+8 copies/g; 5.06E+8 copies/g vs. 4.37E+9 copies/g, p < 0.05). A. muciniphila abundance was depleted in both UC-S and UC-F in contrast with UC-L and HC (median 0.00E+10 copies/g in UC-S and UC-F vs. 3.98E+6 copies/g in UC-L and 5.01E+9 copies/g in HC, p < 0.01). E. coli and F. nucleatum abundance was similar in all subjects studied.

Conclusion: UC patients in long-term, stable remission present an abundance of A. muciniphila and F. prausnitzii that is similar to healthy controls. UC patients may be able to recover some eubiotic characteristics of their microbiota and this could become an important therapeutic end-point in UC.

Disclosure: Nothing to disclose

OP334 COMPARISON OF INTESTINAL MICROBIOTA COMPOSITION IN PATIENTS WITH ULCERATIVE COLITIS DEPENDING ON THE PLACE OF RESIDENCE (URBAN OR RURAL)

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2Republican Clinical Hospital of Tatarstan Republic, Kazan, Russian Federation

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Introduction: The gut microbiota composition differs at the inter-individual level and depends on many factors as food, geographical conditions of human living, genetic factors, age, etc. It is probably the change in the composition of the gut microbiota which can lead to the activation of immune inflammation in ulcerative colitis and Crohn’s disease patients.

Aims and Methods: The aim of the study was to reveal the influence of the place of residence (urban/rural) on the composition of intestinal microbiota in inflammatory bowel diseases (IBD) patients.

Materials and methods: The study included 91 patients with ulcerative colitis and Crohn’s disease (22 living in urban, and 69 – in the urban area). The control group consisted of 96 healthy subjects (25 from rural and 69 from urban area). Total DNA was extracted from stool samples followed by whole genome sequencing (SOLiD 5500 W platform).

Results: The following bacteria were predominant in the samples of healthy subjects living in a rural area: Clostridium (3.20±5.64)%; Eubacterium (16.86±8.19)%; Butyribrio (1.46±0.67)%; Coprococcus (8.82±0.82)%; Roseburia (5.79±4.02)%; Faecalibacterium (7.89±4.93)%; Ruminococcus (12.63±11.51)% and Akkermansia (1.46±0.40)% in contrast to the group of patients, living in a rural area: Clostridium (0.11±1.80)%; Eubacterium (8.34±0.87)%; Butyribrio (0.79±2.59)%; Coprococcus (4.81±1.73)%; Roseburia (3.11±1.53)%; Faecalibacterium (3.64±3.61)%; Ruminococcus (3.92±0.03)%; Akkermansia (0.08±0.21)%; p < 0.05. In the group of healthy urban residents bacteria: Clostridium (0.99±3.58)%; Eubacterium (13.68±9.59)%; Butyribrio (1.77±5.83)%; Coprococcus (5.95±6.46)%; Roseburia (3.48±3.75)%; Faecalibacterium (5.73±5.58)%; Ruminococcus (7.31±6.70)%; Akkermansia (2.29±7.26)% were much more abundant than in IBD patients living in the cities. However the abundance of Bacteroides genus was significantly higher in groups of both rural and urban IBD patients: (14.45±18.02)% and (21.8±19.11)% compared to the control group of healthy subjects living in rural and urban areas (2.73±1.75)%; (9.05±12.08)%, respectively, p < 0.05. The abundance of Bacteroides vulgatus was elevated in IBD patients both from rural (3.84±4.02)% and urban areas (7.28±9.57)% compared to the control group of subjects form rural (0.43±0.52)% and urban areas (2.09±3.46)%; p < 0.05. Comparative analysis of microbiota of IBD patients living in rural and urban areas revealed differences in the representation of only 2 genera of bacteria: the abundance of Methanosphaeribacter (2.30±6.19)% and Catenibacterium (1.18±1.93)% was higher in patients living in the cities (0.71±2.72)% and (0.38±0.85)%, respectively, p < 0.05.

Conclusion: Only 2 genera of bacteria – Methanosphaeribacter and Catenibacterium – differed significantly between urban and rural IBD patients. The abundance of butyrate-producing bacteria with anti-inflammatory properties (Butyribrio, Eubacterium, Faecalibacterium, Coprococcus, Ruminococcus, etc.) was significantly decreased in IBD patients comparing to healthy subjects. The abundance of B. fragilis, which is the cause of diarrhea of different etiology, was statistically different between the groups, but there was an increase in its relative representation in the group of urban IBD patients.

Disclosure: Nothing to disclose

OP335 DONOR MICROBIOTA AS A DETERMINANT FACTOR FOR RESPONSE TO FMT IN PATIENTS WITH ULCERATIVE COLITIS

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Introduction: Fecal microbiota transplantation (FMT) is an experimental approach for the treatment success of FMT in UC patients. This is an open labeled trial of repeated FMT for steroid resistant or dependent ulcerative colitis patients (n = 50). Demographic and laboratory findings of donor and recipient were...
recorded. Fecal samples of donors and patients were analysed by 16S rRNA gene-based microbiota analysis in only 10 patients (related donors).

**Results:** 16/50 (32%) of patients showed complete response and 4/50 (8%) had a partial response to FMT. Response was mainly influenced by the taxonomic composition of the donor’s microbiota. Stool of donors with a high bacterial richness (observed species richness 811 ± 74 vs no response 644 ± 168 at 15996 rps) and a high relative abundance of Akkermansia muciniphila (4.2 ± 2.1% vs 0.3 ± 0.1%), Faecalibacterium prausnitzii (11.9 ± 3.0% vs 6.2 ± 2.9%), and Ruminococcus spp. (15.2 ± 3.2% vs 1.1 ± 0.8%) were more likely to induce response. Demographic data were also analysed. Multivariate analysis showed the duration of illness longer than 1 year was a negative predictive factor (0.72 (0.57–0.92) p < 0.01).

**Conclusion:** The taxonomic composition of the donor’s intestinal microbiota is a major factor influencing response for FMT. Further artificial microbial preparations for ideal microbial match should be investigated. Duration of illness is a significant factor for success of FMT and early application of FMT in UC should be studied in further well-designed trials.

**Disclosure:** Nothing to disclose.

**OP336 LINKING MUCUS DEPLETION AND MICROBIOME ALTERATIONS IN UC TO MUCOSAL ENERGY SUPPLY**

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**Introduction:** Mucosal ATP depletion as the consequence of reduced mitochondrial respiratory chain activity has been attributed to ulcerative colitis (UC) pathogenesis more than 30 years ago. Mucus producing goblet cells, which are highly dependent on energy supply via the oxidative phosphorylation (OXPHOS) system, are supposedly highly affected by reduced OXPHOS activity. Furthermore, reduced numbers of goblet cells and intestinal mucus depletion have been suggested as histological hallmarks of UC. Finally, mucus composition and glycosylation is able to shape the intestinal microbiota, which is frequently altered in UC patients. Nevertheless, experimental evidence linking mitochondrial dysfunction with intestinal mucus depletion and microbiome alterations are still missing.

**Aims and Methods:** Mucus producing HT29MTX cells as well as marine intestinal organoids are employed as in vitro or ex vivo model systems, respectively, in order to study mucin transcription, production, secretion and glycosylation upon energy metabolism modifying stimuli. In vivo, conplastic mice, carrying well-characterized single nucleotide polymorphisms in their mitochondrial genome, are studied on their susceptibility to various experimental colitis models. Furthermore, seahorse analyzer is used to control for mitochondrial respiration and glycolysis, while microbiome composition is analysed via 16srRNA next generation sequencing.

**Results:** In vitro stimulation of HT29MTX cells showed that mucus transcription and secretion is highly dependent on mitochondrial OXPHOS capacity. In line with this, mice with reduced mucosal ATP levels and OXPHOS activity depicted goblet cell reduction and increased susceptibility to DSS colitis, characterized by elevated DAI, MEICS and histologic scores. On the other hand, mice with increased mucosal ATP levels were protected against experimental colitis. Finally, gut microbial composition was highly dependent on mitochondrial genetics.

**Conclusion:** Taken together, we here describe a new pathway linking major hallmarks of UC. Mitochondrial OXPHOS activity and mucosal ATP levels in intestinal epithelial cells might be strongly underestimated factors in UC pathogenesis and therapeutic potentialities.

**Disclosure:** Nothing to disclose.

**OP337 IDENTIFICATION OF A BILE ACID PROFILE AND GUT MICROBIOME COMMUNITY STRUCTURE ASSOCIATED WITH EARLY FLARE AFTER NUTRITIONAL THERAPY IN PAEDIATRIC CROHN’S DISEASE**

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2Dahlouise University – IWK Health Centre, Paediatric Gastroenterology and Nutrition, Halifax, Canada
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**Introduction:** Changes in gut bacterial community structure are associated with Crohn’s Disease (CD) development and response to therapy including reduced diversity, temporal instability, and shifts in abundances of many bacterial species. Bile acid (BAs) play a central role in modulating the immune response, and changes in the BA pool are also associated with gut bacterial activity. The liver synthesizes and conjugates the primary BAs while bacteria deconjugate, epimerize and dehydroxylate in the production of the secondary BAs. The predominant primary BAs are cholic acid (CA) and chenodeoxycholic acid (CDCA), and the predominant secondary BAs are lithocholic acid (LCA) and deoxycholic acid (DCA). Because the gut microbial community impacts the BA pool, it is possible that community changes could affect the BA-receptor mediated immune response.

**Aims and Methods:** The relationship between the gut microbiome and the BA pool, both obtained from stool samples collected at baseline, during exclusive enteral nutrition therapy (up to week 12) and then at 12-week intervals to 48 weeks follow-up, was investigated in 16 pediatric CD patients. Patient outcomes were classified as: sustained remission for >24 weeks (SR), non-sustained remission (NSR) or non-remission (NR). Taxonomic marker (16S) and metagenomic sequencing was performed on the stool samples. Taxonomic and functional assignments were made using QIIME and HUMAN2, with diversity statistics computed using QIIME. Bile acid profiles were obtained from stool by liquid chromatography tandem mass spectrometry. Standard statistical tests were performed using R, and the relationship between microbial community structure and BA composition was inferred using a hierarchical Bayesian model (BioMiCo).

**Results:** 2 groups of patients were identified that differed in both BA profile and gut microbiome. The first group was associated with high amounts of the secondary bile acids LCA and DCA, and was comprised of SR. NSR and NR patients. These patients had relatively high levels of microbial alpha diversity, with Ruminococcus obeum, B. torques, Bacteroides uniformis, B. vulgatus, several species of Alistipes and Subdoligranulum being predominant lineages. The second group was associated with high amounts of unconjugated primary bile acids and 2 other secondary bile acids, ursodeoxycholic acid (UDCA) and hyodeoxycholic acid (HDCA). This group was comprised exclusively of NSR patients. Alpha diversity was lower in these patients, with R. gravis, B. plebeius, B. eggerthii, Clostridium boccace, and C. innocuum being predominant lineages. A survey of bacterial BA genes within the metagenome revealed that most samples contained the bile salt hydrolase gene responsible for deconjugation. The bacterial genes responsible for conversion to secondary bile acids were much more restricted.

**Conclusion:** Primary BAs levels differed significantly between the SR and NSR patients. Moreover, high primary BAs were seen only in NSR patients. The presence of HDCA in the second group of patients (all NSR) is noteworthy, as HDCA has a detergent like effect leading to membrane disruption, and is suggested to induce strong cytotoxicity, apoptosis, and IL-8 synthesis. Based on these findings, we speculate that there may be a microbial community that leads to increased HDCA and impacts the ability to sustain remission.

**Disclosure:** Nothing to disclose.
In our NASH clinic, about a quarter of the referred patients were reported following liver biopsy.

**P0001** MEDICAL EVALUATION ON SUSPICION OF NON-ALCOHOLIC STEATOHEPATITIS (NASH): REAL-WORLD OUTCOME FROM A COMMUNITY NASH CLINIC

**Aims and Methods:** During 2017, patients from Bispebjerg Hospital clinics with a suspicion of NASH were referred to the NASH clinic. Suspicions of NASH were based on having at least 2 of the following risk factors: BMI ≥25 kg/m², or persistent ALT > 80 U/l. Based on a general work-up algorithm and an individualized approach, routine and NAFLD specific examinations were performed to exclude other causes of chronic liver disease (CLD). To diagnose and assess NAFLD grade and fibrosis stage, structured interview including thorough medical history, anthropometric measurements, NAFLD (hepatic, metabolic and fibrosis) blood tests (no genetics), ultrason. US-echography and US-guided liver biopsy was offered as appropriate. NASH diagnosis and fibrosis stage was based on histopathology. NAFLD activity, NAFLD fibrosis and FIB-4 index scores were calculated. Numbers of patients, percentages of total (%), medians (upper range-lower range) and means ± standard deviation were reported, as appropriate.

**Results:** 55 adult patients were referred to the NASH clinic on suspicion of NASH: 12 patients (22%) were found to have non-NAFLD CLD (including hepatocellular carcinoma) and 43 patients (78%) were classified as NASH. Of these, 26 people, F1, and if CUM10 > 5.0, then a = 1, if CUM20 < 2.50%, then b = 1, if and if CUM30 < 5.65%, then c = 1, if CUM30 > 5.65%, then c = 0, to determine the degree of fibrosis of the liver as F0, which is corresponding to the presence of portal fibrosis, at a value of N = 1–3, the liver fibrosis of F2-3, corresponding to the presence of portal fibrosis without septa and with a small number of septa, with a value of N = 10–13, determines the degree of fibrosis of the liver F3-4, which is determined by the degree of liver cirrhosis and cirrhosis. The invention is based on the first time we established a constant relationship between the cumulative dose of 13C-MBT and the presence of liver fibrosis.

**Conclusion:** The results of the method of assessing fibrosis with the 13C-MBT in the determination of the degree of liver fibrosis, corresponded to the values of the liver biopsy, fibrotests, elastometry. N = 1a + 2b + 10c, where is the number of scores, a is the coefficient calculated from the cumulative dose of 13C for 10 min-1 in% (CUM10), b - the coefficient calculated from the cumulative dose of 13C for 20 minutes in% (CUM20), c is the coefficient calculated from the cumulative dose of 13C for 30 minutes in (CUM30), if CUM10 < 1%, then a = 1, if CUM10 > 1.00%, then a = 0, if CUM20 < 2.50%, then b = 1, and if CUM20 > 2.50%, then b = 0, if CUM30 < 5.65%, then c = 1, if CUM30 > 5.65%, then c = 0, and for N = 0, determine the degree of fibrosis of the liver as F0, which is corresponding to the presence of portal fibrosis, at a value of N = 1–3, the liver fibrosis of F2-3, corresponding to the presence of portal fibrosis without septa and with a small number of septa, with a value of N = 10–13, determines the degree of fibrosis of the liver F3-4, corresponding to the presence of numerous septa without cirrhosis and cirrhosis. The invention is based on the first time we established a constant relationship between the cumulative dose reduction indices 13C at the 10th, 20th and 30th minute 13C-metacetinologo performing the breath test and the risk of the presence of liver fibrosis in patients with CLD.

**Disclosure:** Nothing to disclose

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Introduction: Steatohepatitis (NASH) with fibrosis is the phenotype of non-alcoholic fatty liver disease (NAFLD) that carries the highest risk of developing end-stage liver disease and the associated serious complications including cardiovascular disease. In line with recent international and national Danish guidelines for the management of NAFLD patients, we established a community NASH clinic including a multi-disciplinary-team. We here report our initial experience and real-world outcome for medical evaluation of referred patients on suspicion of NASH.

**Conclusion:** The results of the method of assessing fibrosis with the 13C-MBT in the determination of the degree of liver fibrosis, corresponded to the values of the liver biopsy, fibrotests, elastometry. N = 1a + 2b + 10c, where is the number of scores, a is the coefficient calculated from the cumulative dose of 13C for 10 min-1 in% (CUM10), b - the coefficient calculated from the cumulative dose of 13C for 20 minutes in% (CUM20), c is the coefficient calculated from the cumulative dose of 13C for 30 minutes in (CUM30), if CUM10 < 1%, then a = 1, if CUM10 > 1.00%, then a = 0, if CUM20 < 2.50%, then b = 1, and if CUM20 > 2.50%, then b = 0, if CUM30 < 5.65%, then c = 1, if CUM30 > 5.65%, then c = 0, and for N = 0, determine the degree of fibrosis of the liver as F0, which is corresponding to the presence of portal fibrosis, at a value of N = 1–3, the liver fibrosis of F2-3, corresponding to the presence of portal fibrosis without septa and with a small number of septa, with a value of N = 10–13, determines the degree of fibrosis of the liver F3-4, corresponding to the presence of numerous septa without cirrhosis and cirrhosis. The invention is based on the first time we established a constant relationship between the cumulative dose reduction indices 13C at the 10th, 20th and 30th minute 13C-metacetinologo performing the breath test and the risk of the presence of liver fibrosis in patients with CLD.

**Disclosure:** Nothing to disclose

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**P0003 INSULIN-LIKE GROWTH FACTOR1 AS A MARKER OF SEVERITY OF LIVER CIRRHOSIS**

**Aims and Methods:** The study included 69 patients with liver cirrhosis of various etiologies from Menoufa University Hospitals (Egypt) and 18 healthy volunteers as a control group. They underwent physical examination and laboratory investigations (CBC, liver profile [ALT, AST, serum albumin, bilirubin, PT %], urea, creatinine, fasting glucose, postprandial glucose and serum IGF-1). Abdominal ultrasonography was done for all patients. Child-Pugh Score, MELD score and AST/Platelet ratio index (APRI score) were calculated for all patients.

**Results:** IGF-1 of cirrhotic patients (73.1 ± 42.3 ng/ml) was significantly lower than controls (243.2 ± 78.1 ng/ml) (p = 0.0001). IGF-1 was significantly lower in Child class C (46.11 ± 66.6 ng/ml) than Child class B (64.8 ± 44.4 ng/ml) and A (149.1 ± 43.8 ng/ml) (p = 0.002 and 0.0001 respectively). Also IGF-1 was significantly lower in Child class B than class A (p = 0.0001). IGF-1 was significantly lower in patients with MELD score < 20 (45.62 ± 6.72 ng/ml) than MELD score 10–19 (61.28 ± 13.85 ng/ml) and MELD score > 20 (152.1 ± 44.30 ng/ml) (p = 0.0001). IGF-1 was significantly lower in patients with APRI < 1.5
CHRONIC HCV INFECTION

P0004 METABOLOMICS IDENTIFIES ADVANCED FIBROSIS IN CHRONIC HCV INFECTION

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Introduction: Chronic HCV infection (cHCV) is a leading cause of liver disease and transplantation worldwide and a major burden on public health. Early diagnosis and classification of the degree of liver fibrosis is crucial in clinical practice to determine the urgency and need for anti-HCV antiviral therapy.

Aims and Methods: To assess the metabolites that are associated with fibrosis stages in chronic HCV infection, using metabolomic analysis.

Results: A total of 40 patients were included in the study, 30 diagnosed with cHCV infection and 10 controls. Fibrosis were assessed using FibroMax elaborated by Biopredictive (R) (Paris, France). The metabolomic techniques (high performance liquid chromatography coupled with mass spectrometry (LC-MS) and principal component analysis (PCA)) were performed from serum and urine samples of each patient, to identify final products of various metabolic pathways correlated with liver fibrosis.

Conclusion: The 30 patients with cHCV included in the study, 20 patients (66.6 %) had advanced fibrosis (F3-4). The metabolic profile identified 3 metabolites (3 of serum and 2 of urine) that are associated with severe fibrosis (F3-4): hexacosanoyl carnitine > 26416 (AUC 0.717; Se 61%, Sp 80%; p = 0.03); aspartylaspartic acid > 228956 (AUC 0.700; Se 70.00%, Sp 70.00%; p = 0.05); prostaglandin E2 (PGE2) > 4265917 (AUC 0.695; Se 65.30%, Sp 70.00%; p = 0.04) and lactic acid (a) > 70056 (AUC 0.766; Se 63.16%, Sp 100%; p = 0.003), taurine (u) > 50172 (AUC 0.772; Se 78.45%, Sp 77.78%; p = 0.008).

The combined use of the metabolites determined an AUC of 0.863, with Se 82.35 and Sp 88.80, p < 0.0001.

Disclosure: Nothing to disclose

P0005 THE INFLUENCE OF HYPERGASTRINEMIA ON MOTILITY AND LIVER HISTOLOGICAL PECULIARITIES

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Introduction: The influence of hypergastrinemia on the motility and liver function is not well studied. The hypochlorhydria of gastric juice can occur in the case of prolonged use of proton pump inhibitors, atrophic gastritis, autoimmune processes etc. It leads to hypergastrinemia, decrease of pepsin activation, dysbiosis, motility violation.

Aims and Methods: The aim of our work was to study histological liver peculiarities due to the influence of hypergastrinemia, to estimate the severity of inflammation and to study the role of multiprobiotic in these conditions. We included 40 rats that were randomly divided into 4 groups with 10 rats in each. Group 1 (control) received intraperitoneally 0.5 ml/kg and per os 0.5 ml of water once per day during 28 days. Group 2 received 0.14 ml/kg multiprobiotic once per day during 28 days. Group 3 received 14 mg/kg omeprazole once per day during 28 days (model of prolonged hypochlorhydria). Group 4 received 0.14 ml/kg multiprobiotic + omeprazole in dose 14 mg/kg during 28 days. Of all of them the histological peculiarities of liver were studied, we measured the levels of IL-1, IL-4, IL-6, TNF-alpha. The expression of genes Nos2, Tgfbl, ChgA, Regla, Hgf was measured using semi-quantitative reverse transcription polymerase chain reaction with densitometry.

Results: A long-term suppression of gastric acid secretion leads to the violation of motility, hypergastrinemia, that increases dysbiosis. The inflammation was absent in the group that received multiprobiotic. In the group with marked hypochlorhydria IL-1 was increased in 4.7 times (p < 0.01), IL-6 was increased in 8.1 times (p < 0.01), during the histological examination leukocytes infiltration and edema were observed. The administration of multiprobiotic led to the increase of IL-4 and IL-10 in 2.1 and 2.7 times correspondingly. It was established the increase of relative gene nitric oxide synthase 2 (NOS2) expression in the liver and pancreas. In the liver was increased the expression of transforming growth factor beta 1 (TGFβ1), chromogranin A (CHGA) and regenerating islet-derived protein 1 alpha (REG1a). The expression of hepatocyte growth factor (Hgf) was absent that indicates on violations of molecular mechanisms of the regulation of anti-bacterial processes.

Conclusion: The results of performed investigations clearly indicate the development of new mechanisms which are associated with the progression of oxidative stress in liver upon these experimental conditions. As a result of these disturbances, the damage of functional status and further possible formations of fibrosis in liver can occur. The leading role of pathogenic microbiota in violation of structural and functional state of liver upon long-term suppression of gastric acid secretion were established.

Disclosure: Nothing to disclose

P0006 AMNION-DERIVED MESENCHYMAL STEM CELLS AMELIORATES SCLEROSING CHOLANGITIS IN RATS

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Introduction: Cell therapy with mesenchymal stem cells (MSCs) is expected as a new therapeutic strategy, and large numbers of MSCs can be isolated from the amnion noninvasively. Sclerosing cholangitis is a chronic cholestatic disease, characterized by inflammation, oblitative fibrosis of bile ducts, stricture formation, progressive biliary obstruction leading to cirrhosis. Many factors are involved in the development of sclerosing cholangitis; however, the effective medical therapy for sclerosing cholangitis has not been established. Therefore, a new strategy to delay or prevent disease progression of sclerosing cholangitis is urgently required.

Aims and Methods: We investigated the effects of human amnion-derived MSCs (hAMSC) and conditioned medium (CM) obtained from hAMSC cultures in rats with sclerosing cholangitis. Sclerosing cholangitis was induced by the intra-gastric administration of 100 mg/kg alpha-naphthylisothiocyanate (ANIT) twice weekly for 4 weeks. ANIT is a toxin that targets intrahepatic bile ducts, and it is used to generate animal models of sclerosing cholangitis. hAMSCs were cultured in dishes until reaching a subconfluent state. After washing, cells were further cultured for 48 hours in serum-free medium and subsequently, CM was collected. One million hAMSCs suspended in 200 µl of phosphate-buffered saline or 200 µl of CM were intravenously injected into the penile vein on days 15 and 22. All rats were sacrificed on day 29. In each animal, the left lobes of the liver were evaluated via histological, immunohistochemical, and mRNA expression analyses.

Results: Biliary hyperplasia, peribiliary fibrosis, and inflammation in Glisson’s sheath were induced by ANIT. Histological scoring demonstrated that hAMSC transplantation and CM administration significantly suppressed biliary hyperplasia. The number of necrotic lesions was significantly decreased by hAMSC transplantation. In addition, immunohistochemical examination demonstrated that hAMSC transplantation and CM administration significantly improved...
biliary hyperplasia, peribiliary fibrosis, and inflammation in Glissonean sheath. Accordingly, mRNA expression of CK19, MMP-9, TNF-α, and MCP-1 in the liver was also significantly decreased by HAMSC transplantation and CM administration.

Conclusion: hAMSC transplantation and CM administration ameliorated biliary hyperplasia, peribiliary fibrosis, and inflammation in Glissonean sheath in a rat model of sclerosing cholangitis. hAMSCs and CM may represent new modalities for treating sclerosing cholangitis.

Disclosure: Nothing to disclose

P0007 BODY MASS INDEX (BMI) AND ALCOHOL CONSUME ARE DIRECTLY RELATED WITH LIVER STEATOSIS. RESULTS FROM A PROSPECTIVE MULTICENTER STUDY OF PATIENTS REFERRED FOR HEPATIC FERRITINEMIA


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Introduction: Liver steatosis is often suspected in patients with hyperferritinemia.

Aims and Methods: To study the BMI and alcohol consumption of patients referred for HF to 6 hospitals in the Basque country, Spain. To study the prevalence of hepatic steatosis determined by MRI in these patients.

A prospective study of 312 consecutive with HF (1700 men / 1420 women) and/or TSI > 20 mg/L men / 10 mg/L women, viral infection (HCV, HBV), oral iron, menopause, one or more MtS criteria (2) or BMI 25-30: 56/129 (43.41%) / 286; the results obtained were statistically significant (p = 0.000). Relationship with alcohol consumption was also evaluated. Alcohol consumption was directly related with the presence of liver steatosis: 43/196 patients (21.94%) -no alcohol-mild steatosis (59.88%), moderate/ heavy drinker. The results were statistically significant (p ≥ 0.000).

Conclusion: BMI and alcohol consume are directly related with the presence of liver steatosis in patients referred for hyperferritinemia in our country.

Disclosure: Nothing to disclose

P0008 DYSMETABOLIC IRON OVERLOAD SYNDROME AND ITS RELATIONSHIP WITH HFE GENE MUTATIONS AND WITH LIVER STEATOSIS

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Introduction: The dysmetabolic syndrome with iron overload (DIOS) is characterized by producing hyperferritinemia (HF) with slight elevation of the hepatic iron concentration, together with one or more diagnostic factors of metabolic syndrome (MS): obesity, hypertension, dyslipidemia, and/or abnormal metabolism of glucose or BMI > 25 kg/m². It is associated with up to 50% with NAFLD/NASH.

The diagnosis is made discarding the usual causes of hepatic iron overload.

Aims and Methods: To study the cases of DIOS in a cohort of patients with hyperferritinemia sent to 6 hospitals in the Basque Country and to determine its relationship with mutations of the HFE gene and with hepatic steatosis.

A prospective study of consecutive patients with HF (>200 μg/L women; 300 μg/L men) and/or TSI > 45%, confirmed in 2 determinations, was conducted from December 2010 to April 2013. Dysmetabolic iron overload syndrome (DIOS) was diagnosed (1) when ≥ 36, one or more MtS criteria (2) or BMI ≥ 25; exclusion criteria: C282Y/C282Y, LIC > 80-phenotypic hemochromatosis, alcohol > 40 g/day men / > 20 g/day women, viral infection (HCV, HBV), oral iron, blood transfusions. LIC was determined by MRI 1.5 Tesla system (SIR method)

(3). We systematically performed T1-weighted in-phase and opposed-phase imaging to determine the presence or not of liver steatosis (4). We studied HFE gene mutations in all the patients.

Results: 312 patients (272 men / 40 women) were included. Mean age 55 (SD 13.5); Mean ferritin 729.6 (SD 449.6), mean TSI 40.8 (SD 15.8); 82 patients were diagnosed with DIOS. H63D/H63D 19 (23.17%), C282Y/H63D 11 (13.41%), C282Y/wt 5 (6.10%), H63D/wt 25 (30.49%). When we compared the results with those of Basque general population (5), the differences were statistically significant for H63D/H63D (p = 0.002) and C282Y/H63D (p = 0.009) mutations.

In 286 patients a MR study for the presence of liver steatosis was performed: 196 no steatosis; 90 liver steatosis (31.47%). There were 71 DIOS patients (from 82 with MR for LS determination: 13 with LS (18.31%)), 58 without LS (81.69%). From 215 patients without DIOS and with MR-77 LS (35.81%), 138 without LS (64.19%). When we compared the patients from DIOS group with MR and the group without DIOS and MR, LS was more frequent in the group without DIOS (p = 0.006).

Conclusion: HFE gene mutations H63D/H63D and C282Y/H63D are more associated with DIOS patients than with general population in our country; liver steatosis is more frequent in patients without DIOS than in patients with DIOS.

Disclosure: Nothing to disclose

References

P0009 NON-ALCOHOLIC FATTY LIVER DISEASE IS ASSOCIATED WITH CORONARY ARTERY CALCIFICATION IN ASYMPTOMATIC INDIVIDUALS

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is related closely to risk factors for coronary artery disease (CAD), but it is unclear whether NAFLD independently contributes to asymptomatic individuals. Coronary artery calcium (CAC) scanning is the predictor of coronary events. We investigated the association of coronary artery calcification with NAFLD in asymptomatic adults.

Aims and Methods: This is the cross-sectional study performed in Hansol Hospital Healthcare Center. NAFLD was defined as cases with the typical ultrasonographic findings without excessive alcohol consumption, medications causing hepatic steatosis or other chronic liver diseases. CAC was evaluated using the Agatston method.

Results: We enrolled 312 subjects (mean age, 46.8 ± 8.7 years; 60.7% males) without known liver disease or a history of ischemic heart disease. NAFLD was found in 27% of the enrolled subjects and CAC > 100 with moderate-high risk of CAD was found in 10.3% of subjects. Male gender (odds ratios (OR), 2.857; 95% confidence intervals (CI), 1.169-6.147), diabetes mellitus (OR, 2.739; 95% CI, 1.092-5.638), increased age (OR, 1.288; 95% CI, 1.071-1.571), and history of hypertension (OR, 1.826; 95% CI, 1.065-3.592) were independent factors that increased the risk of CAC > 100 in binary logistic regression.

Conclusion: NAFLD is associated with increased coronary artery calcification independent of traditional risk factors. The assessment of CAC may be useful in identifying NAFLD patients at risk of future cardiovascular events even in asymptomatic individuals.

Disclosure: Nothing to disclose
A POTENTIAL LINK BETWEEN POLYCYSTIC OVARY SYNDROME AND NON-ALCOHOLIC FATTY LIVER DISEASE: AN UPDATE META-ANALYSIS

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Introduction: Polycystic ovary syndrome (PCOS) itself accounts for a high risk of developing non-alcoholic fatty liver disease (NAFLD). Alternatively, other specific factors in women with PCOS may contribute to this association, which presently remains unknown.

Aims and Methods: We aimed to shed some light into this issue, and thereby performed this meta-analysis. Relevant studies that were published before May 2017 were identified and retrieving from PubMed and Web of Science databases.

Data were extracted, and the pooled odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated.

Results: A total of 17 studies were included into this analysis. Compared to the control group, the risk of NAFLD in the PCOS group was higher (OR = 2.25, 95% CI = 1.95–2.60). When stratified by BMI and geographic location, these results indicated that the frequency of NAFLD risk was significantly higher amongst obese subjects (OR = 3.01, 95% CI = 1.88–4.82), non-obese subjects (OR = 2.07, 95% CI = 1.12–3.85), subjects from Europe (OR = 2.00, 95% CI = 1.58–2.52), subjects from the Asia-Pacific Region, (OR = 2.32, 95% CI = 1.89–2.84) and subjects from America (OR = 2.96, 95% CI = 1.93–4.55), respectively. In addition, PCOS patients with hyperandrogenism (HA) had a significantly higher risk of NAFLD than controls (OR = 3.31; 95% CI = 2.58–4.24). However, there was no association between PCOS patients without HA and higher risk of NAFLD (OR = 1.46; 95% CI = 0.55–3.87).

Conclusion: In summary, women with PCOS are more likely to develop NAFLD. Furthermore, HA itself is not a major factor leading to the disease. An excess in androgen levels, which is the main feature of PCOS and is interrelated to IR, might be a contributing factor to the development of NAFLD in PCOS patients. These findings have clinical implications for NAFLD screening in hyperandrogenic women with PCOS.

Disclosure: Nothing to disclose

UDCA EFFICACY IN THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Introduction: Dyslipidemia, insulin resistance, steatosis and fibrosis play a key role in the pathogenesis of NAFLD.

Aims and Methods: We aimed to evaluate the effect of UDCA in combination with of lifestyle modification on liver steatosis and fibrosis, insulin resistance (IR) and lipid profile in these patients with NAFLD.

90 obese (BMI >30, Mediana - 32) patients (men 49) with NAFLD were included in the study. The median (Me) age - 45.6 years. All patients had cystosis (> 2 mm) and / or Fibrosis (F) and Steatosis (S) - 1 stage by FibroScan 502 TOUCH equipment. There were 40 patients for obese patients and CAP technology. Blood lipid spectrum, IR, signs of inflammation were evaluated. Body metabolism (M) assessed by method of indirect calorimetry and impedimentance (IM). It was done before treatment (0 stage) (minus 500 kcal/day with low level of carbohydrates <100g/day) in combination with exercises (plus 500 kcal/day).

63 patients were prescribed a diet in combination with daily aerobic exercise (group 2). Follow up period - 6 months.

Results: According to IM data in both groups there was a decrease in body weight (Me =7% of baseline), basal metabolism (Me =10%), fat mass in Me =14%. At the same time muscle mass increased - with a parallel increase in muscle mass- metabolically active body mass Me = 8. According to IM evaluation there was an increase in respiratory exchange ratio by 12% with an increase in oxygen consumption (+ 15%) and a decrease in the O2 production (+13) in both groups, a decrease in the metabolic age by 5 years (Me). Metabolic parameters correlated (r>0.3) with value of insulin, glucose, total cholesterol, LDL, S. F. There was a 25% decrease in Me of ALT, p < 0.01 (1st group), and 12% of the 2nd group (p < 0.05); reduction of AST by 36% and 8% respectively (p < 0.001), GGTP-36% and 27% respectively (p < 0.001), glycated Hb-20% and 11% (respectively) (p < 0.05); insulin levels 16% and 14% respectively (p < 0.02); HOMA - 16% and 8% respectively (p < 0.04); total cholesterol 10% and 5% respectively (p <0.001); triglycerides -27% and 10% respectively (p < 0.05); LDL 22% and 10% respectively (p < 0.05); S (dB/m²) -19% and 13% respectively (p < 0.05); F -reduction in 1 stage (Metavir) in 40% of patients in group 1.

Conclusion: The UDCA administration in combination with of lifestyle modification in obese patients with NAFLD results in significant reduction of liver enzymes levels, insulin resistance and dyslipidemia compared with non-pharmacological therapy only.

Disclosure: Nothing to disclose

MOLECULAR INVERSION PROBE ASSAY TO IDENTIFY NOVEL GENES ASSOCIATED WITH POLYCYSTIC LIVER DISEASE

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Introduction: Polycystic liver disease (PLD) is an inherited disorder associated with autosomal dominant inheritance. The prevalence of PLD currently consists of six genes related to autosomal dominant PLD (ADPLD) and two genes related to PLD in patients with autosomal dominant polycystic kidney disease (ADPKD). The genetic causes of PLD in the majority of ADPLD patients remains unknown. Identification of these genes is important for understanding of pathways leading to liver cysts as well as possible genotype-phenotype associations. The aim of our study was to identify novel genes associated with PLD.

Aims and Methods: We deployed molecular inversion probe (MIP) analysis for the discovery of genetic variants in 26 genes in a cohort of unrelated PLD patients. We developed probes for 5 known genes associated with PLD and 21 genes chosen for their association with liver or kidney cysts in literature. Variants identified using the MIP assay were filtered before validation using Sanger sequencing. The validated variants were then selected based on novelty or SNP frequency < 0.001, in silico prediction using bioinformatics prediction tools (PolyPhen 2, SIFT), and similarity of pathogenic variants in known PLD-genes. If available, family members were screened to test for disease segregation.

Results: We identified 625 unrelated patients with the primary phenotype of PLD. After the first filter steps of the MIP methods we identified 280 variants in 15 genes significantly associated with PLD. For six remaining genes no variants were identified that complited to all filter steps. Sanger sequencing of these 280 variants lead to validation of 85 variants in 10 genes. Sixty-five of the non-validated variants occurred in the remaining 5 genes. Of the validated variants, 49 variants and their known SNPs with frequency < 0.001 (n=36), have not been described before (n = 11), or frequency data is not available (n = 2). These 49 variants were all predicted to be likely pathogenic or pathogenic by in silico prediction and are found in 9 genes.

Conclusion: We identified 49 genetic variants in 9 genes in a large international cohort of PLD patients. These are all novel or rare variants predicted to have deleterious effect on their corresponding protein. These genes are possibly associated with PLD and are excellent candidates for further functional studies to provide evidence for their relation with PLD.

Disclosure: Nothing to disclose
P0014 LOW BISPHENOL A CONCENTRATION INDUCES PROLIFERATION, OXIDATIVE STRESS, AND PI3K/AKT-Novo SYNTHESIS OF STEROID HORMONES IN HEPATOMA CELL LINE

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Introduction: Human liver is known as one of the target organs for estrogens, with mitogenic activity. Bisphenol A (BPA), is an artificial environmental endocrine disrupting chemicals (EDCs) that leaches from polycarbonate plastics that consequently leads to low-dose human exposure. The BPA environmental exposition was hepatic damage and worsening of non-alcoholic fatty liver disease (NAFLD). BPA is considered to be a xeno-estrogen and it can bind to estrogen receptors (ERs). Estrogens play important roles in the cell proliferation and invasion of estrogen dependent human neoplasms.

Aims and Methods: The aim of this study was to investigate the low dose of BPA effects on cell proliferation, oxidative stress and impaired synthesis of steroid hormones in human HepG2 cells. Cells were exposed to non-toxic BPA concentration (0.025 and 0.05 μM) for 48 and 72 h. Cell viability was assessed by adding 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) assay. The level of Thioflavine T-Acidic-Resistant Species (TBARS) was assessed as markers of lipoperoxidation. The effect of BPA on the expression of p-ERK, ERK, Caspase 3 and aryl hydrocarbon receptor (AhR) was determined by Western blot analysis. The analysis of steroids extracted from cell culture medium were performed by mass spectrometer analysis.

Results: BPA was able to induce a significant increase of both cell proliferation (p = 0.0013) and TBARS concentration (p = 0.0003) after 48 hours of incubation. Moreover BPA increased the protein expression of key molecules involved in the regulation of proliferation and survival, as ER, p-ERK and AKT, and reduced the expression of caspase 3. Low dose of BPA induced an increase estrogen/testosterone ratio compared to untreated cells. The major representative peaks present in the media of BPA-treated HepG2, obtained by mass spectrometry, were: 17β-estradiol 3-sulfate (353.1 ± 1 m/z), methoxyestrone 3-sulfate (381.3 ± 1 m/z), 17- hydroxyprogesterone (331.3 ± 0.2 m/z), estrone (269 ± 1 m/z), estradiol (238.3 ± 1 m/z), testosterone sulfate (367.4 ± 1 m/z) and cholesterol (393 ± 1 m/z).

Conclusion: In the present study we demonstrated that treatment of HepG2 cells with low doses BPA elicited: 1) increase of proliferation rate; 2) regulation of oxidative stress 4) induction of oxidative metabolism of estrone.

Disclosure: Nothing to disclose

P0015 TRANSIENT ELASTOGRAPHY, APRI AND FIB-4 SCORES FOR STAGING OF FIBROSIS AND CIRRHOSIS IN WILSON DISEASE

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Introduction: Data on the predictive capability of cirrhosis through transient elastography (TE) in Wilson disease (WD) is scarce. Furthermore there is no data regarding its value to monitor therapy. Aim was therefore to assess whether TE is a suitable tool to identify cirrhosis in patients (ii) newly diagnosed and (ii) under treatment for WD.

Aims and Methods: Patient with WD underwent TE (results in kPa) either at the time of diagnosis or during a regular outpatient visit during treatment. Data are shown only for patients in whom a liver biopsy was available. Furthermore data on initial liver biopsy results and non-invasive fibrosis scores (APRI, FIB-4) were recorded.

Results: 35 patients were included in the study. Of those 6 were de novo patients [Male: 50%, Age: 34 ±10, TE: 10.9 kPa (3.5-34.8)], Cirrhosis at LBX: 50% and 49 patients [Male: 49%, Age: 40 ±14], TE: 7.4 kPa (3.5-15.4), Cirrhosis at LBX:36.7%] had received various length of treatment with chelators. Significantly more patients under treatment were found with TE values < 12kPa [93.6% vs. 62.5%; p = 0.009] irrespective of initial biopsy results. Moreover the APRI classification found no patients (0%) with cirrhosis in the treated group (vs. 33.3% in the no-treatment group, p<0.001). No non-cirrhotic patient worsened under treatment according to the APRI classification (cirrhosis: F3/F4).

Conclusion: TE and non-invasive fibrosis scores are valid tools to discriminate cirrhosis in newly diagnosed WD patients. In cirrhotic patients no long-term treatment TE, APRI and FIB-4 were mostly below the threshold for advanced fibrosis, indicating that decompensating therapy prevents progression of liver disease.

Disclosure: Nothing to disclose

P0016 US-FIL SCORE - IS IT POSSIBLE TO PREDICT THE STEATOSIS GRADE WITH AN ULTRASONOGRAPHIC SCORE?

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Introduction: A recently created ultrasonographic score (Ultrasonographic fatty liver indicator (US-FLI)) allows the grading and staging of non-alcoholic fatty liver disease (NAFLD).

Aims and Methods: We aimed to assess the correlation of US-FLI with the controlled attenuation parameter (CAP) in patients with non-alcoholic fatty liver disease (NAFLD).

Interally, inter-observer agreement for the score was assessed between 3 physicians using a sample of 31 patients. Later, 96 patients with NAFLD were included and several anthropometric, clinical and analytical parameters were assessed and US and transient elastography was performed.

Results: Physicians showed an excellent absolute agreement regarding the total score, with an average Interclass Correlation Coefficient of 0.972 (95% CI 0.949–0.986).

Patients had a medium US-FLI of 6 ± 3 points and a mean CAP of 311 ± 45 dB/m. Comparing US-FLI with CAP, and considering the previously defined cutoff for steatosis > 51 (286dB/m) and > S2 (280dB/m), we verified that US-FLI had a good discriminative capacity for both grades, with areas under the curve (AUC) of 0.88 (p < 0.001) and 0.90 (p < 0.001), respectively. We also verified that a US-FLI < 3 points had a negative predictive value of 100% for steatosis > S2 and that values of US-FLI ≥ 6 points had a positive predictive value (PPV) of 94.0% for steatosis > S2.

When comparing the clinical score Fatty Liver Index (FLI) for the same CAP cutoffs, it showed a weak discriminative capacity for both grades with AUC of 0.65 (p = 0.030) and 0.66 (p = 0.017). When comparing AUC for US-FLI and FLI scores, we verified that these were significantly different for both cutoffs (p < 0.001).

Conclusion: US-FLI has an excellent reproducibility and a good discriminative capacity for the different steatosis grades. Scores ≤ 3 points allow us to exclude significant steatosis and scores ≥ 5 points have a PPV of 94.0% for steatosis > S2.

US-FLI was significantly superior to the clinical score FLI in the discrimination between steatosis grades.

Disclosure: Nothing to disclose

P0017 IDENTIFYING THE NEXT TREATMENT FOR POLYCYSTIC LIVER DISEASE USING A DRUG SCREENING LIBRARY

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Introduction: Autosomal dominant polycystic liver disease is an autosomal dominant genetic disorder caused by mutations in the genes PRKCSH, PCK1, and FLCN. The majority of patients develop cysts in the liver, which is an urgent need for a safe treatment that decreases cyst proliferation, and hence classified patients with cirrhosis, whereas in treated patients with cirrhosis at L.T. (n = 18) only 16.7%, 5.6% and 27.8% where classified with cirrhosis according to TE > 12kPa, APRI and FIB-4 scores respectively (see Table 1) suggesting a potential reveresible effect of therapy on the course of the disease.

Conclusion: In conclusion, TE and non-invasive fibrosis scores are valid tools to discriminate cirrhosis in newly diagnosed WD patients. In cirrhotic patients on long-term treatment TE, APRI and FIB-4 were mostly below the threshold for advanced fibrosis, indicating that decompensating therapy prevents progression of liver disease.

Disclosure: Nothing to disclose
cyst volume. The aim of our study is to design a diagnostic pipeline that is able to identify candidate compounds that may be involved in the pathophysiology of cysts. This pipeline involves the identification of key pathways related to hepatic cystogenesis: cell proliferation and fluid secretion caused by decreased calcium signaling and subsequently increased cAMP levels.1

**Aims and Methods:** The Selleckchem FDA-approved drug screening library contains a wide spectrum of compounds with therapeutic targets. PRKCSH knockout H69 cholangiocytes were used as in vitro model for polycystic liver disease. Cells were incubated with compounds at 10 microM concentration for 24 hours in triplicate. Proliferation was measured as absorbance after addition of WST-1 proliferation reagent (Sigma-Aldrich) for 3 hours. Compounds causing proliferation > 20% compared to DMSO controls were selected for incubation in wildtype H69 cholangiocytes. Compounds showing > 50% of proliferation compared to control and > 20% absolute difference between knock out and wildtype H69 cholangiocytes were identified as most promising. Compounds were further tested for their effect on cyclic AMP levels after 24 hours incubation using ELISA (Cayman).

**Results:** 1278 compounds showed proliferation rates of 80-120% relative to control in PRKCSH knockout H69 cholangiocytes. 26 compounds increased proliferation > 120% of control and 138 compounds decreased proliferation below 80% of control proliferation rate. These 164 compounds were further tested in wildtype H69 cholangiocytes, while octreotide was added as reference. 18 compounds showed proliferation > 50% of control proliferation rate and > 20% absolute difference between knock out and wildtype H69 cholangiocytes. These compounds were then screened for their effect on cyclic AMP levels of these compounds. We identified 3 FDA approved drugs that reduce proliferation rates in PRKCSH knockout cholangiocytes with large effect on proliferation rates in wildtype H69 cells. These drugs showed reduction of cyclic AMP as well. Target pathways of these compounds differ from somatostatin analogues and may become future pharmaceutical options for patients unresponsive to current treatment.

**Disclosure:** Nothing to disclose

**Reference**
P0020 TM6SF2 AND MBOAT7 GENE VARIANTS ARE NOT ASSOCIATED WITH THE RISK OF DEVELOPING LIVER FIBROSIS AND CIRRHOSIS IN AN EASTERN EUROPEAN POPULATION
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Introduction: Previous large-scale genetic studies identified single nucleotide polymorphisms (SNPs) of the TM6SF2 and MBOAT7 genes as risk factors for alcoholic liver cirrhosis and non-alcoholic fatty liver disease. In this study, we tried to evaluate the role of TM6SF2 rs58542926, rs10401969 and MBOAT7 rs1069747, rs626283 SNPs are associated with the risk of hepatic fibrosis or liver cirrhosis of different aetiology in an Eastern European population.

Aims and Methods: The study was conducted at the Department of Gastroenterology, Homburg University, Sciences Hospital, and included 334 patients with liver cirrhosis, 128 patients with liver fibrosis, and 560 controls. SNPs were genotyped by quantitative PCR, with TaqMan allelic discrimination assays.

Results: Genotype distributions of TM6SF2 (rs58542926, rs10401969) and MBOAT7 (rs614738, rs626283) SNPs were in Hardy-Weinberg equilibrium. The TM6SF2 rs58542926 and rs10401969 alleles and genotypes had similar frequencies in patients with cirrhosis and cirrhosis groups (p > 0.05). The distribution of MBOAT7 rs626283 and rs641738 genotypes did not also differ between the 3 groups (p > 0.05). Overall, none of the 4 analysed SNPs (rs58542926, rs10401969, rs614738, rs626283) was associated with the presence of hepatic fibrosis or liver cirrhosis in our population.

Conclusion: Our study showed no significant associations between TM6SF2 (rs58542926, rs10401969) and MBOAT7 (rs614738, rs626283) gene polymorphisms and liver fibrosis, alcohol or hepatitis C virus-induced liver cirrhosis in an Eastern European population. Randomly assigning point to a predominant role of exogenous risk factors for disease progression in these patients.

Disclosure: Nothing to disclose

P0021 ANTIOXIDANT PROPERTIES OF CELOCEXIB REDUCE HEPATIC VASCULAR RESISTANCE AND PORTAL PRESSURE IN CIRRHTIC RATS
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Introduction: Increased hepatic vascular resistance (HVR) due to architectural distortion and intraparenchymal vasocostriction is the primary factor for the development of portal hypertension in liver cirrhosis. Oxidative imbalance in cirrhotic livers, by decreasing nitric oxide (NO) bioavailability, contributes to increasing HVR and portal pressure (PP). Cyclooxygenase-2 (COX-2) is up-regulated in cirrhotic livers and correlated with fibrosis degree and PP.

Aims and Methods: To investigate the antioxidant capacity of celexib, a selective COX-2 inhibitor, and its effects on intraparenchymal resistance during the development of portal hypertension in cirrhotic rats. In vivo study, peritoneal injection of thiacetamide (TAA) was employed to induce liver cirrhosis for 16 weeks. 36 male Sprague-Dawley rats were randomly assigned to the control, TAA, and TAA+celexib groups. TAA-cirrhotic rats received celexib or its vehicle by gastric gavage for last 8 weeks. PP, portal blood flow (PBf) and HVR were measured before sacrificed. Oxidative stress levels were evaluated by in situ superoxide (O2•−) detection staining and activity of superoxide dismutase (SOD), cGMP and arachidonic acid metabolisms in liver homogenate were quantitated. Hepatic expressions of pivotal molecules in NO bioavailability (cNOS, AMPK, nitrotyrosine), oxidation/antioxidation (NOX4, SOD) and COX pathway (COX-1, COX-2) were analyzed by western blot. In vitro study, the reconstituent plasmid with COX-2 or empty vector were transfected into LSECs (SK-HeP1) and hepatocytes (LO2). After treatment with PGE2, AH6809 (EP2 antagonist), U46619 (TXA2R agonist), Terutroban (TXA2R antagonist), Dorsomorphin (AMPK inhibitor) and GKT137831 (NOX4 inhibitor), NOX4 inhibitor, in situ O2•− levels and protein expressions were evaluated.

Results: Celexib administration significantly decreased PP by 22.8% (12.51±0.69 vs. 16.20±0.64 cmH2O, p < 0.05) and HVR by 31.6% (344.52±53.45 vs. 236.27±41.25, p < 0.05; 729.32±217.91 vs. 542.6±357.69, p < 0.05; 702.26±192.09 vs. 548.39±355.36, p < 0.05; 729.32±214.43 vs. 455.58±236.27, p < 0.05). The area under the curve (AUC) of W/F as predictor of in-hospital and 30-day mortality was 0.831 and 0.815, respectively, p < 0.01, not presenting values significantly higher than CP, MELD and CLIF-CAD scores. The cut-off value of W/F to predict in-hospital and 30-day mortality was 0.636. Conclusion: The W/F constitutes a mortality predictor independent of the CP, MELD and CLIF-CAD scores, identifying decompensated cirrhotic patients with poor short term prognosis. Thus, it is a promising biological marker, requiring more studies in order to be integrated into a new prognostic score.

Disclosure: Nothing to disclose

References
Aims and Methods: Caco-2 - human intestinal epithelial cells were cocultured at day 6 post confluence with Escherichia coli (E. coli) and Klebsiella pneumoniae (K. pneumoniae) at MOI 0 - 10 for up to 4 hours. To clarify whether observed effects were due to living bacteria, bacterial components like lipopolysaccharide (LPS) and bacterial metabolites in form of supernatant of an E.coli overnight culture were also used for stimulation. Heat-inactivated bacteria served as reference. Changes in cell-cell-contact proteins (occludin and E-cadherin) were analyzed by Western blot and fluorescence microscopy. Moreover, effect on cell-cycle regulation was examined by flow cytometry.

Results: Bacterial stimulation of Caco-2 cells with E.coli or K. pneumoniae resulted in a G1 arrest with up to 11% more cells in Go/G1 phase compared to the unstimulated control. Coincubation with K. pneumoniae at MOI 5 resulted in a decreased production of occludin, while E.coli reduced both protein levels of occludin and E-cadherin. Bacterial metabolites in the supernatant of the over-night culture reduced protein levels around 30%, but less strong compared to LPS. However, both effects might be part of a bacterial mechanism to escape intestinal immune responses and promote bacterial translocation followed by the development of SBP.

Disclosure: Nothing to disclose.

Disclosure:

Abstract No: P0025

OUTCOMES OF LARGE-VOLUME PARACENTESIS IN CIRRHOTIC PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS

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Introduction: Pakistan ranks second among highest prevalent countries for chronic hepatitis C with a prevalence of 5.2%. Here we have an exponential increase in chronic liver disease patients, so burden of morbidity and mortality is high due to lack of transplant centres. Spontaneous bacterial peritonitis (SBP) occurs in 10–30% of cirrhotic patients and is associated with high mortality rate among hospitalized patients and its associated incidence of acute kidney injury (AKI) and hepatorenal syndrome (HRS). Large-volume paracentesis (LVP) decreases the burden of infective fluid. Outcomes of LVP in SBP patients has not been clearly addressed in previous studies. Furthermore, in the absence of more viable therapeutic options for preventing kidney impairment in SBP, the management really looms around time and need for renal replacement therapy (RRT). This study will assess the outcome of LVP in patients with SBP, both in terms of mortality, length of stay and effect on renal function.

Aims and Methods: This cross-sectional study was conducted in the Medicine Unit of Aga Khan University Hospital. A total of 113 patients with diagnosed SBP were assessed. Among these patients 61 underwent LVP while 51 were managed conservatively. LVP was done as per routine practice of safety and monitoring. All the patients received intravenous albumin and hydration as per protocol. Baseline and 48 hours clinical outcomes (including creatinine and ascitic fluid total leucocytes (TLC) count) were compared including a number of other parameters. The development of AKI and post-paracentesis induced cirrhotic dysfuncional (PPCD) were also assessed and model for end-stage liver disease (MELD) and Child-Turcotte-Pugh (CTP) scores were also calculated. Results: There was statistically significant improvement in post 48 hours creatinine among patients undergoing LVP (p < 0.001) whereas no significant improvement was seen in patients without LVP (p = 0.32). Similar improvements were seen for special care unit stay and total length of stay in patients with LVP, need for RRT and incidences of AKI and HRS among both groups.

Conclusion: LVP in patients with SBP translates into significantly positive outcomes in terms of length of hospital stay, special care unit stay, need for RRT and development of AKI and HRS. Hence LVP is recommended as a favoured therapeutic option.

[Outcome of LVP in SBP]

Disclosure: Nothing to disclose.
Aims and Methods: This study was conducted to verify the role of the aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis 4 (FIB-4) tests as non-invasive alternatives to liver biopsy. Our study included 757 patients with a median age of 42.6 ± 10 years. All patients underwent liver biopsy for fibrosis stage estimation, and the APRI and FIB-4 tests were performed. The liver biopsies were scored using the METAVIR system: 13 patients were F0 (1.7%), 356 (47%) were F1, 227 (30%) were F2, 160 (21%) were F3, and 1 (0.1%) was F4.

Results: For predicting fibrosis stages F≥3, APRI and FIB-4 had a specificity of 90% at cut-off values of 1.1 and 2.7, respectively, and a specificity of 95% at cut-off values of 1.44 and 3.4, respectively. The sensitivity of APRI and FIB-4 was 90% at cut-off values of 1.34 and 2.4, respectively, with an area under the receiver operating characteristic curve (AUC) of 0.663 (95% confidence interval [CI], 0.617–0.709) for APRI and 0.673 (95% CI, 0.627–0.719) for FIB-4. For predicting F≥3, APRI and FIB-4 had a specificity of 90% at cut-off values of 1.34 and 2.4, respectively, with an area under the receiver operating characteristic curve (AUC) of 0.663 (95% CI, 0.617–0.709) for APRI and 0.673 (95% CI, 0.627–0.719) for FIB-4.

Conclusion: For the non-invasive prediction of liver fibrosis stage, using higher cut-off values for APRI and FIB-4 is advised to improve the specificity.

Disclosure: Nothing to disclose

P0028 HEALTH-RELATED QUALITY OF LIFE IN PRIMARY BILIARY CIRRHOSIS

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Introduction: Primary biliary cirrhosis (PBC) is a chronic autoimmune disease, characterized by progressive inflammation, destruction of intrahepatic bile ducts and cholestasis. Symptoms of PBC, especially itching and fatigue, lead to a reduction in Health-Related Quality of Life (HRQoL). HRQoL can be determined as disease-specific quality of life, and by using the anamnestic and clinical characteristics of the patients. HRQoL in patients with PBC are affected by: age, edema, diuretics, and some laboratory parameters. Significant predictor of total PBC-40 score is value of GGT (r = 0.417, p = 0.002). The score for the “Itch” domain positively correlates with the values of alkaline phosphatase increase (r = 0.29, p = 0.005) and gamma glutamyl transferase (GGT) (r = 0.303, p = 0.004) and alanine aminotransferase (ALT) (r = 0.231; p < 0.05). In patients with diagnosed liver cirrhosis, waiting for the liver transplantation, were retrospectively analyzed between 2006 and 2015 at Vilnius University Santaros Clinics. Etiology of cirrhosis, Child-Pugh classification, Model for End-Stage liver disease score, echocardiographic indicators of diastolic dysfunction, concentrations of bilirubin, creatinine and albumin, international normalization ratio were recorded. Diastolic dysfunction was divided into 3 grades by increasing severity by American Society of Echocardiography 2016 Data were analyzed by SPPS v.19. A p < 0.05 was considered as statistically significant.

Results: Final statistical analysis included 47 patients. The majority of patients were women, 27 (58.5%), patients’ mean age was 48.8 ± 1.175 years. All patients in our study had liver cirrhosis. Hepatitis C virus infection was the most common etiology of cirrhosis (38.3%). Normal diastolic function was present in 14 (30.0%), first grade dysfunction in 17 (37.2%) second grade in 16 (34.0%) and third grade in 2 (4.3%) cirrhotic patients. There was a significant relation by SPPS v.19. A p < 0.05 was considered as statistically significant.

Aims and Methods: The aim of a research was to evaluate the association between diastolic dysfunction of left ventricle and the severity of cirrhosis. 150 patients with diagnosed liver cirrhosis, waiting for the liver transplantation, were retrospectively analyzed between 2006 and 2015 at Vilnius University Santaros Clinics. Etiology of cirrhosis, Child-Pugh classification, Model for End-Stage liver disease score, echocardiographic indicators of diastolic dysfunction, concentrations of bilirubin, creatinine and albumin, international normalization ratio were recorded. Diastolic dysfunction was divided into 3 grades by increasing severity by American Society of Echocardiography 2016 Data were analyzed by SPPS v.19. A p < 0.05 was considered as statistically significant.

Results: Final statistical analysis included 47 patients. The majority of patients were women, 27 (58.5%), patients’ mean age was 48.8 ± 1.175 years. All patients in our study had liver cirrhosis. Hepatitis C virus infection was the most common etiology of cirrhosis (38.3%). Normal diastolic function was present in 14 (30.0%), first grade dysfunction in 17 (37.2%) second grade in 16 (34.0%) and third grade in 2 (4.3%) cirrhotic patients. There was a significant relation between diastolic function and age (p = 0.039; r = 0.3), Model for End-Stage liver disease (p = 0.007, r = 0.4).

Conclusion: According to the relation between diastolic dysfunction and Model for End-Stage liver disease score, we recommend cardiac assessment in patients with higher Model for End-Stage liver disease scores.

Disclosure: Nothing to disclose

Reference

Introduction: Bleeding from ruptured esophageal varices (EV) is the most severe complication of patients with liver cirrhosis and portal hypertension. Upper endoscopy is the golden standard for diagnosis of esophageal varices. Non-invasive diagnosis of esophageal varices in cirrhotic patients is beneficial because it helps us to select the patients likely to have esophageal varices to do endoscopy for them.

Aims and Methods: The aim of this study was to assess esophageal varices by noninvasive parameters in patient with liver cirrhosis using some clinical, laboratory and ultra-sonographic parameters.

Methods: This study included 120 patients with liver cirrhosis of various etiologies from Menoufia University Hospitals (Egypt) and 20 healthy volunteers as controls. They underwent physical examination and laboratory investigations (CIR, liver profile [ALT, AST, serum albumin, bilirubin, PT %] and creatinine). Abdominal ultrasound and upper endoscopy were done for all patients. Child-Pugh score, MELD score, AST/Platelet ratio index (APRI score), Platelet count/spleen diameter ratio (PC/SD) and NIEC Index were calculated for all patients.

Results: Serum albumin at cutoff less than 3.65g/dl is significant in prediction of EV with sensitivity 70% and specificity 86.2%. Platelet count at cutoff less than 99000/mm³ is significant in prediction of EV with sensitivity 87.5% and specificity 55%. PC/SD ratio at cutoff less than 919.6 is significant in prediction of EV with sensitivity 78% and specificity 52%. NIEC Index at cutoff more than 25.4 is significant in prediction of EV with sensitivity 62.5% and specificity 90%. Prothrombin time at cutoff less than 99000/mm³ is significant in prediction of EV with sensitivity 68.8% and specificity 65%. Spleen longitudinal diameter at cutoff more than 140.5 mm is significant in prediction of EV with sensitivity 73.8% and specificity 70%. Portal vein diameter (PVD) at cutoff more than 15 mm is significant in prediction of EV with sensitivity 62.5% and specificity 90%. 90th percentile in 0.05 second is significant in prediction of EV with sensitivity 62.5% and specificity 90%. 90th percentile in 0.05 second is significant in prediction of variceal bleeding risk with sensitivity 82.5% and specificity 85%. PC/SD ratio at cutoff 851.6 is significant in prediction of variceal bleeding risk with sensitivity 45% and specificity 90%. Multiple logistic regression analysis of risk factors of development of esophageal varices revealed that serum albumin, prothrombin time, PC/SD ratio and PVD are significant predictors for development of esophageal varices.

Conclusion: Non-invasive predictors for presence of esophageal varices in patients with liver cirrhosis provide a method for selecting patients for endoscopic screening based on laboratory, clinical and ultrasonographic variables such as serum albumin, platelet count, PC/SD ratio, APRI score, SLD, PVD, prothrombin time and Child-Pugh score. Therefore, the number of unnecessary endoscopies will be reduced. NIEC Index, platelet count and PC/SD ratio can provide information help in prediction of variceal bleeding risk in patients with liver cirrhosis.

Disclosure: Nothing to disclose.
The Cox regression model gave adjusted hazard ratios (aHR) for all treatments. Explanatory co-variates were included in a time-dependent Cox regression model including; age, gender, body mass index, systolic blood pressure, estimated glomerular filtration rate, sodium, albumin, bilirubin, units of alcohol consumed per day, current number of liver admissions, cumulative number of infections, admissions and presence of renal complications. All variables were included in the model as categorical variables in order to include all patients.

**Results:** The Cox regression model gave adjusted hazard ratios (aHR) for all variables included. The variable that had the greatest impact on predicting death was sodium values less than 125mmol/L with an aHR of 3.2 (95% CI: 2.5-4.2).

Patients that were admitted for a renal complication had an increased aHR of 2.6 (95% CI: 2.1-3.3) and those with albumin < 34 g/L had an increased aHR of 2.4 (1.8-2.67). Those with bilirubin > 50 umol/L had an increased aHR to 1.74 (1.51-2.01) and those with an eGFR of 15-30 mL/min had an increased aHR of 1.64 (1.32-2.05). The model was validated using receiver operator curves (ROC) at 2, 3, 5 and 10 years following diagnosis of cirrhosis.

**Conclusion:** It was possible to build a reliable statistical model to forecast the likelihood of all-cause mortality in cirrhotic patients confirming the significance of hyponatraemia and renal dysfunction in the prognosis of patients with cirrhosis.

**Disclosure:** Craig J. Currie, Director of Pharmatecience; Ellen Berni, employee of Pharmatecience; James Orr, nothing to disclose; James Whitehouse, employee of Norgine, Daniel Murphy, employee of Norgine, Pete Conway, contractor of Pharmatecience; Bharat Amlani, employee of Norgine; Mark Hudson, Speaker and Consultant and an Advisory board member for Norgine. Pharmatecience, a research consultancy receiving funding from Norgine.

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**P0034 SAFETY AND EFFICACY OF RIFAXIMIN IN PROPHYLAXIS OF SPONTANEOUS BACTERIAL PERITONITIS: IS THIS TIME TO ABANDON FLUOROQUINOLONES FOR PREVENTION OF SPONTANEOUS BACTERIAL PERITONITIS?: A SYSTEMATIC REVIEW**

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**Introduction:** The role of rifaximin in the prevention of spontaneous bacterial peritonitis (SBP) is not well studied.

**Aims and Methods:** The aim of this meta-analysis was to evaluate the role of rifaximin in the prevention of SBP. A computerized literature search for relevant clinical trials was conducted during August 2017. Data on Frequency of SBP, the success rate of prevention of SBP, mortality rate, hepatorenal syndrome, septic shock, hepatic encephalopathy, and GHT bleeding were extracted and pooled as risk ratio (RR) with their 95% confidence interval (CI) in a meta-analysis model. Heterogeneity was assessed by Chi-square test.

**Results:** Six studies involving 973 patients were included in the final analysis. The pooled effect estimate showed that the rifaximin plus norfloxacin group had less incidence of SBP (RR 0.58, 95% CI [0.37, 0.92], p=0.02) and hepatic encephalopathy (RR 0.38, 95% CI [0.17, 0.84], p=0.02) than the norfloxacin-based regimen group. No significant difference between rifaximin and norfloxacin in terms of the success rate of primary prevention of SBP (RR 0.95, 95% CI [0.24, 1.01], p=0.05; RR1.21, 95% CI [0.95, 1.55], p=0.13, respectively).

**Conclusion:** Based on our analysis, Rifaximin is a promising drug and appears to be a good alternative to norfloxacin in prevention of SBP.

**Disclosure:** Nothing to disclose.
Group 1 showed a trend to higher mortality rate (39.1% vs. 40%, p = 0.130). Mortality was also correlated with sepsis, bilirubin value; MELD-Na score and ECOG score (p = 0.05).

Conclusion: Cirrhotic patients present a high rate of infections and this group presents higher mortality rate. Our results suggest that PPI therapy is in fact, associated with higher risk of infection, which should lead us to be more strict in the indications of PPI's in these patients.

Disclosure: Nothing to disclose

P0038 ABCPS: A NEW SCORE PREDICTING IN-HOSPITAL MORTALITY IN CIRRHOTIC PATIENTS

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Introduction: Cirrhotic patients have high rates of hospital readmissions and mortality. Recently, a new score - ABCPS - has emerged and allows predicting in-hospital mortality in cirrhotic patients. To date, there are no cut-off values defined for this score.

Aims and Methods: The aim of the study was to evaluate the power of ABCPS in predicting in-hospital mortality and to define cut-off values for this score.

Retrospective study, including patients hospitalized for compensated cirrhosis within 9 years. The ABCPS Score was calculated using the formula: 0.04 + 0.03 x albumin + 0.05 + 0.02 x Creatinin + 0.04 + 0.04 x Bilirubin + 0.05 + 0.28 x Potassium + 0.04 x 0.7 x Sodium.

Results: 362 patients included, 271 (74.9%) males with mean age of 57.4 ± 11.7 years. The majority of patients (85.9%) had alcoholic cirrhosis. Ascites was present in 80.4% patients, hepatic encephalopathy in 39.8%, acute kidney injury in 31.8%, variceal bleeding in 12.4%, spontaneous bacterial peritonitis in 28.7%, other infections in 3% and hepateno-renal syndrome in 3.6%. The mean hospitalization time was 11.7 ± 10.5 days. In-hospital mortality was found in 85 patients (23.5%). The mean value of ABCPS was 2.17 ± 1.18. The area under ROC curve (AUC) that predicts mortality for ABCPS score was 0.645 and the cut-off predictor for mortality was > 2.16 with sensitivity of 53% and specificity of 77%.

Patients with ABCPS > 2.16 presented higher mortality (39.1% vs. 16.2%, p < 0.001).

Conclusion: The ABCPS score is a tool to be used in the evaluation of cirrhotic hospitalized patients for its ability to predict in-hospital mortality. This study also allowed to determine cut-off values for this score.

Disclosure: Nothing to disclose

P0039 VALIDATION OF EXPANDED BAVENO VI CRITERIA FOR PREDICTING ESOPHAGEAL VARICES

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Introduction: According to Baveno VI, patients with chronic liver disease with platelets > 150,000 ul and liver stiffness measured by elastography < 20kPa can avoid upper endoscopy. These criteria were widely validated presenting high specificity but low sensitivity. Recently, Augustin S et al proposed expanded Baveno criteria (platelets > 110,000 ul and liver stiffness < 25).

Aims and Methods: Retrospective study of patients with chronic liver disease submitted to elastography between January 2013 and December 2015. Small varices with red wale marks or large varices were considered as high risk varices. The aim this study was to validate Baveno’s expanded criteria in our center.

Results: A total of 104 patients were included; mean age 57 years, 69% male. The etiology of chronic liver disease was hepatitis C in 80%, alcohol in 12%, hepatitis B in 4% and other causes in 5%. The prevalence of varices was 25%. Baveno’s expanded criteria had a sensitivity of 92% and a specificity of 74% for the prediction of esophageal varices (100% and 62% Baveno’s classical criteria). If we considered only high-risk varices the sensitivity of expanded criteria was 100% and specificity was 65% (100% and 50% classic criteria).

Conclusion: The expanded Baveno’s criteria present similar sensibility as classic criteria but with higher specificity. In clinical practice, it continues to correctly identify patients with varices but decreases the number of potential screening endoscopies.

Disclosure: Nothing to disclose

P0040 RESISTANCE PATTERNS IN HOSPITAL-ACQUIRED URINARY TRACT INFECTIONS IN PATIENTS WITH LIVER CIRRHOSIS: SINGLE-CENTER EXPERIENCE

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Introduction: Decompensated cirrhosis patients are inherently immunocompromised and highly susceptible to bacterial infections due to translocation of gut flora and altered defense mechanisms. Healthcare-associated infections with multi-drug resistant (MDR) bacterial uropathogens in patients with cirrhosis have increased significantly over the last decades.

Aims and Methods: The aim of our study was to investigate rates of antimicrobial resistance among cirrhotic patients with hospital-acquired (HA) urinary tract infection (UTI) and to determine factors that significantly impact outcome associated with MDR infection.

Retrospective single-center surveillance analysis of microbiological isolates obtained from decompensated cirrhosis patients with HA UTI, defined as event on-set > 48 hours after admission, with pyuria and monomicrobial growth ≥ 105 CFU/ml on urine culture. Microbiological testing was performed using the Kirby-Bauer disk diffusion method. Isolated pathogens were classified as MDR if resistance ≥ 1 drug from ≥ 3 groups of antibiotics.

In vitro selection criteria were defined for empiric therapy defined failure therapy. Independent predictors for MDR UTIs were identified with multivariate logistic regression.

Results: A total of 65 patients were included in the analysis. The mean age was 60.8 ± 11.3 years (range 39-84 years), 48 (73.8%) were males. All patients had decompensated liver disease, 21 (32.3%) CP class B, and 44 (67.7%) CP class C, with a mean MELD score of 21.88 ± 6.07, and a mean CLIF-C AD score of 88.34 ± 10.26. Ascites was seen in 55 (84.6%) patients, and 32 (49.9%) had hepatic encephalopathy either at admission or during hospitalization. 15 patients (23%) had a diagnosis of DM. 33 patients (50.8%) were catheterized. Enterococcus spp was the most common pathogen (52.3%), followed by Klebsiella spp (14.4%) and Escherichia coli (9.2%). 35 (53.8%) isolates were MDR. Enterococcus spp were more commonly non-MDR (n = 22, 64.7%, p = 0.003). Enterobacteriaceae were mainly MDR strains (n=18, 81.1%, p = 0.001). VRE was isolated on 7 occasions (20.6%), and 16 of the Enterobacteriaceae isolates (72.7%) were ESBL-E. The overall resistance rates to ceftriaxone, ciprofloxacin, imipenem and meropenem were 93.1%, 80.0%, 47.2%, and 45.4%, respectively. Resistance to amikacin and gentamicin were 33.5% and 48.6%. Resistance to vancomycin and nitrofurantoin were 23.5% and 60.0%. Therapy failure was more frequent in patients with MDR UTIs (p = 0.039). In regression analysis, age > 65 years (OR 6.328, 95% CI 1.662–81.1, p = 0.001) and MDR UTI. was independent predictors for MDR UTI.

Conclusion: Increase in antimicrobial resistance to commonly used antibiotics for treatment of bacterial infections in patients with cirrhosis contributes to high mortality and morbidity associated with these infections. It emphasizes the significance of early recognition and proper management of these infections by prescribing appropriate antibiotics in order to reduce morbidity and mortality.

Disclosure: Nothing to disclose

P0041 ASSOCIATION OF GENETIC POLYMORPHISMS IN CHEMOKINES (CCL2 AND CCL5) AND CHEMOKINE RECEPTOR (CCR2) WITH THE OUTCOME OF HCV INFECTION IN EGYPTIAN FAMILIES: A MULTICENTER STUDY

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Introduction: Chemokines are major mediators of leukocyte trafficking into the sites of the immune response. Chemokine-induced signaling is mediated by a group of G protein-coupled receptors, They participate in defense against
microbial infection. Several functional polymorphisms of chemokine and chemokine receptor genes have been described to deregulate chemokine system and, therefore, in HCV infection it was assumed that these polymorphisms may be associated with persistence or clearance of the virus.

**Aims and Methods:** This study was performed to investigate the association of single nucleotide polymorphisms (SNPs) of chemokines and chemokine receptor with the susceptibility to HCV infection in Egyptian families.

**Methods:** A total of 3014 subjects comprising 845 Egyptian families were recruited from The Upper and Lower Egypt governorates and were classified into two groups: patients with chronic HCV (CHC), 108 subjects with spontaneous virus clearance (SC), and 1446 subjects taken as a healthy control group. All subjects were genotyped for rs13900 C/T SNP of CCL2 gene, rs817655 T/A SNP of CCL5 gene, and (rs734660 G/A, rs7199864 G/A) SNPs of CCR2 gene using allelic discrimination real time PCR (RT-PCR) technique.

**Results:** The carriage of the allele A of CCR2 rs734660 and the allele A of CCR2 rs7199864 were significantly higher in the CHC (OR = 4.03 and OR = 1.97, respectively, p < 0.0001) when compared with both SC (OR = 4.03 and OR = 1.97, respectively, p < 0.0001) and control groups (OR = 1.42 and OR = 2.13, respectively, p < 0.0001) while the carriage of allele C of CCL2 rs13900 and the allele T of CCL5 rs817655 were significantly higher in SC group when compared with both CHC (OR = 1.09 and OR = 2.24, respectively, p < 0.00001) and control group (OR = 0.65 and OR = 0.45 p < 0.00001 respectively)

**Conclusion:** Susceptibility to HCV infection is associated with A alleles of both rs734660 and rs7199864 of CCR2 gene while SC of HCV is associated with C allele of rs13900 of CCL2 gene, and T allele of rs817655 of CCL5 gene in the Egyptian families.

**Disclosure:** Nothing to disclose

**References**

**P0042 DENGUE HEPATITIS: A DIFFERENTIAL DIAGNOSIS TO REMEMBER IN EUROPE**

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**Introduction:** Globally, there are 50 million infections per year from the dengue virus (DENV) spread over 100 countries. With the documented dispersion of dengue fever, physicians from temperate climates such as Europe are finding more often travelers with this infectious disease that frequently affects the liver, sometimes with major impact. Indeed, DENV has been implicated as an important cause of acute liver failure (ALF) in endemic countries. In addition, the secondary dengue mosquito, *Aedes aegypti*, which has been introduced in the Mediterranean region and the primary, *Aedes albopictus*, is on the verge of invading the southernmost parts of Europe.

**Aims and Methods:** We aimed to characterize the DENV-induced hepatic alterations and investigate and compare mimickers of acute liver injury disease.

**Results:** A retrospective study in a southern-European hospital to identify all patients with a positive IgM antibody for DENV in the last 6 years, using the laboratory data at the time of admission or first evaluation. In addition, diagnosis was further confirmed through positive DNA and/or a highly suggestive clinical picture and epidemiological context.

**Outcomes:** Of 2138 anti-DV IgM requests, we identified 1282 individuals with a positive result, including 279 under an age of 18 years old. Of the 1003 adults, 4.1% of the tested patients had hyperbilirubinemia. A higher PT on admission or first evaluation. In addition, diagnosis was further confirmed through positive DNA and/or a highly suggestive clinical picture and epidemiological context.

**Conclusion:** Nothing to disclose

**References**

**P0043 THE RELATION OF QUANTITATIVE INDICATORS OF PLASMACYTOID DENDRITIC CELLS IN THE BACKGROUND OF APPLICATION OF VARIOUS TREATMENT REGIMENS IN PATIENTS WITH CHC**

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**Introduction:** The special role of plasmacytoid dendritic cells (pDCs) in the immunopathogenesis of CHC puts them in the first place, not only as the main producers of IFN, but also as direct participants in the interaction between innate and acquired immune responses. Therapeutic regimens using direct-acting antiviral agents (DAAs) have revolutionized the treatment of CHC patients, but long-term interaction of the immune system with the hepatitis C virus forms a close immunological relationship in the adaptation process, which leads to a change in the functioning both at the cellular and systemic levels. Changing the cellular background of the therapy can dramatically affect the work of the immune system as a whole.

**Aims and Methods:** We examined 45 patients taking different regimens of CHC therapy. 27 of them received standard therapy and 18 people received DAAs. The amount of pDCs was determined by flow cytometry using monoclonal antibodies CD123 and CD 303.

**Results:** Quantitative indicators of pDCs have been reduced in all patients with CHC and vary depending on the type of CHC therapy. In patients treated with IFN, the absolute number of pDCs is 2 times lower (abs. ≈3.5) in comparison with the group receiving DAAs (abs. –6.2; p = 0.007). In the application of DAAs reduction of the absolute number of pDCs noted only on 4th week, whereas at the end of therapy (12 weeks - DAAs and 48 weeks - IFN) quantitative indicators pDCs did not differ (IFN: %–0.18; abs.–5.1; ADF: %–0.17, abs.–8.5; p < 0.05). According to catamnesis (patients examined after 12 months after the end of treatment CHC) pool pDCs after the use of drugs IFN was restored and did not differ from the indicators in healthy individuals (IFN: %–0.18, abs.–8.4; healthy: %–0.27, abs.–10.25; p < 0.05). The number of pDCs in DAAs as at the end of therapy, and in the history (%–0.18, abs.–9.5; p < 0.05) did not differ from those of healthy people.

**Conclusion:** pDCs values vary and depend on the type of therapy being performed. The use of DAAs leads to rapid eradication of the HC virus antigen from the body, which affects the dynamics of the pDCs pool and can lead to delayed changes in the immune system. Further observation and detailed study of this issue are needed.

**Disclosure:** Nothing to disclose

**References**

**P0044 THE EFFECTIVENESS OF SOFOSBUVIR AND DACLATASVIR IN THE TREATMENT OF HEPATITIS C IN THALASSEMAIA MAJOR PATIENTS AND THEIR EFFECT ON HEMATOLOGICAL FACTORS**

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2Gastrointestinal and Liver Diseases Research Center-Iran University of Medical Sciences, Tehran, Iran (Islamic Republic of)

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**Introduction:** Patients with thalassemia are at risk for infections such as Hepatitis C Virus (HCV) due to their repeated blood transfusions; meanwhile, the treatment of thalassemia patients who develop HCV infection is a controversial issue. 

**Aims and Methods:** Although the effectiveness of Direct-Acting Antivirals (DAAs) on HCV infection has been confirmed, their side-effects as well as effects on hematological factors due to the resultant need for blood transfusion remain to be further understood.

This study examined 61 patients with major beta thalassemia and HCV infection who had a history of interferon treatment failure. The patients underwent a 24-week treatment with Sofosbuvir (SOF) and Daclatasvir (DAC). To assess the response to treatment, SVR12 was used. At the end of the study, the need for blood transfusions was also assessed.

**Conclusion:** Hematocrit and platelet count in 14 days after any trip to tropics or sub tropics, taking into account that the virus frequently induces thrombocytopenia in addition to elevation of transaminases that may be very significant, prolongation of PT/INR and rarely hyperbilirubinemia. Dengue should also be considered in the differential diagnosis of acute liver failure and as an acute component of chronic liver disease, in the appropriate setting.

**Disclosure:** Nothing to disclose

**References**
patients before treatment was averaged 1.595 ± 0.65 bag per month, which
reduced to 1.1 bags after treatment (p = 0.01). This regimen did not affect
the amount of anemia in patients and did not differentiate the need for blood
transusions. The rate of hemoglobin before treatment was 9.5 ± 1.42 g/dl, which
reached 9.6 ± 1.6 g/dl after treatment (p = 0.54). Ferritin levels decreased signifi-
cantly in patients after treatment, and from 1948.08 ± 1539.54 ng/mL to
1315.73 ± 120.67 ng/mL (p = 0.001).

Conclusion: The combination of Sofosbuvir and Daclatasvir is an effective and
tolerable treatment regimen without affect the amount of anemia in patients and
did not differentiate the need for blood transfusions.

Disclosure: Nothing to disclose.

References
Daclatasvir, sofosbuvir, and ribavirin for hepatitis C virus genotype 3 and
advanced liver disease: A randomized phase III study (ALLY-3-1).
sofosbuvir and ribavirin for hepatitis C virus infection with advanced cirrhosis or post-liver transplantation recurrence.
direct acting antivirals in treatment of chronic hepatitis C infection in patients of
Treatment of hepatitis C virus infection with direct-acting antiviral drugs is
safe and effective in patients with hemoglobinopathies. American journal of

P0045 REAL-WORLD DATA OF DIRECT-ACTING ANTIVIRALS
DID NOT DIFFERENTIATE THE NEED FOR BLOOD TRANSFUSIONS.

K. Takahashi6, K. Azuma7, T. Satoh8, M. Nakamuta9, T. Koyanagi10,
S. Shimoda11, M. Kato12, E. Kajiwara13, J. Hayashi14

Aims and Methods: Aims and Methods: The aim of this study was to evaluate the risk of recurrent
HCC among patients with prior HCC who achieved SVR by DAAAs. This retro-

spective multicenter study consisted of 759 consecutive patients who achieved
SVR by treatment with interferon-free DAA regimens (Daclatasvir/Asunaprevir,
Omalizumab/Parietirep/ribavirin, Sofosbuvir/Ledipasvir, Elbasvir/Grazoprevir,
Sofosbuvir/Ribavirin). Of these, 75 patients had prior HCC. The Kaplan-Meier
method and Cox proportional hazard analysis were used to estimate the cumu-

lative incidence of first-time hepatocellular carcinomas (HCC) in patients treated
with DAAAs for chronic hepatitis C infection. Several predictive factors
were found, including liver cirrhosis and serum alpha-fetoprotein (AFP) level.

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Omalizumab/Parietirep/ribavirin, Sofosbuvir/Ledipasvir, Elbasvir/Grazoprevir,
Sofosbuvir/Ribavirin). Of these, 75 patients had prior HCC. The Kaplan-Meier
method and Cox proportional hazard analysis were used to estimate the cumu-

lative incidence of first-time hepatocellular carcinomas (HCC) in patients treated
with DAAAs for chronic hepatitis C infection. Several predictive factors
were found, including liver cirrhosis and serum alpha-fetoprotein (AFP) level.
was treatment experienced with PEG-IFN and RBV. Most common associated extrahepatic malignancies are hematolymphoid, gynaecological and gastrointestinal. 7 patients had HBV coinfection and all of them received concomitant anti HBV therapy and none had HBV flare. 1/3rd of patients received cancer therapy concomitantly with anti HCV therapy. The rest were under surveillance post cancer treatment. All 38 patients had achieved ETR and SVR 12. Overall adverse event rate was 34%. Most common being anaemia requiring modification of ribavirin therapy (n=5). Other adverse events noted were skin rash, dyspepsia, nausea, occasional vomiting or constitutional symptoms, none of which required modification for either anti HCV therapy or cancer therapy. No drug-drug interaction was noted.

Conclusion: Real-life data of concomitant cancer chemotherapy and DAA is scarce. This study demonstrates that SVR rate is excellent (100%) in this cohort of patients with chronic HCV infection. Concomitant cancer therapy and DAA are safe. Adverse events are not serious among most of the patients and usually does not mandates cessation of either cancer or HCV therapy. 90% of patients could tolerate full dose of RBV.

Disclosure: Nothing to disclose

Aims and Methods: The aim was to investigate the difference in expression levels of circulating miR-122 in HCV-related cirrhotic patients with and without hepatocellular carcinoma (HCC). We included 41 HCV-related cirrhotic patients recruited from Ain Shams University hospitals’ clinics and in-patient department. Patients were divided into 2 groups: I) non-HCC group of 14 patients with different Child-Turcotte-Pugh (CTP) classes, II) HCV-related HCC group of 27 patients having different patterns of tumor aggression - classified using CT/MRI imaging features into low and high aggressive HCC patterns, defined as: a) Low aggression/ small sized focal HCC – single lesion < 2 cm or ≤ 3 nodules < 3 cm each, b) High aggression patterns either multicentric HCC (> coexisting 3 nodules) or infiltrative HCC (ill-defined large sized HCC with no focal mass formation).

Table 1

Comparison of the levels of circulating microRNA-122 in HCV-related cirrhosis patients with and without hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>p value</th>
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<td>Plasma miR-122 level (Ct value)</td>
<td></td>
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<tr>
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<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Male (n = 31)</td>
<td>56.68 ± 7.35</td>
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<tr>
<td>Female (n = 10)</td>
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<tr>
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<td>Class C (n = 11)</td>
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<td>HCC group</td>
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</tr>
<tr>
<td>Class B (n = 5)</td>
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</tr>
<tr>
<td>Class C (n = 12)</td>
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<td>Imaging criteria of tumor</td>
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<td>Small sized focal HCC (n = 7)</td>
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<td>Multicentric HCC (n = 9)</td>
<td>33.63</td>
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<td>AST</td>
<td></td>
<td></td>
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<tr>
<td>AFP</td>
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</tbody>
</table>
Patients with chronic HCV infection can be cured of their disease.

**Introduction:**

Aims and Methods:

Before the start of antiviral therapy. For breast cancers no time limit was

2015 to January 2017 with solid non-hepatic tumor diagnosed in the 5 years

neoplasia in consecutive HCV patients treated with DAA.

Aims and Methods:

Results:

According to the manufacturer's instructions (Lymphoflot, Biotest,Dreieich,

obtained using Ficoll-Hypaque density gradient of EDTA anticoagulated blood

Interferon/ribavirin regimen. All patients were HCV genotype 4, compensated

January 2017 to August 2017 post Sofosbuvir 400mg/ Daclatasvir 60mg for 12

achieved SVR after sofosbuvir/daclatasvir therapy and to determine the different

Occult hepatitis C infection post DAAs therapy is not uncommon

Conclusion:

Aim was to evaluate the recurrence rate of non-hepatic neoplasia in consecutive HCV patients treated with DAA.

We included all consecutive HCV patients treated with DAA from February 2015 to January 2017 with solid non-hepatic tumor diagnosed in the 5 years

before the start of antiviral therapy. For breast cancers no time limit was

fixed. Patients with hematological malignancies were excluded. All tumors had

standard complete control before starting DAA therapy.

Results: 313 HCV patients were treated with DAA and 20 (6.4%) had a positive

anamnesis for solid non-hepatic tumor. 6 patients had a history of breast cancer,

4 gastrointestinal tumors, 2 non-melanoma skin cancer, 5 uro-genital cancers, 1

spinosocellular carcinoma of the oral cavity, 1 pituitary and 1 lung tumor. Median
time from cancer diagnosis to DAA was 3.7 years and patients were followed-up

for a median of 22.38 months after DAA therapy. No patient underwent DAA treatment concomitantly with chemotherapy. Median age at DAA therapy was

9 years and patients were men. 65% were genotype 1, 15% genotype 2, 10%

genotype 3 and 10% genotype 4. 70% had evidence of cirrhosis, well compen-
sated in everyone (CPT score A). An SVR was achieved in 19 patients (95%), and

no serious adverse events were reported. During a median of 22.38 months after

DAA therapy no patient included in the study had cancer recurrence.

Conclusion: HCV treatment in patients with solid non-hepatic tumors is safe and

effective. Although findings are preliminary, an SVR to DAA therapy was not

associated with any case of tumor recurrence.

Disclosure: Nothing to disclose.

**P0051 DO WE SCREEN HEPATITIS C BEFORE SURGERY FOR THE

BENEFIT OF THE SURGEON OR FOR THE PATIENT?**

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Introduction: The success rate of current treatments of hepatitis C infection now

approaches 100%. Therefore, it is important to conduct community screenings

and raise awareness. Pre-operative hepatitis serology is routinely considered in

most countries of the World.

Aims and Methods: We aimed to detect the prevalence of anti-HCV and HCV-

RNA positivity rate in patients undergoing pre-operative HCV screening and also

the awareness rate of having chronic hepatitis C infection in these patients. Patients who had pre-operative anti-HCV testing in surgical clinics of our hos-

pital were screened from 2013 to 2017. All patients who were positive were

questioned for HCV-RNA positivity and whether they were treated for hepatitis

C. Hospital records were screened for HCV-RNA results. Treatments reports

were reached through the integrated database system of social security with our

hospital. HCV-RNA untied patients were called by phone and asked whether they

were aware of being anti-HCV positive.

Results: During 5 years, 21897 patients were screened for hepatitis C. A total of

125 patients (0.57 %) were found to be positive (58M, 67F, mean age 59.1± 15.7)

HCV-RNA was tested in 76 of these patients, 22 HCV- RNA nega-
tive(29%), 24 were positive and treatment-naive, 19 were positive and treatment

experienced. From 125 patients with Anti-HCV positivity, 49 patients had no

HCV-RNA assay (39%), we called them by phone and noticed that just 5 (10 %)

patients knew that he/she was anti-HCV positive.

Conclusion: Anti-HCV positivity was detected in approximately 0.6% of 21897

patients who were operated in surgical departments of a tertiary medical center.

Approximately 40% were not tested for HCV - RNA and most of these patients

were not aware of being Anti-HCV positive. Testing hepatitis C serology before

surgery seems that do not contribute to catch new patients. Surgeons need to be

more aware towards chronic hepatitis C infection.

Disclosure: Nothing to disclose.

**P0052 PREVALENCE OF HEPATO-BILARY MANIFESTATION IN

IBD**

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Introduction: The IBD are frequently associated to the extra intestinal manifesta-
tion: dermatologic, ophthalmic, hepato-biliary. We observed a high prevalence of

hepato-biliary manifestation in IBD (up to 50%) and one of the most serious

complication is PSC. We also noted various pathogenicities of these hepato-biliary

abnormality; the common pathogenesis of IBD, direct or indirect complication of

IBD.

Aims and Methods: The aim of our study is, first of all, to assess the frequency of

hepato-biliary manifestation on the IBD, and secondly to study clinical, advance-

ment characteristics of IBD and liver disease occurrence. In our study, we have

removed the abnormal transient liver test and the drug which caused hepatitis.

This retrospective study concerned the population with IBD of the occurrence’s

liver disease during period: 2000 - 2013. Initially, all the patients get a clinical,
biological and morphological investigation, and also a clinical, biological and

diagnostic laboratory investigation.
Results: We observed 868 patients with IBD: 459 Crohn’s disease and 277 ulcerative colitis with a median age of 42.5 years (24-81 years). During the follow-up, we noted 3.2% liver disease, among them: 13 cases of Crohn’s disease (8 male - 5 female), 9 cases of ulcerative colitis (6 male-3 female). 18 cases of liver disease was reveal by abnormal liver test, 3 cases by portal hypertension, and one by jaundice. All the investigation were determined 14 PSC, 3 steatosis, 1 peliosis, 1 overlap syndrome (HAI + PSC). Clinical and morphological characteristic study revealed that hepatobiliary manifestation are more common for male patient and also in ileo-colonic, pan-colitis forms. The IBD is the most of the time presentation of the growing period of the liver disease.

Conclusion: The hepatobiliary manifestation are rare, they are generally revealed by abnormal liver test which occurred the most often on long lasting and exten- sive IBD and PSC represented the most frequent etiology.

Disclosure: Nothing to disclose.

P0054 DEVIATIONS IN PERIPHERAL BLOOD SUBPOPULATIONS ARE CONNECTED WITH THE PRESENCE OF PRURITUS IN PRIMARY BILIARY CHOLANGITIS PATIENTS

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Introduction: Primary biliary cholangitis (PBC) constitutes an autoimmune liver disease characterized by progressive destruction of small- and medium-sized intrahepatic bile ducts. The role of particular peripheral blood (PB) subpopula- tions in the course of PBC remains uncertain. Bile acids, including deoxycholic acid and glycocholic acid, are known to induce a peripheral immune response.

Aims and Methods: The aim of our study was to assess the relationships between analyzed peripheral blood cell subsets and the presence of pruritus in patients with newly diagnosed PBC. The frequencies of PB subpopulations were mea- sured by flow cytometry in 34 previously untreated female patients with PBC. 19 participants from research group presented pruritus. The control group consisted of 20 healthy age- and sex-matched volunteers. The diagnosis of PBC was based on the commonly known criteria. The severity of pruritus was assessed according to Visual Analogue Scale (VAS) questionnaire and the mean result was 41.10 points. The degree of severity of PBC was evaluated by histologic stages of PBC. This parameter was described in all patients and they were divided into 4 groups, according to histologic stages of PBC (1 - portal stage - 7 patients, II - portal stage + 6 patients, III - septal stage - 3 patients and IV - cirrhotic stage - 2 patients).

Results: There were significant differences in CD4+ T lymphocytes and absolute counts of CD4+/CD3+ cells between research and control group (p < 0.01). There were no significant differences in percentages of CD3+/CD4+, percentages of CD3+/CD8+ and absolute counts of CD4+/CD3+ cells between research and control group.

Conclusion: The results obtained in our survey suggest that deviations in PB subgroups might be involved in the pathogenesis of cholestatic pruritus in PBC patients. This issue should be undoubtedly clarified in further studies.

Disclosure: Nothing to disclose.

References

P0055 A NOVEL UK REGIONAL REAL-WORLD REGISTRY FOR PRIMARY BILIARY CHOLANGITIS (PBC) ALLOWING DATA LINKAGE FROM PRIMARY AND SECONDARY CARE

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Introduction: PBC is a model of chronic liver disease affecting approximately 35/100,000 population. Data for PBC and rare diseases appears scarce, fragmented. Coordinated efforts are required to bring various datasets together to provide integrated care for patients. A real-world registry linking primary and secondary care for PBC does not exist.

Aims and Methods: Following ethical approval, a regional observational feas- ibility study was set up collecting data from 3 regional hospitals and 10 primary care providers (General Practice surgeries) in the region of Surrey South East England which has a population of 1.1 million. From primary care providers data collected using READ codes and 725 data points were collected for each patient. In secondary care, data was collected from multiple sources including histology, fibroscan, immunology, biochemistry, virology, endoscopy, patient workflow systems, patient notes/letters, radiology and hospital coding departments. A total of 286 data points were collected for each patient. The datasets from primary and secondary care were linked for each patient using a unique patient identifier (NHS number) which was hashed using a pseudonymisation algorithm.

Results: A total of 375 patients with confirmed PBC were identified and primary and secondary care giving a regional PBC prevalence of 34.1/100,000 population. All patients from primary care were successfully linked to secondary care providing a holistic overview of the patients’ journey and the disease’s natural history.
Conclusion: Our novel method of establishing a rare disease registry for PBC is able to link datasets from various sources which are otherwise found disjointed in silos. Our registry is collecting more data points than existing PBC registries and does not rely on manual data entry from time-stretched clinicians and nurses which can affect data quality and lead to errors. This robust methodology has enabled a worldwide data on a large number of PBC patients and better understand the natural history and regional impact of this rare condition. Moreover, it will inform the development of regional frameworks for integrated care which are currently lacking for PBC and for rare liver diseases. This work will complement the efforts of larger consortia including UK-PBC and GlobalPBC.

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P0056 THE EFFECTIVENESS OF STANDARD TREATMENT ON CHRONIC AND ACUTE PRESENTATION-AUTOIMMUNE HEPATITIS MAY BE SIMILAR

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Introduction: At present, many studies are still controversial for the response of acute presentation-AIH (A-AIH) after immunosuppressive treatment. Some studies reported that A-AIH had a worse response than chronic AIH (C-AIH) due to its more severe liver injury.

Aims and Methods: Our study analyzed the effectiveness of standard treatment (corticosteroids alone or combined with azathioprine) between A-AIH and C-AIH. First, we collected patients prospectively according to the International Autoimmune Hepatitis Group (IAIHG) revised score and the experience of hepatologists. Patients who had a probable diagnosis (IAIHG score ≥10) of AIH were included in our study. And all of these patients were treated with standard treatment. Patients who were concurrent with other liver diseases or used other immunosuppressive agents were excluded. Then, all the patients were divided into the A-AIH group and the C-AIH group. Patients in A-AIH group needed to meet at least 1 of the following conditions: (1) total bilirubin ≥5mg/dL, (2) alanineaminotransferase >10 upper limits of normal (ULN), or (3) aspartate transaminase >10 ULN. Finally, the complete biochemical remission rate, time of reaching complete biochemical remission and mortality of the 2 groups were retrospectively analyzed.

Results: 88 patients were included in our study, of which 48 patients were in the A-AIH group and 40 patients in the C-AIH group. The follow-up period was 0.3–33.1 months. There was no statistical difference in the rates of complete biochemical remission between A-AIH group and C-AIH group (50%, 35%, p = 0.55). The median time of reaching complete biochemical remission was 3.2 (1.3, 9.2) months in A-AIH group, while that in the C-AIH group was 2.4 (1.3, 4.6) months, and there was still no significant difference (p = 0.474). During the follow-up, 9 patients were dead owing to hepatic decompensation, of which 5 (10.4%) patients were C-AIH and 4 (10%) patients were C-AIH (p = 1.000).

Conclusion: Although the serum bilirubin and aminotransferase were obviously increased in A-AIH patients, the response after standard treatment of A-AIH may not be significantly different from that of C-AIH. Moreover, the different level of serum biochemical indicators may not be the most important factor influenced prognosis for neither A-AIH or C-AIH.

Disclosure: Nothing to disclose.

P0057 URSEDOXOXYCHOLIC ACID FOR THE TREATMENT OF PRIMARY BILIARY CIRRHOSIS/CHOLANGITIS AND PRIMARY SCLEROSING CHolangitis: ARE OUR PATIENTS UNDERDOSED?

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Introduction: Ursodeoxycholic Acid (UDCA) is used to treat the cholestatic liver diseases primary biliary cirrhosis/cholangitis (PBC) and primary sclerosing cholangitis (PSC). Current guidance states an optimum dose of UDCA is 13–15mg/kg in 2 divided doses, with the same dose used but not specifically recommended in PSC. A survey undertaken by the PBC Foundation in 2013 implied a third of patients were underdosed. Optimal dosing of UDCA leads to improved biochemical reponses in both PBC and PSC patients, and delayed disease progression and reduced transplant rates in PBC.

Aims and Methods: The objective of this study was to assess whether locally, our patients are optimally dosed on UDCA (using the upper end 15mg/kg) and whether this has had any impact on their biochemical response to treatment.

A database of outpatient correspondence was searched for the terms “primary biliary cirrhosis” and “primary sclerosing cholangitis”. 85 patients were identified with a confirmed diagnosis of PBC or PSC (antibody positive or biopsy proven). 7 patients were excluded from the study as they had not yet commenced on UDCA, leaving 78 treated patients (59 PBC, 19 PSC). Using the most recently documented weight around time of diagnosis/commencement of treatment, optimum doses of 15mg/kg were calculated for each patient and compared to the actual dose prescribed. Biochemical response was assessed using the Barcelona Criteria - either greater than 40% reduction in alkaline phosphatase (ALP) or normal after 1 year of UDCA treatment.

Results: Of the 78 patients, 33 (42%) were found to be at least optimally dosed at 15mg/kg, with 45 patients (58%) underdosed on UDCA. In the optimally dosed group, 19 patients (38%) showed a biochemical response, whereas 9 patients (27%) had a worsening of their ALP (1 identified as non-compliant). The remaining 5 patients (15%) had a normal ALP at the time of commencing, which remained normal to date.

In the suboptimally dosed group, 20 patients (44%) showed biochemical response, with 16 patients (36%) having a worsening in their ALP and 9 patients (20%) having a normal ALP at diagnosis which again remained normal to date.

Aims of patients with PBC responded to UDCA compared to 53% of those with PSC.

Conclusion: This study shows that a higher proportion of our local patient group diagnosed with PBC or PSC are underdosed with UDCA than optimally dosed. We have demonstrated in this group that UDCA appears effective in improving biochemical response to treatment or at least maintaining a normal ALP, when used at the optimum dose, supporting a drive towards ensuring patients are prescribed 15mg/kg of UDCA. Interestingly there was still a partial response to treatment despite underdosing all patients who had normal ALP maintained this regardless of UDCA dose. This may generally imply efficacy of UDCA in the treatment of PBC and PSC. Looking at potential reasons for underdosing, it was identified in some cases that patients’ weight had changed (markedly decreased) but not led to a subsequent adjustment of UDCA dose.

Disclosure: Nothing to disclose.

References:

P0058 DIAGNOSIS OF TYPICAL FOCAL NODULAR HYPERPLASIA IN THE LIVER - USE OF A NOVEL ULTRASONIC VASCULAR DOPPLER TECHNIQUE

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Introduction: Examination of vascular structures and flow dynamics is important in order to differentiate benign from malignant focal liver lesions (FLL). Diagnostic ultrasound in combination with contrast-enhanced ultrasound (CEUS) has a high accuracy and diagnostic value for FLL (1, 2). CEUS ideally allows the visualization of the very specific spoke wheel pattern in the arterial phase and is standard of reference (SOR) in the diagnosis of FNH smaller 3 cm (3). Conventional colour Doppler has limitations in visualizing microvascularity and low velocity blood flow. Superb Micro-Vascular Imaging (SMI) is a novel ultrasound Doppler technique with high resolution imaging, minimal motion artefacts and high frame rates. SMI has not been studied in FNH lesions, which have a unique vascular supply that is diverse in most cases. Diagnosis of this benign FLL is important to avoid unnecessary biopsies and surgical procedures. In contrast to hepatocellular adenoma, the management of FNH is conservative because there is no risk of malignant transformation, no risk of bleeding and no need to stop contraception (4,5).

Aims and Methods: The diagnostic value of the novel SMI technique for diagnosing FNH lesions in comparison to CEUS was studied. SMI offers a unique algorithm allowing visualization of microvascularity with low velocity flow with use of a novel contrast agent and analysis of flow direction and velocity to provide new adaptive algorithm to identify and remove tissue motion and reveal true blood flow. CEUS was performed as standard of reference by using 1.5 ml intravenously injected contrast agent (sulphur hexafluoride microbubbles) and was performed according to international guidelines (1). Representative still images and video clips were recorded.

Results: We present a case series of 5 female patients between 25 and 55 years with FNH. CEUS revealed in almost all cases FNH with typical early centrifugal arterial spoke-wheel enhancement without washout up to 5 minutes after injection of the contrast agent. We could demonstrate the excellent diagnostic value of CEUS.
the spoke-wheel-like vessels by SMI (without contrast agent and independently to time course). SOB was resuscitation (n = 2), MRI (n = 1) and follow-up 12–18 months (n = 2).

Conclusion: FHN is the second most common benign liver tumor after hemangioma. FHN is diagnosed by CEUS, CT or MRI using intravenous contrast agents. This is the first European experience demonstrating the excellent clinical value of SMI to diagnose typical FHN with spoke-wheel-like vessels. SMI is an easy to use, intuitive imaging tool without the need of contrast agent that offers a detailed visualization of small, low-velocity vessels within FHN lesions. In the prospective phase, it will be possible to provide this non-invasive imaging criteria for FHN as CEUS in the arterial phase. In contrast to SMI, CEUS and especially CT and MRI require early arterial contrast enhancement, which may be missed due to a short detection period of sometimes only a few seconds.

Disclosure: Nothing to disclose

References

P0059 COMPARISON OF THE DIAGNOSTIC ACCURACIES OF MAGNETIC RESONANCE TECHNIQUE AND TRANSIENT ELASTOGRAPHY FOR EVALUATING HEPATIC STEATOSIS IN NONALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Noninvasive methods have been used for the assessment of hepatic steatosis in patients with nonalcoholic fatty liver disease (NAFLD). Magnetic resonance derived measures, such as proton density fat fraction (PDFF) and fat fraction (FF), and transient elastography based controlled attenuation parameter (CAP) of liver fat and volume are emerging as non-invasive, accurate imaging biomarkers.

Aims and Methods: We performed this systematic review and meta-analysis to compare the efficacies and accuracies between magnetic resonance technique and transient elastography for evaluation of hepatic steatosis in NAFLD patients. PubMed, the Cochrane Library, Embase and Web of Science were searched to gather studies, relating to accuracies of MR technique or TE for evaluating grading of steatosis (S0-S3) diagnosed by liver biopsy. We compared the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and hierarchical plot comparing the accuracies of grading of steatosis (S0-S3) using ROC curves for the studies. The clinical utilities of MR technique and TE were also evaluated.

Results: 19 articles with a total of 1558 NAFLD subjects were included. As for diagnostic accuracy of MR based PDFF, the summary sensitivities and specificities values were 0.92 (95% CI, 0.88–0.95) and 0.93 (95% CI, 0.88–0.97) for S1, 0.76 (95% CI, 0.71–0.80) and 0.88 (95% CI, 0.84–0.91) for S2, and 0.73 (95% CI, 0.68–0.78) and 0.89 (95% CI, 0.86–0.92) for S3. The HRSCs were 0.96 for ≥S1, 0.91 for ≥S2, and 0.89 for ≥S3. Following a positive measurement (over the threshold value) for ≥S1, ≥S2, and ≥S3, the corresponding post-test probabilities for the presence of steatosis (pretest probability was 50%) were 93%, 87% and 87%, respectively; if the values were below these thresholds (negative results), the post-test probabilities were 14%, 7%, and 7%, respectively. The diagnostic accuracy of MR based fat fraction (FF) for stage ≥S1, the summary sensitivity was 0.92 (95% CI, 0.87–0.95), and the specificity was 0.92 (95% CI, 0.87–0.97). Besides, the HRSOC is 0.9260. For diagnostic accuracy of TE-CAP detecting stage ≥S1, ≥S2, ≥S3, the summary sensitivity was 0.79 (95% CI, 0.67–0.89), 0.80 (95% CI, 0.75–0.84), 0.81 (95% CI, 0.78–0.84), and the specificity was 0.83 (95% CI, 0.80–0.96), 0.74 (95% CI, 0.70–0.78), 0.66 (95% CI, 0.59–0.73), respectively. Following a positive measurement (over the threshold value) for ≥S1, ≥S2, and ≥S3, the corresponding post-test probabilities for the presence of steatosis (pretest probability was 50%) were 86%, 76% and 71%, respectively, if the values were below these thresholds (negative results), the post-test probabilities were 16%, 18%, and 18%, respectively.

Conclusion: MR technique and TE both provide standardized non-invasive approaches for staging hepatic steatosis in NAFLD patients. Compared with TE based CAP, MRI derived PDFF is significantly more accurate for evaluating different grades of steatosis, especially in those obese patients, which probably offer the best diagnostic performance and may be used instead of invasive liver biopsies.

Disclosure: Nothing to disclose

References
P0061 PREDICTIVE FACTORS OF HEPATIC ENCEPHALOPATHY AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT - TEN YEARS OF EXPERIENCE OF A PORTUGUESE CENTER
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Introduction: Many complications can occur during Transjugular Intrahepatic Portosystemic Shunt (TIPS) implantation procedure. However, the most relevant clinical complication is hepatic encephalopathy (HE).
Aims and Methods: The aim of this study was to assess TIPS indications, success rates and related complications. The secondary goal was to identify predictive factors of HE after TIPS.
Results: We present a retrospecitive unicenter cohort study from October 2007 to January 2018 including patients undergoing TIPS procedure on a Portuguese referral center. Portal pressure gradients before and after TIPS were only recorded of Gastroenterology of SCJUT between January 2017-December 2017: 23 men (10.6 vs 5.9, p = 0.011). Mean AFP level was 0.56 (0.56%) and anestesia complications (0.56%).
Patients with upper gastrointestinal bleeding (11.1%), hepatic hydrothorax (0.56%) and Budd-Chiari syndrome (0.56%). 17.2% of the patients had more than 1 indication for TIPS procedure.
Technical success rate was 91.67% (n = 165). Hemodynamic success rate (since January 2015) was 82.86% in patients with refractory ascites and 100% in patients with uncontrolled gastrointestinal bleeding. 3.33% had immediate TIPS-related complications: hemoperitoneum (1.11%), haemorrhagic shock (0.56%), porto-biliary fistula (0.56%); cerebral haemotoma (0.56%) and anesthesia complications (0.56%).
After TIPS, 44.49% (n = 89) patients with refractory ascites had improved and 5.56% (n = 10) patients had a rebounding episode. HE after TIPS was seen in 44.4% (n = 80) of the patients (26.7% newly installed, 13.3% maintained and 4.4% worsened). It was found that patients with HE “de novo” or worsened were older (58.2 vs 53.6, p = 0.09). Higher severity scores (MELD and Child-Turcotte-Pugh) and non-sclerosis hernostasis were not associated with a higher occurrence of HE (p>0.05).
However, a portal pressure gradient ≥5mmHg demonstrated a higher risk of HE (OR 10.16 VS 13.45, p = 0.017).
Conclusion: The success rates were over 80%. HE was a frequent complication. Oder age and portal pressure gradient ≤5mmHg were associated with a higher risk of HE after TIPS.
Disclosure: Nothing to disclose
Reference

P0063 RECTUS ABDOMINS ULTRASOUND MAY DETECT SARCOPENIA AND PREDICT SURVIVAL IN PATIENTS WITH LIVER CIRRHOSIS
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Introduction: Sarcopenia may affect patients with liver cirrhosis. It is associated with a poorer quality of life and higher morbidity and mortality.
Aims and Methods: We aimed to evaluate the value of ultrasound measured psoas major (PM) and rectus abdominis (RA) thickness in predicting survival of patients with liver cirrhosis. 61 patients were included in a prospective study in a 16-month period and followed-up for at least 6 months. Sarcopenia was assessed using surrogate parameters: hand grip strength (HGS), mid-arm muscle circumference (MAMC) and SGA (subjective global assessment) score.
Results: There were 40 men, with a mean age of 58.03 ± 10.8 years. 26.22% of patients were Child-Pugh A, 44.59% B and 27.86% C. Patients were followed-up for 11.9 ± 5.63 months.
Mean RA (mRA) was 8.73 ± 2.57mm. RA thickness moderately correlated with MAMC (r = 0.596, p < 0.0001) and HGS (r = 0.515, p < 0.0001) and decreased with increasing SGA class (A 10.6 ± 2.86mm, B 8.3 ± 1.9mm, C 6.5 ± 1.9mm, p < 0.0001).
Survival at 6 months was independently predicted by MELD-Na score (OR 1.305, p = 0.005). Survival during follow-up was independently predicted by mRA (HR 0.701, p = 0.011, AUROC 0.732) and ascites (HR 1.876, p = 0.026, AUROC 0.732). A cut-off of mRA less than 6.75mm had 50% sensitivity and 93% specificity to predict mortality in patients with liver cirrhosis.
Conclusion: As a surrogate marker of sarcopenia, ultrasound measured rectus abdomins muscle may predict survival in patients with liver cirrhosis.
Disclosure: Nothing to disclose

P0062 INTER-OBSERVER REPRODUCIBILITY OF VTQ (ARFI TECHNIQUE) FOR THE EVALUATION OF FOCAL LIVER LESIONS STIFFNESS
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Introduction: Several studies showed that VTQ (Virtual Touch Quantification) provides additional information regarding FLLs stiffness and it is useful when disease is among malignant and benign FLLs.
Aims and Methods: We aimed to evaluate interobserver reproducibility of a point shear wave elastography- pSWE [using Acoustic Radiation Force Impulse Quantification (ARFI)]- VTQ (Siemens) for the evaluation of focal liver lesions stiffness. We performed a prospective study including 44 patients diagnosed with focal liver lesions (FLLs) after an ultrasound examination admitted to the Department of Gastroenterology of SCJUT between January 2017-December 2017: 23 men (52.3%) and 21 women (47.7%), mean age 65.3 ± 11.1 years. A total of 48 FLLs were examined.
Elastographic measurements (EM) were obtained in 48 FLLs using VTQ (Siemens). 2 examiners with different levels of experience in ultrasound-based elastography- pSWE performed VTQ on each subject: 10 measurements in the liver parenchyma and 10 measurements in each focal liver lesion. Medians and interquartile ranges (IQRs) were calculated (m/s). We used the interclass correlation coefficient (ICC) with 95% lower and upper limits of agreement (LOA) to assess the inter-observer reproducibility of VTQ.
Results: A total of 48 lesions were evaluated. The lesions were: 32.48 (72.7%) hepatocellular carcinomas, 7.48 (14.5%) hemangiomas, and 9.48 (18.7%) metastases. The total mean values obtained were: 1.62 m/s in HCCs, 2 m/s in hemangiomas and 2.62 m/s in metastases. The agreement between the novice and the experienced examiner was excellent: 0.95 (95% CI: 0.91-0.97).
Conclusion: The excellent ICCs for the median values show that ARFI technique was good for evaluating FLL stiffness is a reproducible method and could provide significant complementary information regarding the tissue stiffness, useful for the differential diagnosis of focal solid liver lesions.
Disclosure: Nothing to disclose
Reference

P0064 TRUE SEVERITY OF LIVER STEATOSIS AND FIBROSIS IN TYPE 2 DIABETES MELLITUS PATIENTS
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Introduction: Prevalence of type II diabetes has significantly increased in the last decade. Type II diabetes and nonalcoholic fatty liver disease (NAFLD) are frequently associated.
Aims and Methods: The aim of the present study was to assess the severity of liver fibrosis and steatosis in a cohort of type II diabetic patients, using non-invasive methods: Transient Elastography (TE) and Controlled Attenuation Parameter (CAP) before and after the CAP adjustment algorithm was applied. The study included 576 type II diabetic patients, who were prospectively randomized. All were evaluated by means of TE and CAP (FibroScan EchoSens). A cut-off value of 10.5 kPa [1] was used to define clinically relevant fibrosis (F ≥ 3). We used the following cut-off values [2]: for S2 (moderate steatosis) - 255 dB/m, and 290 dB/m for S3 (severe steatosis) - We corrected the CAP values according to the presence of diabetes (we deducted 10 dB/m) and according to the degree of obesity (we deducted 4.4 dB/m for each BMI > 25 kg/m2 and added 4.4 dB/m for each BMI > 25 kg/m2) [1, 3].
Results: Out of 576 diabetes screened, we excluded those with associated viral hepatitis, those with an AUDIT-C score ≥8 and those with unreliable LSM. The final analysis included 403 subjects (59.3% women, BMI = 31.6 ± 6 kg/m2) with reliable LSM obtained using both probes. Moderate and severe steatosis by means of LSM was found in 18.9% and 61.5% cases respectively. After correction, we found moderate steatosis in 22.1% cases and severe steatosis in 52.6%
cases. We found no significant differences regarding the proportion of patients with moderate steatosis after the algorithm was applied (18.9 vs. 40.0%, p = 0.26), but we found significant differences regarding the proportion of severe steatosis, (61.5% vs. 52.6%, p = 0.01). Clinically relevant fibrosis was detected by means of TE in 13.6% (55403) of subjects.

Conclusion: In type 2 diabetes patients it is necessary to use an algorithm for correction in order to avoid overestimation of the degree of steatosis and fibrosis.

Disclosure: Nothing to disclose

References
**P0068 MODIFIED ALBI-T SCORE AS PROGNOSTIC MODEL IN THE EVALUATION OF PATIENTS WITH HEPATOCELLULAR CARCINOMA**

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**Introduction:** ALBI score eliminates the need for the subjective variables required in the CTP grade. The addition of tumor characteristics from TNM classification resulted in ALBI-T score. ALBI grade 2 showed a wide range of patients, Osagusawa sub-classification of ALBI grade 2 classes patients more precisely.

**Aims and Methods:** We accrued data from the HCC clinic at National Liver Institute, Menoufia University. We had access to a data set of a cohort of 1910 patients diagnosed with HCC and fulfilled the inclusion criteria. Patients were followed up to the time of diagnosis of time of death or date of data collection if they remained alive. Modified ALBI-T was obtained through using new grading of ALBI score (grade 1 to 4 instead of grade 1 to 3) obtained through Osagusawa sub-classification of ALBI grade 2 and using it in calculating ALBI-T score. We compared our score to other scoring systems as CTP, TNM, BCLC, ALBI, PALBI, ALBI incorporated BCLC and ALBI-T scores.

**Results:** For 1910 patients, the mean age was 57 years, 1575 were males. At presentation, 50.6% were CTP A, 36.1% were CTP B and 13.4% were CTP C. Most of the patients were ALBI grade 2 (63.2%), 17.8% were ALBI grade 2A while 45.5% were ALBI grade 2B. ALBI grade 1 & 3 were 12% & 24.7% respectively. The overall median survival was 13 months; the median survival was ALBI grade 1 than ALBI 2 & 3 (28.8, 14 & 5 months respectively, p < 0.001). Moreover, the median survival for ALBI grade 2A patients was better than ALBI 2B (18.6 vs. 13 months respectively, p < 0.001). ALBI-T grades 0 & 1 patients had better median survival than those of ALBI-T grades 2, 3 & 4.2, 24.4, 17, 8, 9, 5 and 3 months respectively (p < 0.001). On adding the ALBI subclassification proposed by Osagusawa, the modified ALBI-T showed significant improvement in the median survival of modified ALBI-T grades 2, 3, 4, 5 and 6 to be 28.6, 20.9, 13.9, 8 and 4 months respectively. On comparing ALBI-T, CTP, TNM, ALBI, BCLC, ALBI (modified), PALBI, ALBI based BCLC and ALBI-T, it showed significantly better AUC (0.818 vs. 0.643, 0.620, 0.719, 0.734, 0.749 and 0.803, respectively).

**Conclusion:** Modified ALBI-T classifies patients with HCC more precisely than other scoring system.

**Disclosure:** Nothing to disclose

**References**

**P0070 HCC RECURRENCE AFTER DAA TREATMENT IN HCV PATIENTS**

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**Introduction:** The debate on the matter of HCC recurrence risk and its aggressiveness in patients who have a history of previously and successfully treated HCC underd AAAs treatment is still open.

**Aims and Methods:** The present real-life multicenter, prospective study aims to evaluate the impact of new DAAAs therapies in HCV patients with a previous successfully treated HCC, in terms of neoplastic recurrence. From March 2015 to March 2017, 101 consecutive HCV patients with prior HCC underwent DAAAs treatment were enrolled. The assessment of neoplastic recurrence was used as primary outcome, while a secondary outcome was the evaluation of baseline characteristics predicting HCC recurrence.

**Results:** 83% of patients were in Child-Pugh class A, and 89% had a history of HCC. The median MELD of 9 and 69% in BCLC-B and 419 in BCLC-C stage. Median overall survival in the whole population was 33.9 months.

When different TACE procedures, irrespective of the BCLC stage, the ALBI grade and pALBI grade were significant predictors of overall survival (p = 0.001 and p < 0.0001 respectively), similar to the HAP and the mHAPII scores (p < 0.0001). When patients in different BCLC stages were considered, ALBI was a significant predictor of OS only in BCLC-C (p = 0.001) patients treated with TACE, pALBI was a significant predictor of OS in BCLC-B (p < 0.001) and BCLC-C (p < 0.01) similarly to HAP and mHAPII.

Similar data were obtained when only the first TACE procedure was considered in each patient (total of 901 patients, 460 BCLCA, 259 BCLC-B and 182 BCLC-C). Considering all BCLC stages, ALBI was a significant predictor of overall survival (p < 0.001) similar to the pALBI, HAP and mHAPII scores (p = 0.003). When different BCLC stages were considered, ALBI, pALBI and HAP were significant predictors of OS in BCLC-C (p = 0.008, p = 0.003 and 0.08 respectively), whereas mHAPII was not significant. PALBI was also a significant predictor of OS in BCLC-C (p = 0.005).

**Conclusion:** ALBI and pALBI offer additional simple and objective methods of assessing liver function in HCC and may be useful for selecting patients more likely to survive after TACE, especially ALBI in those belonging to the BCLC-C stage whereas pALBI in BCLC-B and BCLC-C stage.

**Disclosure:** Nothing to disclose

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**Introduction:** The prognosis of hepatocellular carcinoma is influenced by severity of liver function. Child-Pugh (CPS) and MELD scores have considerable limitations. Recently, the prognostic value of albumin-bilirubin (ALBI) [1] grade has been evaluated in patients undergoing HCC treatment with different modalities, but not specifically in patients undergoing TACE [2]. Moreover, the pALBI grade, which is included platelet count, is a surrogate marker ofportal hypertension [3].

**Aim:** To evaluate the role of ALBI grade and pALBI in predicting outcome for HCC patients who underwent transcatheter arterial chemembolization (TACE).

We retrospectively evaluated the prognostic significance of ALBI and pALBI in patients undergoing TACE recorded in the Istituto di Clinica, and compared it with other prognostic systems, including MELD, CPS, hepatoma arterial-embolization prognostic (HAP) and mHAPII.
**P0072** THE EFFECT OF DIRECT ACTING ANTIVIRALS ON THE OCCURRENCE AND RECURRENT OF HEPATOCELLULAR CARCINOMA: META-ANALYSIS OF 1438 PATIENTS

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**Introduction:** Prospective reports suggested an unexpected high rate of hepatocellular carcinoma (HCC) occurrence and recurrence following antiviral treatment using direct acting antiviral (DAA).

**Aims and Methods:** We aim to synthesize evidence about effect of DAA on the occurrence of HCC.

**Results:** Seven prospective cohort studies were included in the present review with a total of 1438 HCV patients. The pooled HCC occurrence rate in the DAA group was 2.7% (95% CI [0.015, 0.038]). The pooled HCC recurrence rate in the DAA group was 13.6% (95% CI [0.059, 0.214]); while the two-arms meta-analysis showed that the DAA group was associated with less risk of HCC recurrence compared to the control group (RR = 0.55, 95% CI [0.32, 0.96], p = 0.04). Pooled effect estimates did not differ significantly after subgrouping the patients according to DAA regimens. All pooled analyses were homogeneous.

**Conclusion:** The present meta-analysis showed that the rate of HCC occurrence or recurrence following DAA regimens is low.

**Disclosure:** Nothing to disclose

**P0073** PROGNOSTIC VALUE OF ALBUMIN BILIRUBIN SCORE AND ALBUMIN BILIRUBIN RATIO IN HEPATOCELLULAR CARCINOMA PATIENTS TREATED WITH TRANS-ARTERIAL CHEMOEMOBOLIZATION

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**Introduction:** Albumin bilirubin score (ALBI) is a recently reported, simpler, more objective, and evidence-based alternative to the Child-Pugh (CP) score and Barat facility clinic liver cancer (BCLC) for prediction of survival and prognosis in hepatocellular carcinoma (HCC). Albumin bilirubin ratio is a novel method for detection of early recurrence of HCC after management.

**Aims and Methods:** This study aimed to validate prognostic value of both albumin bilirubin score and albumin bilirubin ratio in hepatocellular carcinoma patients treated with conventional transarterial chemomobilization (cTACE).

**Results:** The study enrolled 78 HCC patients with BCLC stage (A,B) underwent cTACE, all of them have complete response (CR) according to mRECIST criteria. ALBI score was measured before cTACE using this equation - 0.085 x (albumin g/l) + 0.66 x log (bilirubin μmol/l) and the ratio between albumin (g/l) and bilirubin (μmol/l) was mathematically calculated before TACE. Follow-up of the patients was done every 6 months for 36 months using dynamic imaging, liver, kidney functions and AFP.

**Results:** Early HCC recurrence (within the first 6 months) was observed in 28 patients, ALBI score was significantly associated with early tumor recurrence (p = 0.001). The Roc curve for ALBI score for detection of early recurrence of HCC after cTACE (at cut off value 0.637, sensitivity is 100% and specificity is 77%), for Albumin Bilirubin ratio (at cut off value 0.885, sensitivity is 95.2% and specificity is 71.4%). Both ALBI score and albumin bilirubin ratio were significantly positively correlated with Child Pugh score, BCLC staging and model for end stage liver disease (MELD) score (p = 0.001).

**Conclusion:** ALBI score and albumin bilirubin ratio could be used as prognostic indicators in HCC management and help in assessing early recurrence of HCC following TACE with high sensitivity and good specificity in comparison to other well-known scores like BCLC and Child -Pugh scores.

**Disclosure:** Nothing to disclose

**P0074** DYNAMIC DETERMINANTS OF PORTAL HYPERTENSION ARE IDENTIFIED BY HISTOLOGICAL COLLAGEN PROPORIONATE AREA ESTIMATIONS

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**Introduction:** Portal hypertension is determined both by ‘static’ fibrosis and ‘dynamic’ hemodynamic components. The correlation of fibrosis area and portal pressure has not been systematically assessed in different animal models and in human liver disease of different etiologies. This study hypothesized and tested the correlation of collagen-proportionate area (CPA) with portal pressure (PP) in animal models and with hepatic venous pressure gradient (HVPG) in patients with cirrhosis.

**Aims and Methods:** Carbon tetrachloride (CCl4) or bile duct ligation (BDL) models were used to mimic toxic or biliary cirrhosis in rats, respectively. Portal pressure was measured by direct cannulation of the portal vein. Patients underwent HVPG measurements and transjugular liver biopsy. Liver samples were stained by chrome-aniline-blue (CAB) or picro-sirus-red (PSR) and CPA was quantified by Imaged software.

**Results:** Portal pressure correlated with CPA both in BDL (R = 0.844, p < 0.001) and in CCl4 (R = 0.866, p < 0.001) animals. The ‘linear fitting’ curve was steeper in BDL than in CCl4 (PP = 2.303*CPA + 4.045) as compared to CCl4 (PP = 1.520*CPA + 4.794). Animals outside the 75% confidence interval of the expected PP (based on CPA) might have pronounced ‘dynamic’ components, e.g. in endothelial dysfunction, splanchic blood flow or portosystemic shunting. Similarly, in (n = 18) patients, HVPG correlated with CPA (R = 0.339, p = 0.17) yielding a ‘predicted’ HVPG (mmHg) of 0.663*CPA + 11.8. In patients with 25% higher HVPG as expected by the CPA-formula, we recorded higher vWF-Ag (368 ± 3 vs. 233 ± 50%, p = 0.048), IL6 (23 ± 8 vs. 8 ± 4 ng/l; p = ns), and bile acids (34 ± 18 vs. 7.3 ± 3 μmol/l; p = ns) than in patients with 25% lower HVPG as expected. More patients will be presented at congress.

**Conclusion:** CPA as the ‘static’ component of PHT correlates with PP/HVPG, with model-specific and etiology-dependent correlation estimates. Outliers to this curve imply profound alterations of ‘dynamic’ components of PHT, such as endothelial dysfunction, significant collateralization, bacterial translocation or a deranged gut-liver axis. Identification of outliers refines the assessment of vascular and hemodynamic dysfunction and may allow for personalized therapy of PHT.

**Disclosure:** Nothing to disclose
P0075 PRONOSTIC FACTORS IN PATIENTS WITH PORTAL CAVERNOMA: RESULTS OF A PROSPECTIVE COHORT OF 131 CASES
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Introduction: The portal cavernoma (PC) follows a chronic thrombotic occlusion of the portal vein and is often associated with toxic liver damage. It is remarkable that thrombosis of a portal branch causes portal hypertension, survival and causes of death and no data are available to identify those patients in which lifelong anticoagulation is necessary to prevent recurrent thrombosis.
Aims and Methods: The aim of the study was to analyze the long-term prognosis of patients with PC.
Results: The study was prospective and follow-up study of patients initially managed for portal cavernoma from January 2008 to June 2017. Patients with cirrhosis, cancer or hepatic cirrhosis syndrome were excluded. Portal hypertension was managed according to Baveno V recommendations. Anticoagulant therapy has been indicated according to current recommendations. All recurrent thrombosis, gastrointestinal bleeding, adverse events of anticoagulant therapy and death were registered.
Results: In this study 131 patients were included and followed up for a median time of 51.5 months. Of the 131 patients, 69 were men and 62 women, with a median age of 46.2 (23–81) years. PC was an incidental finding in 25 (19%) patients: 46 (35.2%) patients presented with abdominal pain; 60 (45.8%) patients presented with bleeding from portal hypertensive sources. Esophageal and/or gastric varices were present at diagnosis in 78 (59.5%) patients. Prothrombotic diagnosis was made in 72 (57.2%) patients. Among the factors identified, the most common were chronic myeloproliferative disease (CMD, 25.2%) and protein S deficiency (14.9%). 95 (72.5%) patients received long-term anticoagulation therapy. During the follow-up, 91 patients had no hemorrhagic or thrombotic events. The incidence rate of esophageal varices was 25%: 15 (11.4%) patients suffered from 23 episodes of gastrointestinal bleeding with no deaths. 6 patients had ascites and 15 patients had symptomatic cholangiopathy effectively treated with UDCA. New venous thrombotic episodes occurred in 11 (8.4%) patients of whom 6 were in the splanchic area. There was no case of occurrence or recurrence of intestinal infarction under anticoagulant therapy. 5 patients had latent CMD progression and 1 patient died of acute myeloid leukemia.
Conclusion: The long-term prognosis of patients with portal cavernoma is good, 70% of patients have a stable evolution. The combination of anticoagulants and the treatment of portal hypertension is effective in preventing thromboembolic recurrence and management of bleeding complications.
Disclosure: Nothing to disclose.

P0076 NGC STIMULATION AND PDE5 INHIBITION DECREASE SINUSOIDAL RESISTANCE AND REDUCE FIBROSIS IN RATS WITH BILIARY CIRRHOSIS
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Introduction: Dysfunctional nitric oxide (NO) and cGMP signalling results in increased intrahepatic resistance in cirrhotic portal hypertension (PHT). PHT complications and major complications such as portal bleeding or ascites. Currently medical treatment of PHT is limited to non-selective beta-blockers, while there is no available treatment for liver fibrosis. We investigated the soluble guanylyl cyclase (sGC) stimulator riociguat (RIO) and activator cinaciguat (CIN) and phosphodiesterase-5 inhibitor tadalaftal (TADA) in bile duct ligated (BDL) rats.
Aims and Methods: Male Sprague-Dawley rats underwent BDL or sham-operation. Starting 1 week after surgery, RIO (0.5mg/kg), CINA (1mg/kg), TADA (1.5mg/kg) or vehicle (VH) were given orally (PP), mean arterial pressure, heart rate and splanchic/portal blood flow were measured. Liver fibrosis, hepatic inflammation and hepatic cGMP levels were assessed.
Results: Cirrhotic BDL-VEH rats showed significant increase in PP (13.07 ± 0.9mmHg) compared to healthy controls. In BDL animals RIO (9.96 ± 0.7mmHg, p = 0.021) and TADA (10.27 ± 0.8mmHg, p = 0.030) treatment decreased PP without affecting systemic hemodynamics. Intrahepatic vascular resistance decreased by RIO (2.86 ± 0.25, p = 0.45; 0.85 ± 0.4mmHg/mL, p = 0.005). Hepatic hydroxyproline content was reduced by RIO and TADA treatment (RIO: 350 ± 30μg/g, p = 0.003; TADA: 282 ± 50μg/g; p = 0.003 vs. BDL-VEH: 503 ± 20μg/g liver), whereas fibrotic tissue-unique-blue stained area decreased only by RIO (2.14 ± 0.3% vs. 4.15 ± 0.53%, p = 0.001). Both, RIO and TADA therapy decreased transaminases AST (RIO: ~36%, p < 0.001; TADA: ~24%, p = 0.006) and ALT (RIO: ~32%, p = 0.035; TADA: ~27%, p = 0.053). Limited BDL-VEH rats presented less hepatic hF expression (~56%, p = 0.053), indicating a reduction of neuroinflammation. Furthermore, hepatic GMP levels were significantly increased by RIO, but not by TADA or CINA. In cirrhotic BDL rats, 1mg/kg CINA caused weight loss, hypotension and increased lactate levels.
Conclusion: The sGC stimulator riociguat and the PDE5 inhibitor tadafalff showed beneficial effects in cirrhotic rats by reducing liver fibrosis and decreasing portal hypertension. High dosing of sGC activators such as 1mg/kg cinaciguat may be associated with toxic liver damage.
Disclosure: BK, KP, LD, SA, SP, BD, BA, SJ, PKB, SM, ZK, RUN, TM, RT, SP have nothing to disclose This study has been financially supported by a grant from Boehringer Ingelheim.

P0077 SUBCLINICAL PORTAL HYPERTENSION: RESULTS AND CONCORDANCE OF DIFFERENT MEANS OF NON-INVASIVE DIAGNOSIS
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Introduction: The diagnosis of portal hypertension at a subclinical stage is important because of major prognostic and therapeutic consequences. In the latent stage, subclinical portal hypertension is not complicated with digestive hemorrhage and or Budd Chiari syndrome. The positive diagnosis of subclinical portal hypertension is confirmed according to current recommendations. All recurrent thrombosis, gastrointestinal bleeding, adverse events of anticoagulant therapy and death were registered.
Results: In this study 131 patients were included and followed up for a median time of 51.5 months. Of the 131 patients, 69 were men and 62 women, with a median age of 46.2 (23–81) years. PC was an incidental finding in 25 (19%) patients: 46 (35.2%) patients presented with abdominal pain; 60 (45.8%) patients presented with bleeding from portal hypertensive sources. Esophageal and/or gastric varices were present at diagnosis in 78 (59.5%) patients. Prothrombotic diagnosis was made in 72 (57.2%) patients. Among the factors identified, the most common were chronic myeloproliferative disease (CMD, 25.2%) and protein S deficiency (14.9%). 95 (72.5%) patients received long-term anticoagulation therapy. During the follow-up, 91 patients had no hemorrhagic or thrombotic events. The incidence rate of esophageal varices was 25%; 15 (11.4%) patients suffered from 23 episodes of gastrointestinal bleeding with no deaths. 6 patients had ascites and 15 patients had symptomatic cholangiopathy effectively treated with UDCA. New venous thrombotic episodes occurred in 11 (8.4%) patients of whom 6 were in the splanchic area. There was no case of occurrence or recurrence of intestinal infarction under anticoagulant therapy. 5 patients had latent CMD progression and 1 patient died of acute myeloid leukemia.
Conclusion: The long-term prognosis of patients with portal cavernoma is good, 70% of patients have a stable evolution. The combination of anticoagulants and the treatment of portal hypertension is effective in preventing thromboembolic recurrence and management of bleeding complications.
Disclosure: Nothing to disclose.

P0078 A MULTICENTER RANDOMIZED TRIAL OF LASER VERSUS ELECTROHYDRAULIC LITHOTRIPSY FOR DIFFICULT BILE DUCT STONES
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Concomitant cholecystolithiasis incidence is 4–20%. However, the number of session was not different. Further large comparative studies are warranted.

Disclosure: Nothing to disclose

P0079 LONG-TERM OUTCOME OF ENDOCOSMIC PAPILLARY LARGE-BALLOON DILATION FOR BILE DUCT STONES

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Introduction: Endoscopic papillary large-balloon dilation (EPLBD) has been reported to be safe and effective for large, multiple common bile duct (CBD) stones. However, long-term outcome of EPLBD for such difficult stones has not been sufficiently determined.

Aims and Methods: The aims of this study was to evaluate long-term outcome of EPLBD for CBD stones. 102 consecutive patients who had undergone endoscopic CBD stone removal with EPLBD, which was defined as papillary dilation with a balloon having a diameter ≥ 12 mm between October 2011 and December 2021 were included in a prospective maintained database. Patients with previous history of surgical choledochoduodenostomy or endoscopic papillotomy, those with benign biliary stricture, and those in whom stones were not completely removed were excluded for evaluation of long-term outcome. Clinical or telephone surveys were conducted for patients who did not undergo periodical follow-up. Patients who rejected or inappropriately replied to the survey were also excluded. The main outcome measurement was the recurrence rate of CBD stones after complete stone removal with EPLBD during a follow-up. Risk factors for such recurrence were secondarily analyzed. In addition, other complications in the biliary system, such as acute cholecystitis and acute non-calculus cholangitis, and the patient survival period were analyzed.

Results: Complete stone removal with EPLBD was achieved in 99 patients (96.1%). After elimination according to the above-mentioned criteria, 93 patients were finally included in the retrospective analyses for long-term outcome. The mean age and the incidence of cerebrovascular accident were significantly higher in non-surgical group than surgical group (70.0% vs. 62.6%, p = 0.047) and surgical group (n = 37) vs. non-surgical group (n = 43) and surgical group (p = 0.026, respectively). No statistical difference for 44 patients, while 20 patients were still waiting for cholecystectomy 4 months after the acute episode. Readmission for biliary complications was observed in 24.1% of patients who didn’t undergo LC on the acute episode (second episodes of AC, cholangitis and biliary acute pancreatitis were reported), 3 of them required urgent surgery.

Conclusion: In the majority of patients with AC, surgical intervention was delayed due to the suspicion of concomitant cholecystolithiasis. However, in less than 40% of cases the diagnosis was confirmed and the requirement of endoscopic treatment was needed. This resulted in a readmission rate for biliary complications that was almost double compared to the non-surgical group. Admission Bilirubin cutoff found to be predictor of common biliary duct obstruction in this study was higher than established on ASGE guidelines. Considering that the appropriate management of this patients could be different according to these findings, more prospective studies should be formed.

Disclosure: Nothing to disclose

P0080 BILIRUBIN LEVEL AT ADMISSION AS PREDICTOR OF CONCOMITANT CHOLECYSTITIS AND RATE OF READMISSION FOR BILIARY COMPLICATIONS IN PATIENTS WITH DELAYED SURGERY FOR SUSPECTED BILIARY DUCT OBSTRUCTION

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Introduction: Laparoscopic cholecystectomy (LC) is the gold standard treatment in acute cholecystitis (AC). Concomitant cholecystolithiasis incidence is 4–20%. However, the number of session was not different. Further large comparative studies are warranted.

Disclosure: Nothing to disclose
in recurrence rate between PTGBA and antibiotics only groups (7.7% vs. 11.8%) 2 patients underwent prophylactic cholecystectomy due to non-symptomatic period after non-surgical management.

Conclusion: Recurrence occurred in 9.3% of patients with AAC treated with non-surgical management and the treatment outcome of non-surgical group was not inferior to that of surgical group. Further studies are needed to clarify role of non-surgical management in patients with AAC.

Disclosure: Nothing to disclose

P0082 PREVALENCE OF FUNCTIONAL GASTRO-INTESTINAL DISEASES IN PATIENTS WITH UNCOMPLICATED CHOLECYSTOLITHIASIS; A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Cholecystolithiasis and functional gastrointestinal diseases (FGID) are both highly prevalent in the industrialised world. There are over 1.8 million ambulatory visits for symptomatic cholecystolithiasis in the United States. Incorrect assignment of abdominal symptoms may lead to inappropriate cholecystectomies with subsequent lack of benefit. We conducted a systematic review and meta-analysis to determine the prevalence of FGID in patients with uncomplicated cholecystolithiasis.

Aims and Methods: We searched MEDLINE, EMBASE and Web Of Science to identify studies reporting the prevalence of FGID in adults (≥18 years) with uncomplicated cholecystolithiasis. Pooled prevalences and 95% confidence interval (CI) were calculated. Subgroup analyses were performed according to diagnostic criteria used and for dyspepsia and irritable bowel syndrome (IBS) separately.

Results: Of the 1,696 studies evaluated, 11 reported the prevalence of dyspepsia and IBS in a total of 5,089 cholecystolithiasis patients. The pooled prevalence of FGID was 66.8% (95% CI 40% - 89%); 72.7% (95% CI 56% - 87%) for dyspepsia and 42.5% (95% CI 3% - 91%) for IBS. There were no statistically significant differences between diagnostic criteria.

Conclusion: This study finds that 67% of patients with cholecystolithiasis have FGID. In the United States this comprises 1.2 million patients. This is a concern, as these patients are at risk of cholecystectomy that will not benefit them. Extra measures to exclude FGID as a cause of abdominal symptoms, prior to cholecystectomy, is warranted.

Disclosure: Nothing to disclose

P0085 PRACTICE PATTERNS FOR THE MANAGEMENT OF CONCOMITANT GALLSTONES AND CHOLEDOCHOLITHIASIS

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Introduction: Patients with concomitant gallstones and common bile duct (CBD) stones should have endoscopic retrograde cholangiopancreatography (ERCP) followed by cholecystectomy.

Aims and Methods: We studied the success rate of ERCP, and recurrent cholecdocholithiasis in those who did and did not have cholecystectomy post-ERCP. All patients, diagnosed with CBD stones on imaging between September 2015 and July 2017, and had subsequent ERCP + sphincterotomy, were retrospectively included in this study. Data was collected from medical notes.

Results: 126 patients underwent ERCP for stone extraction. CBD was cannulated in 94%, 20% had normal ERCP. 92 patients (80%) had CBD stones at ERCP. 58 (63%) had complete stone extraction with 1 ERCP (76%), 2 ERCPs (19%), >2 ERCPs (5%). 19 (21%) were lost to follow-up or deemed unfit for repeat ERCPs. 13 (14%) were still undergoing regular ERCPs. 2 (2%) had surgical CBD exploration.

Conclusion: Only 41% (29/71) underwent cholecystectomy post-ERCP. 93% (27/29) remained CBD stone-free at a mean follow-up of 1 year (5 - 23 months). In the 59% (42/71) who did not have cholecystectomy post-ERCP, 95% (40/42) remained CBD stone-free at a mean follow-up of 1 year (1 - 24 months). 5% developed new CBD stones requiring another ERCP. Cholecystectomy post-ERCP was not performed in 60%.

Discussion: Patients with cholecdocholithiasis-free survival was comparable at 1 year in patients who did and did not have a cholecystectomy post-ERCP. This suggests strong benefits from sphincterotomy alone, however cholecystectomy would still be necessary to prevent cholecystitis, biliary colic, cholangitis or biliary pancreatitis.

Disclosure: Nothing to disclose

P0086 PREVALENCE AND RISK FACTORS OF CHOLELITHIASIS IN CROHN’S DISEASE

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Introduction: Cholelithiasis occurs in patients with Crohn’s disease more frequently than in a healthy population. The cause of this difference has not been satisfactorily explained, nor its risk factors.

Aims and Methods: The aim of our study was to determine the prevalence of cholelithiasis in CD patients, to compare prevalence with a control group and to analyze the risk factors of cholelithiasis. We performed a monocentric retrospective case-control study. The cohort consisted of all CD patients who underwent abdominal ultrasound from January 2007 to January 2018 at the IH Center of the 5th Department of Internal Medicine in Bratislava. The control group consisted of 505 patients, who underwent ultrasound at the same department because of dyspepsia and were age and gender matched. Medical records were reviewed and patients demographics, behavior, localisation, duration and number of flare of CD, number and type of bowel resections, number and length of total hospitalization, number of total parenteral nutrition treatments and presence of cholelithiasis and its characterization were noted. An univariate and a multivariate analysis were performed using logistic regression analysis (with cholelithiasis as the dependent variable). Prevalence and odds ratios were calculated with their 95% confidence intervals.

Results: The study cohort consisted of 238 CD patients and 238 controls. The prevalence of cholelithiasis in CD group was 12.6% and 9.2% in control group (RR 1.36, p=0.24). In the univariate analysis, we observed cholelithiasis association with multiple risk factors such as - age, age at CD diagnosis, inflammatory versus aggressive disease behaviour, duration of disease, abdominal resection, number of intestinal resections, length of ileal resection, number of corticosteroid treatments, hospitalizations and total parenteral nutrition treatments. The age (OR 1.077, 95% CI 1.043–1.112, p < 0.001) and the number of total parenteral nutrition treatments (OR 1.812, 95% CI 1.131–2.903, p = 0.013) were determined as independent risk factors for cholelithiasis in CD patients by multivariate analysis.

Conclusion: The prevalence of cholelithiasis in our CD patient population was significantly higher than in the control group. We identified the age of patient and the number of parenteral nutrients as the independent risk factors of cholelithiasis in CD patients.

Disclosure: Nothing to disclose
P0087 P8 DEFICIENCY LEAD TO ELEVATED PANCREATIC BETA CELL MASS BUT DOES NOT CONTRIBUTE TO INSULIN RESISTANCE IN MICE FED WITH HIGH FAT DIET

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Introduction: Nuclear Protein 1, Transcriptional Regulator gene (NUPR1, p8) was first described as an overexpressed gene in pancreatic carcinomas and encodes a ubiquitous nuclear and cytoplasmic stress protein. Analysis of insulin sensitivity and glucose tolerance in p8 haplodeficiency and p8-knockout mice revealed counterintuitive results. Thus, we analyzed glycemic control of p8 in mice fed with standard (SD) and high-fat diet (HFD).

Aims and Methods: p8+/− mice and wild type (p8+/+) littermates were used to study glucose homeostasis. We determined glucose (immunohistochemistry) and insulin levels (ELISA) from isolated pancreatic islets and analyzed beta cell mass. In addition, hyperinsulinemic- euglycemic glucose clamp technique, i.p. glucose tolerance test (ipGTT), i.p. insulin tolerance test (ipITT) and metabolic chamber analysis over 72 hours were performed in SD (4% fat) and HFD (55% fat) groups.

Results: p8+/− mice showed no differences in glucose content but higher levels of insulin in pancreatic islets upon glucose stimulation compared to wildtype littermates. p8 deficiency resulted in elevated beta cell mass but was not associated with increased insulin resistance in ipGTT in both SD and HFD groups. Glucose clamp tests also revealed no evidence of association of p8 deficiency with insulin resistance. Metabolic chamber analysis showed equal energy expenditure in p8+/− mice and wildtype animals.

Conclusion: Complete p8 depletion may contribute to glucose metabolism by means of stress-induced insulin production and beta cell mass. Nevertheless, p8 knockout showed no impact on insulin resistance in SD and HFD fed mice.

Disclosure: Nothing to disclose

P0088 HISTOLOGICAL ANALYSIS OF THE OBESTATIN/G-PROTEIN COUPLED RECEPTOR 39 (GPR39) SYSTEM IN HUMAN PANCREAS

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Introduction: Obestatin, a 23-amino acid peptide encoded by the ghrelin gene, and the GPR39 receptor were reported to be involved in the control of mitogenicity of gastric cancer cells. Our data strongly suggest the involvement of the obestatin/GPR39 system in the pathogenesis and/or clinical outcome of human gastric cancer in which in addition, GPR39 expression was shown to be closely related to proliferation and poor prognosis.

Conclusion: Disclosure: Nothing to disclose

P0089 OBESTATIN PROMOTES MIGRATION AND INVASION OF ACTIVATED HUMAN PANCREATIC STELLATE CELLS

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Introduction: There is evidence that the mature adult pancreas has the ability to regenerate, similar to the liver, although to a lesser extent. Studies in animal models confirmed the plasticity and regeneration of both exocrine and endocrine pancreatic cells. Pancreatic stellate cells (PSC) play a major role in pancreas regeneration after partial pancreatectomy. Obestatin, a peptide derived from preproghrelin, and its receptor GPR39 have been described in the endocrine pancreas. Recent studies showed that the expression of GPR39 in the stellate cells is increased in the area of ischemia.Receptor expression in rat pancreas undergoing ischemia injury is increased.

Conclusion: Disclosure: Based on the previous background, the main objective of the present study was to evaluate the regulatory function of the obestatin/GPR39 system in the human pancreatic stellate cells (RLT-PSC).

Disclosure: Nothing to disclose

P0090 THE RELATIONSHIP BETWEEN CHOLECYSTOKININ SECRETION, INSULIN RELEASE AND PANCREATIC DUCTAL ADENOCARCINOMA IN HUMAN SUBJECTS AFTER PARTIAL PANCREATICODUODENECTOMY

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Introduction: The uptake of 11C]-methionine ([11C]MET) is associated with pancreatic endocrine and exocrine activity such as insulinogenic index and pancreatic digestive enzyme release. However, studies that examine both, the impact of endocrine and exocrine function, on methionine uptake of the pancreas are rare. Cholecystokinin (CCK), a trigger of pancreas secretion is altered after operations that accelerate gastric emptying, such as gastroectomy. Similarly insulin release is modified due to elevated glucose plasma concentrations and via GLP-1. The purpose of this study was to shed light on the relationship between the secretion of CCK, insulin release and [11C]MET uptake in subjects having undergone partial pancreateicoduodenectomy (PD).

Disclosure: Nothing to disclose
Aims and Methods: 19 tumor-free survivors after PD (age mean ± SD: 61 ± 8.7 yr; 13 males) were given a mixed meal, and pancreatic CCK, insulin and glucose concentrations were measured before and at 10, 20, 30 and 60 minutes after ingestion. Simultaneously 800 MBq of [11C]MET were administered and the activity (maximum tissue standardized uptake values [SUVmax]) over the pancreas was measured using PET-CT at 15, 30 and 60 minutes after injection. Beta cell function was calculated from basal plasma glucose and insulin concentrations. Area under the curve [AUC] was calculated for insulin, CCK and SUVmax (methionine uptake).

Results: CCK AUC0-60 (R2 = 0.26, p = 0.05), beta cell function (R2 = 0.54, p < 0.01) and insulin AUC0-60 (R2 = 0.66, p < 0.01) correlated with the SUVmax AUC0-60. Multivariate analysis revealed CCK, basal beta cell function and post-prandial insulin (AUC0a) concentrations as significant independent predictors of [11C]methionine uptake (R2 = 0.64, p < 0.01, Table 1, Figure 1).

Table 1. Multiple linear regression on the dependent variable ‘methionine SUVmax AUC0-60′ in patients after PD (R2 = 0.84, p < 0.01).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Standard error</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>3.33</td>
<td>76.36</td>
<td>0.9658</td>
</tr>
<tr>
<td>Betas cell function</td>
<td>1.73</td>
<td>57.07</td>
<td>0.0094</td>
</tr>
<tr>
<td>Insulin AUC060 (mU/l x min)</td>
<td>0.07</td>
<td>0.02</td>
<td>0.0141</td>
</tr>
<tr>
<td>CCK AUC060 (pmol/l x min)</td>
<td>0.72</td>
<td>0.33</td>
<td>0.0457</td>
</tr>
</tbody>
</table>

Conclusion: The association between CCK secretion, beta cell function and post-prandial insulin release with pancreatic [11C]MET uptake might suggest the representation of digestive enzyme and insulin metabolism. Further studies are needed to evaluate the relative impact of exocrine and endocrine pancreatic function on the uptake of this tracer.

Disclosure: Nothing to disclose.

References

PO092 CLINICAL STUDY OF IMPROVEMENTS IN PANCREATIC BLOOD FLOW AS MEASURED BY PERFUSION TOMOGRAPHY IN PATIENTS WITH SEVERE ACUTE PANCREATITIS AND ADMINISTERED RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN

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Introduction: Pancreatic circulation failure due to disseminated intravascular coagulation (DIC) is a significant factor in determining the severity of pancreatitis. Pancreatic circulation failure affects walled-off necrosis (WON) caused by severe acute pancreatic necrosis. A study has shown that patients with severe acute pancreatitis (SAP) administered recombinant human soluble thrombomodulin (rTM) exhibit significant improvements in coagulation anomalies and inhibited sepsis development [1]. Peripheral blood perfusion imaging (PCT) in advanced imaging technique for evaluating blood circulation in SAP, can accurately diagnose the development of pancreatic necrosis in the early stages of SAP. PCT can also be used to predict the severity of acute pancreatitis [2].

Aims and Methods: This study applies PCT to investigate whether rTM improved pancreatic blood flow (PBF) in cases of SAP involving pancreatic necrosis.

We retrospectively analyzed 27 SAP patients with pancreatic necrosis treated from January 2015 to January 2018 at Osaka Saiseikai Nakatsu Hospital. All patient data was gathered from an electronic database. The 27 SAP patients were divided into two groups: SAP patients with DIC treated with rTM (380 U/kg for 30 minutes, once daily: the rhTM(DIC(-)) group) and patients without and did not get treated with rTM (DIC(+)) group, 13 patients. To determine a diagnosis of pancreatic necrosis, we measured PBF with PCT within 48 hours and set a criterion of 25% or greater reduction of PBF in a region of 1 cm² or more compared to normal pancreatic parenchyma. We assessed the extent of pancreatic necrosis based on the ratio of ischemic pancreatic PBF/nor mal pancreatic PBF. We calculated the PBF ratio, APACHE II SOFA, JPN prognostic factor (by the Japanese severity scoring system), and JAAM DIC scores within 48 hours of hospitalization and again on the seventh day of hospitalization (day 7).

Results: The background data for the subjects is as follows: mean age 62.6 years; male/female ratio: 18:9; cause: 11 alcohol, 5 gallstone, 6 idiopathic, 3 cases of EIRC, 2 other, and 1 fatality. In the Revised Atlanta Criteria, the rTM(DIC(-)) group was significantly severer: the rTM+(DIC(+)) group vs. DIC(-) group (7 severe; 6 moderate vs. 1 severe; 9 moderate). We found no differences in SOFA scores between the two groups as of the time of hospitalization (i.e., rTM+(DIC(+)) vs. DIC(-)): 3.8 ± 2.1 vs. 2.8 ± 2.4. However, we found significant differences with respect to the prognostic factor (3.5 ± 1.6 vs. 1.8 ± 1.3), mean APACHE II scores (12.5 ± 5.8 vs. 8.2 ± 4.1), and JAAM DIC scores (3.7 ± 1.5 vs. 1.9 ± 1.3) (p < 0.05). PBF ratios within 48 hours of hospitalization did not differ between the rTM+(DIC(+)) and DIC(-) groups: 0.560 ± 0.144 vs. 0.673 ± 0.241. The PBF ratio for rTM+(DIC(+)) group was significantly higher (0.760 ± 0.218) on day 7 (p < 0.01). The PBF ratio for the DIC(-) group without rTM treatment failed to improve (0.670 ± 0.119) on day 7. The PBF ratio for the rTM+(DIC(+)) group on day 7 was significantly higher than for the DIC(-) group (0.760 ± 0.218 vs. 0.670 ± 0.119) (p < 0.05). WON occurred in 12 cases (44.4%).

Conclusion: Since pancreatic ischemia is defined as a reduction in PBF of 25% or more, we considered ischemia in many of the patients meeting this criteria was significant, although the syndrome of the rTM+(DIC(+)) group had significantly worse, improvements in the PBF ratio were significantly better. Since rTM improved coagulation anomalies, we considered it may improve PBF and that rTM offers a new therapeutic option in treating pancreatic ischemia.

Disclosure: Nothing to disclose.

References

Aim of the Study: The purpose of the study is to evaluate the efficacy of an innovative combination of medications, compared to the conventional treatment, in the management of acute pancreatitis.

Methods: A randomized controlled trial was conducted in patients diagnosed with acute pancreatitis at the Department of Gastroenterology, University of Debrecen, Hungary.

Results: The results showed a significant decrease in the duration of hospitalization and the severity of the disease in the group treated with the innovative combination, compared to the control group.

Conclusion: The innovative combination of medications offers a promising approach in the treatment of acute pancreatitis.

Disclosure: Nothing to disclose.

References
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Introduction: Both alcohol consumption and cigarette smoking have been recognized as risk factors on the pancreas. These adiposity effects are very close together, so careful investigations are crucially needed to understand their independent/synergic effects on the pancreas.

Aims and Methods: To examine the clinical effects of alcohol consumption and/or smoking in patients with acute pancreatitis (AP).

A total of 1435 adult patient were enrolled from 2012 to 2017 with the diagnosis of AP in 28 healthcare centres by the Hungarian Pancreatic Study Group. Specific questionnaires for AP including information on cigarette smoking and alcohol consumption were used, whereas detailed clinical data such as the results of laboratory parameters and imaging, the course and the outcome of AP episodes were collected.

Results: 692 (48.32%) of the patients were non-drinkers and non-smokers (ND-N), 615 of the patients were drinkers (D) (43.0%), 279 (45.4%) of the drinkers did not smoke (D-NS), whereas 336 (54.6%) of them were smokers (D-S) as well. The age of onset was 61.1y in the ND-NS group, 55.1y in the D-NS and 46.3y in the D-S group. The female/male ratio was 0.6 in the ND-NS group, 3.15 in the D-NS and 1.4 in the D-S group. Smoking alone had an effect on the BMI (ND-NS: 28.2, D-NS: 28.2), but smoking in addition to drinking decreased it (D-S: 25.7). Concerning the parameters on admission the ND-NS, D-NS and D-S groups were as follows: amylase (U/L): 1310 ± 1351, 1609 ± 1194, 737 ± 1237; lipase (U/L): 3233 ± 4911, 2617 ± 3350, 2035 ± 6617; CRP (mg/L): 53 ± 77, 51 ± 72, 63 ± 80; WBC (G/L): 13 ± 5.5, 13.3 ± 6.4, 13.6 ± 5.7. Smoking had synergic effect with drinking on local complications (ND-NS: 34.4%, D-NS: 37.5%, D-S: 44.1%) such as necrosis (8.8%, 11.0%, 15.6%), development of pseudocyst (0.9%, 9.2%, 13.3%) and fluid collection (28.3%, 31.3%, 35.5%). The percentage of moderate AP copied the same pattern (24.9%, 26.8% and 31.9%). We could see no difference in mortality and the rate of severe AP. Deaths were higher among the other 2 groups. Of the abdominal adiposity phenotypes we also elevate the risk for acute recurrent pancreatitis (ARP). 18.9% of the patients had ARP in the ND-NS, 23.5% in the D-NS, whereas 31.9% in the D-S groups.

Conclusion: Drinking and smoking together result in the onset of pancreatitis 15 years earlier. It elevates the risk for recurrence of the disease. Drinking and smoking synergize with each other and increase the rate of local complications.

Disclosure: Nothing to disclose

P0094 IMPACT OF VISCERAL ADIPOSITY ON SEVERITY OF ACUTE PANCREATITIS

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Introduction: Acute pancreatitis (AP) is a sudden inflammation of the pancreas. The early evaluation and accurate prediction of AP severity is vital, as severe AP can result in multiple organ failure (POF) and mortality.

Aims and Methods: This study is to explore the predictive significance of visceral adiposity (VFV) and visceral adiposity index (VAI) on AP severity, which may go together, therefore careful investigations are crucially needed to understand the differences in abdominal adiposity and ectopic fat phenotypes and pancreatitis-related factors (aetiology, severity) in individuals after AP have never been studied.

Aims and Methods: The aim is to investigate phenotypic differences in distribution of abdominal adipose tissue and ectopic fat between individuals after AP (with and without diabetes) using magnetic resonance imaging (MRI). The secondary aim was to determine pancreatitis-related factors associated with abdominal adiposity and ectopic fat phenotypes. A total of 156 patients had been diagnosed prospectively with AP were included in this study. They were recruited after an average time of 28 months after last episode of AP.

Results: Of the abdominal adiposity phenotypes, VFV was significantly higher in the diabetes (2715.3 ± 1077.6 cm3) as compared with no diabetes (1982.3 ± 1092.4 cm3) and healthy (1162.6 ± 740.4 cm3) groups (p < 0.001). Moreover, V/S ratio was significantly higher in the diabetes (0.97 ± 0.27) as compared with no diabetes (0.68 ± 0.42) and healthy (0.52 ± 0.34) groups (p < 0.001). Of the ectopic fat phenotypes, PF% was significantly higher in the diabetes (10.2 ± 1.2%) as compared with no diabetes (9.2 ± 1.7 %) and healthy (7.9 ± 1.9 %) groups (p < 0.001). Other studied phenotypes did not differ significantly between the groups. C-reactive protein levels during hospitalization for AP were associated with significantly increased VFV in unadjusted (β = 3.32; 95% CI, 1.68, 4.96; p < 0.001) and adjusted (β = 2.71; 95% CI, 1.24, 4.19; p < 0.001) models. Biliary aetiology of AP was associated with a significantly increased PF% in adjusted model (β = 0.67; 95% CI, 0.01, 1.33; p = 0.047).

Conclusion: The findings of this study show, for the first time, that individuals after an episode of AP have abnormal adiposity phenotypes, particularly increased visceral fat and pancreatic fat depots. Further, these depots are significantly associated with the presence of diabetes after AP. Levels of C-reactive protein during hospitalisation for AP are significantly associated with VFV whereas biliary aetiology of AP is significantly associated with PF%.

Disclosure: Nothing to disclose

Reference

P0096 DIETARY FAT PATTERNS AND OUTCOMES IN ACUTE PANCREATITIS

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Introduction: Lipolysis of adipocyte triglycerides by pancreatic lipases results in the release of free Fatty Acids (FA) seem to be an important factor in the release of low-density lipoprotein (LDL-C) and triglycerides (TG) on the development of atherosclerosis. We aimed to investigate if differences in dietary fat patterns are associated to different composition of fat storages, and thus to a different frequency of complications and death in AP.

Aims and Methods: Our aim was to investigate whether different patterns of fat intake are associated to worse outcomes in AP. We used data from the Atlantis project, a 23-center prospective nation-wide Spanish database aiming to investigate the determinants of morbidity and mortality in acute pancreatitis. Dietary fat intake (fat intake, proportion of fats, SFAs, mono and polyunsaturated fats) from different regions of Spain were retrieved from the ANIBES (Anthropometry, Intake and Energy Balance in Spain) cross-sectional study using a nationally representative sample of the Spanish population. Outcome variables included: necrotizing pancreatitis (pancreatic gangrene, pancreatic fat necrosis), persistent organ failure (POF) and mortality. Variables addressing dietary fat intake were divided according to their median value into low and high intake. Univariate (Chi-square) and multivariate (binary logistic regression) analysis were performed. The variables included on the multivariate analysis model were: Charlson comorbidity index ≥ 3 (includes also age), alcohol etiology, gender, obesity and recurrent AP; adjusted Odds Ratio (aOR) were calculated.

Results: 1,653 episodes of AP were analyzed. Etiology was biliary in 28.3%, 54% of the patients were male, AP was associated to necrosis in 17%, to persistent organ failure (POF) in 7% and mortality was 4%. On univariate and multivariate

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analysis, a high SFA intake was independently associated to a lower risk of necrosis [15 vs. 19%, aOR 0.746 (0.570–0.978), p = 0.034], a lower risk of POF [5 vs. 9%, aOR 0.550 (0.367–0.822), p = 0.004] and mortality [3 vs. 6%, aOR 0.548 (0.329–0.914), p = 0.021].

Conclusion: Our study suggests that a high saturated fatty acid intake is associated to improved outcomes in acute pancreatitis, resulting in a 50% lower risk of persistent organ failure and mortality.

Disclosure: Nothing to disclose

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**P0097 BODY-MASS INDEX CORRELATES WITH SEVERITY AND MORTALITY IN ACUTE Pancreatitis - A META-ANALYSIS**

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Introduction: During the past decades, obesity rates have increased sharply. As there is a growing number of cases in which acute pancreatitis (AP) is accompanied by obesity, we found it clinically relevant to investigate how body-mass index (BMI) affects the outcome of the disease.

Aims and Methods: Our aim was to quantify the association between subgroups of BMI and the severity and mortality of AP. A meta-analysis was performed using the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols. 3 databases (PubMed, EMBASE and Cochrane Library) were searched for articles containing data on BMI, disease severity and mortality rate of AP. English-language studies from inclusion to 19 June 2017 were checked against our predetermined eligibility criteria. The included articles reported all AP cases with no restriction on the etiology of the disease. In severity analyses we only involved studies that classified AP cases according to the Atlanta Criteria. Odds ratios (OR) and mean differences (MD) were pooled using the random effects model by the DerSimonian-Laird estimation and displayed on forest plots. The meta-analysis was registered in PROSPERO under number: CRD42017077890.

Results: Altogether 19 articles were included in our meta-analysis, containing data on 9,997 patients. Severity: The subgroup analysis shows a direct association between AP severity and BMI. BMI > 25 compared to normal BMI and BMI 25–30 subgroups. A BMI > 30 results in a 3 times higher risk of persistent organ failure and mortality compared to the non-severe group (MD 5 vs. 9%, aOR 0.548 (0.329–0.914), p = 0.021).

Adipose tissue specific adipokines, omentin and vaspin, hold promise for future clinical investigation of tissue-specific IR.

Disclosure: Nothing to disclose

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**P0098 GENERAL AND ADIPOSE TISSUE-SPECIFIC INSULIN RESISTANCE AFTER AN EPISODE OF ACUTE Pancreatitis**

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Introduction: Emerging evidence indicates that individuals after an episode of acute pancreatitis (AP) are at an increased risk of developing metabolic derangements, in particular new-onset prediabetes or diabetes after AP.1 The link between general obesity and insulin resistance (IR) was established decades ago, however the impact of body fat distribution on IR has gained attention only recently and is not completely understood. In the setting of AP, the association between abdominal obesity and IR, and a comprehensive assessment of various IR indices in post-pancreatitis setting, is lacking.

Aims and Methods: The aim of this study was to investigate associations between abdominal obesity and IR (general and adipose tissue-specific) in patients with AP independent of the effect of covariates including diabetes mellitus, and to determine the relative accuracy of several indices of IR in characterising abdominal obesity. Patients were eligible for this cross-sectional study if they were previously admitted with a primary diagnosis of AP, established prospectively. Fasting venous bloods were collected to measure glucose, insulin, free fatty acids, glycerol, adiponectin (AD), omentin (OM), and vaspin(VAS). The IR indices - homeostasis model assessment of IR (HOMA-IR), adipose tissue IR (Adipo-IR), insulin*glycerol (IG) index, HOMA-AD, HOMA-OM, and HOMA-VAS were calculated. Abdominal obesity was defined according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines.2 Modified Poisson regression was conducted, with statistical model adjusting for patient-, metabolic-, and pancreatitis-related risk factors. Areas under the receiver operating characteristic (ROC) curves were calculated to determine the relative accuracy of the studied indices followed by determination of agreement between the two new indices (HOMA-OM, HOMA-VAS) and HOMA-IR.

Results: Of the 92 individuals recruited, 41 had abdominal obesity. The median (interquartile range) time since AP was 24 (7-46.5) months. Insulin resistance indices HOMA-IR, IG index, HOMA-OM, and HOMA-VAS were significantly associated with abdominal obesity, both in unadjusted and adjusted models (Table 1). Area under ROC curves for HOMA-IR was 0.698 (95% CI, 0.591, 0.791; p < 0.001), for IG index was 0.695 (95% CI, 0.585, 0.791; p < 0.001), for HOMA-OM was 0.756 (95% CI, 0.648, 0.845; p < 0.001), and for HOMA-VAS was 0.735 (95% CI, 0.625, 0.827; p < 0.001). There was a good agreement between observed HOMA-IR values and values obtained from HOMA-OM (p = 0.733) and HOMA-VAS (p = 0.595).

Conclusion: Individuals with abdominal obesity after AP have a significantly higher IR, independent of diabetes and other covariates. Visceral adipose tissue specific adipokines, omentin and vaspin, hold promise for future clinical investigation of tissue-specific IR.

References

Disclosure: Nothing to disclose

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**Abstract No: P0098**

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inhibit Hpa activity both
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Introduction: pancreatic (AP) is one of the most common diseases in gastroenterology. However, neither the etiology nor the pathophysiology of the disease is fully understood and no specific or effective treatment has been developed. We previously showed that heparase (Hpsa) appears to play an important role in the pathogenesis of AP and that Hpsa inhibitors significantly reduced the severity of the AP in an animal model. Aspirin has also been demonstrated to inhibit Hpa activity both in vitro and in vivo. We hypothesize that combination of Aspirin and aspirin can ameliorate AP more efficiently than each drug alone.

Aims and Methods: The current study examines whether combination of Aspirin with PG545 or Roneparstat (SST0001), 2 inhibitors of Hpsa, exerts superior pancreateo-protective effect in cerulein-induced AP in mice, vs each compound alone.

Heparase-overexpressing transgenic mice (Hpsa-TG) and wild-type (WT) BALB/c mice (n = 7–8) were intraperitoneally injected with either cerulein (50 mg/kg; 5 times, at 1 hour apart) or vehicle, with or without either PG545 (0.4 mg/kg, kind gift of Dr. Edward Hammond, Zucero Therapeutics, Brisbane, Queensland, Australia), Roneparstat (2 mg/mouse, kind gift of Dr. Alessandro Noseda, Leadiant Biosciences S.A., Mendrisio, Switzerland), Aspirin (250 mg/kg, kind gift of Dr. Harald Noseda, Leadiant Biosciences S.A.). The animals were sacrificed 24 hours following the induction of pancreateitis. The severity of AP and architectural structure changes were evaluated by serum pancreatic enzyme (amylase and lipase) levels, inflammatory markers, histological examination (determined by organ-specific characteristics). The costs of care were 25% less in group A.

Disclosure: Nothing to disclose

P0101 CENTRALIZED CARE OF ACUTE PANCREATITIS SIGNIFICANTLY IMPROVES ITS OUTCOMES

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Conclusion: Administration of either Aspirin or Hpa inhibitor exerts protective effects against Cerulein-induced AP. Interestingly, combination of Aspirin and Hpa inhibitors completely abolished AP, providing a rational basis for the treatment of this clinical setting.

Disclosure: Nothing to disclose

P0099 COMBINATION OF HEPARASE INHIBITORS AND ASPIRIN DYNAMICALLY AMELIORATES ACUTE PANCREATITIS IN AN ANIMAL MODEL

Aims and Methods: The current study examines whether combination of Aspirin with PG545 or Roneparstat (SST0001), 2 inhibitors of Hpsa, exerts superior pancreateo-protective effect in cerulein-induced AP in mice, vs each compound alone. Results: Results: 195 patients in the specialized center (group A) and 160 patients in the general medical hospital (group B). There was no difference in the mean age (57.02, ±71.6 vs. 57.31, ±16.50, p = 0.872) and sex ratio (56% males vs. 57% males, p = 0.837) between group A and B; allowing comparison without selection bias. Gender differences (42.0% vs. 51.7%, p = 0.13) were also observed in group A and that Hpsa inhibitors significantly reduced the severity of the AP in an animal model. Aspirin has also been demonstrated to inhibit Hpa activity both in vitro and in vivo. We hypothesize that combination of Aspirin and aspirin can ameliorate AP more efficiently than each drug alone.

Aims and Methods: The current study examines whether combination of Aspirin with PG545 or Roneparstat (SST0001), 2 inhibitors of Hpsa, exerts superior pancreateo-protective effect in cerulein-induced AP in mice, vs each compound alone.

Heparase-overexpressing transgenic mice (Hpsa-TG) and wild-type (WT) BALB/c mice (n = 7–8) were intraperitoneally injected with either cerulein (50 mg/kg; 5 times, at 1 hour apart) or vehicle, with or without either PG545 (0.4 mg/kg, kind gift of Dr. Edward Hammond, Zucero Therapeutics, Brisbane, Queensland, Australia), Roneparstat (2 mg/mouse, kind gift of Dr. Alessandro Noseda, Leadiant Biosciences S.A., Mendrisio, Switzerland), Aspirin (250 mg/kg, kind gift of Dr. Harald Noseda, Leadiant Biosciences S.A.). The animals were sacrificed 24 hours following the induction of pancreateitis. The severity of AP and architectural structure changes were evaluated by serum pancreatic enzyme (amylase and lipase) levels, inflammatory markers, histological examination (determined by organ-specific characteristics). The costs of care were 25% less in group A.

Disclosure: Nothing to disclose

P0013 DIAGNOSIS, TREATMENT AND LONG-TERM OUTCOMES OF AUTOIMMUNE PANCREATITIS


Conclusion: Our data suggests that treatment of AP in specialized centers improves its mortality, the quality of care, the length of hospitalization and reduces the costs of care.

Disclosure: Nothing to disclose

P0102 GENESTIN INHIBITS THE ACTIVATION OF PANCREATIC STELLATE CELLS BY PI3K/akt/mTOR SIGNALING PATHWAY

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Conclusion: Administration of either Aspirin or Hpa inhibitor exerts protective effects against Cerulein-induced AP. Interestingly, combination of Aspirin and Hpa inhibitors completely abolished AP, providing a rational basis for the treatment of this clinical setting.

Disclosure: Nothing to disclose
Aims and Methods: We aimed to determine clinical presentation together with biochemical features of AIP in Japan. This was a single-center, retrospective, cohort study of patients with histologically confirmed or highly probable diagnosis of AIP according to ICDC criteria. Clinical/radiological characteristics, type of treatment and its outcomes were collected and was used for statistical analysis.

Results: 71 patients with AIP (87.3% with type 1), were evaluated at Karolinska University Hospital between 2004 and 2018; 49.2% males, mean age 49.2 years (range 44.7–53.8). Among them, 28.1% were histologically confirmed, 35.2% presented with jaundice, 22.5% with acute pancreatitis, 19.4% had non-specific symptoms such as weight loss or abdominal pain, 40.8% displayed other organ involvement (OOL). Radiologically, 40.5% displayed a focal mass, 36.2% a focal pancreatic enlargement, 27.5% a sausage-like pattern, 27.5% signs of acute pancreatitis, 10.1% had multiple pancreaticat. In total 58 patients (81.6%) underwent treatment comprising different medications: 46 (79%) cortisone, 7 (12.0%) atazanavir, 5 (8.6%) other immunosuppressives drugs. 26 (36.6%) underwent biliary stenting and 12 (16.9%) surgery due to suspicion for pancreatic malignancy. All (100%) of patients treated with cortisone, displayed a clinical response. After a mean follow-up of 46.7 months, 97.1% of patients were alive, 70% displayed a radiological complete response, 89.6% were treatment-free. None developed pancreas cancer but 1 patient (1.4%) developed mucinous cystic neoplasm (MCN) with high-grade dysplasia and was therefore successfully operated. 59.3% of patients developed pancreatic exocrine insufficiency (PEI) of which 76.4% had a severe form (fetal elastase-1 < 0.01 μg/g) and 23.6% of patients developed diabetes mellitus (pancreatic endocrine insufficiency) of which 73.3% requiring insulin.

Conclusion: AIP is a challenging disease for diagnosis and treatment. Cortisone treatment is generally successful and provides clinical remission in the large majority of patients. In the further course of the disease, the number of patients develop PEI (up to 60% of pts) and diabetes (up a quarter of pts). Only a quarter of patients exhibit the characteristic “sausage-like” pancreas, approximately 40% had a focus mass that can be misdiagnosed as pancreatic malignancy.

Disclosure: Nothing to disclose

P0104 DEFICIENCY OF FAT-SOLUBLE VITAMINS, MINERALS AND TRACE ELEMENTS IN PATIENTS WITH CHRONIC PANCREATITIS OF DIFFERENT ETIOLOGY

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Introduction: Malnutrition with deficiencies of fat-soluble vitamins and trace elements are well-known consequences of maldigestion and poor absorption of nutrients, and have been frequently identified in patients with pancreatic exocrine insufficiency (PEI). The prevalence of abnormal laboratory nutritional markers in chronic pancreatitis has been investigated in several studies, but most of them were restricted to patients with alcoholic chronic pancreatitis (CP) and had limitations due to the small number of patients. We are presenting results of the largest study so far comparing markers of malnutrition in relation to different etiological groups of CP.

Aims and Methods: We performed a retrospective analysis of medical records of patients with CP. Etiology of CP was determined according to M-ANNHEIM classification. The following demographic, clinical and demographic parameters were analyzed: age, gender, smoking (pack years), consumption of alcohol (units per day/years), fecal elastase-1 (FE1), albumin, calcium, magnesium, iron, triglyceride, cholesterol, hemoglobin, vitamin A, vitamin E, vitamin D and zinc.

Results: Altogether, 226 patients were included in the analysis: 131 (58.0%) male and 95 (42.0%) female, mean age 51.8 ± 17.9 years (range 18–89). The different etiologies of CP comprised: autoimmune (n = 69; 30.5%), alcohol (n = 65; 28.8%), efferent duct factors (n = 20; 8.8%) and idiopathic (n = 27; 12.0%). FEI was normal (FEI > 200mg/g) in 83 (41.7%) patients. Mild to moderate PEI (FEI 100–200mg/g) was found in 22 (11.1%) of patients and severe PEI (FEI < 100mg/g) in 94 (42.7%) of patients. Prevalence of deficiencies in serum nutritional panel was as follows: vitamin D 51.3%, albumin 34.2%, zinc 26.0%, hemoglobin 15.8%, cholesterol 14.1%, cobalamin 11.0%, iron 10.5%, vitamin A 8.3%, vitamin E 6.9%, magnesium 14.7%, folate 4.4%, 1,25(OH)2D3 11.5% and calcium 0%, with no statistical significant differences between nutritional deficiencies and different etiologies of CP. Factors associated with low zinc values were age > 70 years (p = 0.003) and current smoking status. (p = 0.02). Factors associated with low vitamin D levels were age > 60 years (p = 0.03), male gender (p = 0.007), insulin treated diabetes mellitus (p = 0.05) and severe PEI (p = 0.05). In patients who bone mineral density was performed, 21 (24.1%) of patients had osteopenia and 9 (10.3%) osteoporosis.

Conclusion: A large number of CP patients exhibits signs of malnutrition with vitamin deficiencies. Deficiencies of fat-soluble vitamins, minerals and trace elements appear not to be related to CP etiology. Noteworthy, more than a third of patients had a focus mass that can be misdiagnosed as pancreatic malignancy.

Disclosure: Nothing to disclose

P0105 PREDICTION OF PANCREATIC ATROPHY AFTER STEROID THERAPY USING EQUILIBRIUM CONTRAST CT IMAGING IN AUTOIMMUNE PANCREATITIS

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Introduction: Previous reports showed pancreatic atrophy 6 months after the initiation of steroid therapy with diabetes control worsening and incidence of new onset of diabetes in patients with autoimmune pancreatitis (AIP). However, predictor for pancreatic atrophy after steroid therapy at the diagnosis of AIP remains unknown.

Aims and Methods: We aimed to evaluate the role of equilibrium computed tomographic (CT) imaging for the prediction of pancreatic atrophy 6 months after steroid therapy. 33 steroid treated AIP patients, who underwent CE-CT examinations before and after steroid therapy, were included in this study during December 2005 to October 2015. CT attenuation (Hounsfield units [HU]) values in noncontrast (NC) and equilibrium phase (EP) images were measured by placing 3 regions of interest (ROIs) from the anterior to the posterior part of the organ. The degree of difference of each HU value with the degree of atrophy was evaluated.

Results: Pancreatic atrophy was observed in 11 patients and not in 22 patients after the steroid therapy. Pancreatic atrophy was not associated with the thickness of pancreatic body on CE-CT before steroid therapy, other organ involvement, pattern of pancreas swelling (diffuse/focal) and serum IgG4 levels. The HU values in NC and EP subtracted HU values in AIP with atrophy were significantly higher than those without atrophy (113.2 ± 16.1 vs. 100.0 ± 11.8, p = 0.01, 70.7 ± 18.0 vs. 57.8 ± 13.9, p = 0.03). Thickness of pancreatic body after steroid therapy was also associated with HU values in EP and subtracted HU values (less than 10–15mm: median 13.5 ± 10mm vs. 70.6 ± 9.2, 92.7 ± 10.9, p = 0.002, 70.7 ± 18.0 vs 63.6 ± 11.7: 50.4 ± 13.5, p = 0.01).

Conclusion: Equilibrium contrast CT imaging at the diagnosis of AIP would be a potential predictor for pancreatic atrophy after steroid therapy. The use of other therapies, such as immune-modulating agents, might be recommended for those patients.

Disclosure: Nothing to disclose

P0106 INCIDENTAL FINDINGS OF FATTY PANCREAS ON COMPUTED TOMOGRAPHY ASSOCIATED WITH IMPAIRED BONE METABOLISM

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Introduction: Fatty pancreas (FP) is an increasingly recognised entity associated with obesity and the metabolic syndrome. It correlates with non-alcoholic fatty liver disease (NAFLD) and progression to cirrhosis. It is hypothesised that a similar process exists resulting in chronic pancreatitis, fibrosis and pancreatic exocrine insufficiency (PEI) with associated malnutrition-related complications; such as vitamin D deficiency and impaired bone metabolism.1,3 FP as a cause of PEI has not been thoroughly assessed, with published studies largely comprising small case reports.4–5

Aims and Methods: This study assessed the relationship between FP and PEI, by examining the correlation with impaired bone metabolism. Cases were identified by a search of computed tomography (CT) reports from January 1st, 2010 to June 30th, 2017 at Melbourne Health, using keywords of FP and its synonyms; including pancreatic lipomatosis, fatty replacement or infiltration of the pancreas, lipomatous pseudo-hypertrophy of the pancreas, and pancreatic steatosis.6 Controls were identified using keywords of normal pancreas. All images were reviewed by a radiologist to confirm CT report diagnoses. Retrospective clinical data was obtained from existing medical records and pathology. Data of interest included features of impaired bone metabolism, namely osteopenia and osteoporosis. Patients without available medical records were excluded. Cases and controls were assessed for baseline characteristics, including gender and age. Outcomes of impaired bone metabolism were assessed as categorical variables and statistical analysis undertaken on identified trends. Chi-square test for independence was used with a statistical significance level of p < 0.05; Fisher's exact test was used for small sample sizes with a statistical significance level of p<0.05. Sub-analyses were completed to remove confounding variables of age and gender.
Results: 133 cases and 117 controls were identified. There were no statistically significant differences in gender distribution or age between the cohorts. Both groups comprised 59% males. The mean age of cases and controls was seventy-seven years and sixty-seven years respectively [case range 43–99 years; control range 42–94 years; \( p = 0.15 \)]. There was a statistically significant difference in impaired bone mineral density (BMD) between cases and controls in 41.4% and 20.5% respectively [OR 2.73, RR 2.02]. This difference was independent of gender [males OR 3.53, RR 2.65; females OR 2.28, RR 1.63] and age greater than sixty-five years [total OR 2.83, RR 2.02; males OR 3.44, RR 2.53; women greater than 65 years demonstrating a positive trend without statistical significance [OR 2.19, RR 1.56].

Conclusion: The study showed a statistically significant relationship between incidental FP and impaired bone metabolism with a RR of 2.02. This was independent of gender and increased age, except with women greater than 65 years of age showing a positive trend but no statistical significance. This suggests that FP is not a benign finding and is associated with PEI. Recognising these patients is of clinical importance, as early detection and treatment of PEI may improve the associated morbidity and mortality.

Disclosure: Nothing to disclose.

References:

P0107 METABOLIC BONE DISEASE IN CHRONIC PANCREATITIS; A SINGLE-CENTRE EXPERIENCE

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Introduction: Chronic pancreatitis is associated with metabolic bone disease which increases the risk of fracture. The National Institute of Clinical Excellence (NICE) guidance recommends that all patients aged 50 or over should be considered for DEXA scanning at risk (1). Previous data has shown under-utilisation of DEXA scanning in this population despite increased risk of osteoporotic fracture. The primary aim of this study was to assess compliance with metabolic bone assessment in patients with chronic pancreatitis, assess the prevalence of abnormal DEXA scans and the impact of this assessment on appropriate management.

Aims and Methods: Retrospective analysis of outpatient coding for “chronic pancreatitis” during 2017 from Freeman Hospital. DEXA scan results were retrieved for chronic pancreatitis patients from the radiology department. Aetiology recorded as alcohol (n = 52), idiopathic (n = 25), autoimmune (n = 4), hereditary (n = 3), anatomical (n = 1) and biliary (n = 102). Patients were also assessed for the prescription of bone protection. Those not requiring pancreatin replacement therapy (PERT) (n = 201) were included with aetiology recorded as alcohol (n = 52).

Conclusion: The study found that the impact of DEXA scanning on prescription of bone protection was also assessed. The impact of DEXA scanning on prescription of pancreatic enzyme replacement therapy (PERT) and osteoporosis treatment was investigated in patients with chronic pancreatitis, assessing the prevalence of abnormal DEXA scans and the impact of this assessment on appropriate management. The study found that DEXA scanning was underutilised in chronic pancreatitis patients compared to the general population. Abnormal DEXA scans were significantly associated with appropriate prescription of bone protection.

Disclosure: Nothing to disclose.

References:

P0108 DIFFERENCES IN IMAGING STUDY BETWEEN LOCALIZED AUTOIMMUNE PANCREATITIS AND PANCREATIC CANCER: A MATCHED CASE-CONTROL STUDY

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Introduction: Although the differential diagnosis between autoimmune pancreatitis (AIP) and pancreatic cancer (PC) is important in clinical settings, it is difficult to distinguish PC and localized type AIP which mimics PC in clinical presentation. However, the difference in imaging study between them has not been fully discussed.

Aims and Methods: The aim of this study was to compare the imaging findings between localized AIP and PC. 81 patients were diagnosed as AIP by International Consensus Diagnostic Criteria (ICDC) from April 2007 to October 2017, and 22 of them who showed the focal enlargement in pancreatic imaging were analyzed retrospectively (Group AIP; definitive 18, probable 4). During the same period, 191 patients were diagnosed as PC after surgical resection, and 44 of them were selected as a control (Group PC) in this study. To minimize the selection bias, the patients in Group PC was extracted by 1:2 ratio optimal matching, which was adjusted for age, gender, mass location, tumor size using propensity score. Measured outcomes were the findings of contrast enhanced CT, MRCP, and EUS. The statistical evaluations were conducted using Mantel-Haenszel test.

Results: Median ages of Group AIP and PC were 69 (range, 49–80) and 71 (range, 49–82) years old, respectively. The male to female ratios of them were 57:28 and 26:18. The mass location and the patients in Group AIP was pancreatic head in 11 and body/tail in 11 while that of the patients in Group PC was pancreatic head in 22 and body/tail in 22. Median tumor sizes of them were 21 (range, 5–40) and 23 (range, 10–23) mm. On CT imaging, the rates of the patients with high attenuation lesion in equilibrium phase or apparent capsule like rim were not different between Group AIP and PC (95% vs. 98%; 95% vs. 2%). However, a high attenuation lesion as compared to normal pancreatic parenchyma in equilibrium phase was observed more in the patients of Group PC (27% vs. 55%, \( p < 0.007 \)). More than half of main pancreatic duct (MPD) dilation was also noticed more in the patients in Group PC (27% vs. 64%, \( p = 0.008 \)). MRCP was carried out to 19 patients of Group AIP and matched 30 patients of Group PC. Among them, MRCP stricture at the lesion was observed in 84% of Group AIP and 80% of Group PC. However, MRCP stricture apart from the lesion was also included in 53% of Group AIP and 7% of Group PC, which showed a significant difference between them. As for EUS, the significant differences were not present in the findings regarding the boundary or echogenicity of the lesion. Moreover, the presence of hyperchoic foci inside the lesion was observed more in the patients of Group AIP (91% vs. 7%, \( p < 0.007 \)).

Conclusion: While a high attenuation tumor in equilibrium phase or more than 4mm of MPD dilation on CT were observed more frequently in PC, specific findings of MRCP was the MRCP stricture apart from the lesion on MRCP and presence of hyperchoic foci inside the lesion on EUS.

Disclosure: Nothing to disclose.
is to understand the modifying effect of the number of acute episodes which contribute to CP. The Hungarian Pancreatic Study group has built up a prospective register of subjects with AP. In the last 6 years, precise clinical data were collected from 1435 patients. In this study, data on the number of episodes from 1315 patients with high data accuracy were analyzed.

**Results:** In our cohort, 983 (74.75%), 270 (20.53%), 62 (4.72%) patients had a single episode of AP, ARP, and CP, respectively. In the ARP group, 173 patients (64.07%) had 2 episodes, 43 (15.93%) had 3 episodes, 24 (8.89%) had 4 episodes, and 30 (11.11%) had 5 or more episodes. 13 biomarkers were significantly different between AP, ARP, and CP. The significant difference between AP and CP disappeared after the second episode of AP concerning 8 biomarkers (gender, age, biliary etiology, alcohol consumption, pseudocyst development, gammaGT, amylase, and red blood cell count), as did after the third episode concerning 3 biomarkers (gender, body mass index, ASAT) as did after the fourth and fifth episodes concerning 2 biomarkers (ALAT and smoking). As an average, the significant differences between AP and CP disappeared from 2.63 attacks. The average number of acute episodes of patients with pre-existing morphological alterations in the pancreas is to understand the modifying effect of the number of acute episodes which contribute to CP. The Hungarian Pancreatic Study group has built up a prospective register of subjects with AP. In the last 6 years, precise clinical data were collected from 1435 patients. In this study, data on the number of episodes from 1315 patients with high data accuracy were analyzed.

**Conclusion:** A definition of early CP may be 3 or more previous attacks of AP without chronic morphological alterations in the pancreas.

**Disclosure:** Nothing to disclose.
Introduction: Pancreatic ductal adenocarcinoma (PDAC) is one of the most frequent gastrointestinal cancers and the fourth leading cause of cancer-related death. Despite several new developed anti-cancer drugs, the survival rates in advanced stages remain disappointing. Thus, innovative therapeutic approaches are urgently needed. On molecular levels, oxidative stress (ROS) is important for the development and progression of the disease. There was, highly reactive compound methylglyoxal (MGO) is an important source for ROS. MGO is a by-product of glycolysis and mainly detoxified by Glyoxalase-I (Glo-I). Overexpression of Glo-I has been shown in different tumours and linked to multi drug resistance in cancer therapy. Until now, the importance of Glo-I in PDAC has not been elucidated. Thus, we analysed the role of Glo-I for proliferation, migration and colony formation in PDAC.

Aims and Methods: Expression of Glo-I was determined in 7 PDAC cell lines (BxPC3, Capan-1, Capan-2, CFPPAC, HS776T, MiaPaca2, Panc-1) via immunocytochemistry (DAB-staining) by means of Cytospin centrifugation. Analysis of cell proliferation (Wst-assay), migration (scratch assay) and colony formation (clonogenic assay) was performed in all cell lines and correlated to Glo-I expression.

Results: HS776T and MiaPaca2 cells showed highest expression of Glo-I. Capan-2 and CFPPAC revealed low Glo-I staining intensity whereas BxPC3, CFPAC and HS776T exhibited average Glo-I expression. Interestingly, HS776T and MiaPaca2 also showed highest rates of proliferation and colony formation but not migration. In contrast, Capan-2 and CFPPAC revealed minor proliferation and colony formation but only CFACP indicated high cell migration. Proliferation, migration and colony formation of BxPC3, Capan-1 and Panc-1 was at average levels.

Conclusion: Glo-I is expressed in all examined PDAC cell lines. High expression of Glo-I was positively correlated with proliferation and colony formation but not migration. Ongoing studies analyses the effects of Glo-I knockdown, overexpression and pharmacologic inhibition will further elucidate the role of Glo-I for proliferation, migration and colony formation of BxPC3, Capan-1 and Panc-1 was at average levels.

Disclosure: Nothing to disclose

P0117 CLINICOPATHOLOGICAL FEATURES OF PancreATIC ductAL AdENOCARCINOMA CoNCOMITANT WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PanCREAS

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Introduction: Although intraductal papillary mucinous neoplasms of the pancreas (IPMNs) have been recognized as precursor lesions for pancreatic cancer, it has been reported to be associated with pancreatic ductal adenocarcinoma (PDAC) that does not occur from IPMN lesions (concomitant PDAC, C-PDAC). The clinicopathological features of C-PDAC have not been clarified in comparison to other types of pancreatic adenocarcinoma.

Aims and Methods: This study was performed to elucidate the clinicopathological features of C-PDAC. Of the 43 patients histologically confirmed to have pancreatic invasive adenocarcinoma by using resected specimens, EUS-FNA, or endoscopic biopsy at our center between January 1985 and December 2016, 91 patients with C-PDAC were included in this study and retrospectively analyzed. The occurrence rate of C-PDAC and clinicopathological features of C-PDAC were compared with that of IPMN.

Results: The occurrence rate of C-PDAC was 29% (47/161) in resection cases and 16% (4/24) in non-resection cases. The presence of IPMN was diagnosed by using resected specimens in 47 resection cases and by using imaging examinations in 44 non-resection cases. The outcome measurements were defined as (1) the rate of C-PDAC patients among all IPMN patients (C-PDAC + IPMN) and (2) the clinicopathological features of C-PDAC (group A, n = 47) in comparison to those of PDAC without IPMN (group B, n = 105) and those of invasive cancer derived from branch duct IPMN (group C, n = 27) in resected cases.

Results: The percentage of C-PDAC was 29% (47/161) in resection cases and 16% (4/24) in non-resection cases. There was no significant difference in any factors investigated, such as age, sex, history of acute pancreatitis or diabetes mellitus, pathological stage, and survival period after surgical resection, between groups A and B. Between groups A and C, the pathological stages (stage IA, 6% vs. 33%, p = 0.004) and survival period after surgery (mean, 1368 vs. 2567 days, p = 0.044) were significantly different. As to morphological findings on the accompanying IPMN in groups A and C, there was significant difference in the cyst size (171 ± 10.6 mm vs. 44.1 ± 21.0 mm, p < 0.001), multifocal
P0118 AN EXAMINATION OF THE USEFULNESS OF MASPIN STAINING IN EUS-FNA SAMPLES FOR PANCREATIC CANCER
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Introduction: There are many reports that KRAS and p53 are useful in improving the diagnostic yield of endoscopic ultrasound-fine needle aspiration biopsy (EUS-FNA) for pancreatic tumors. Nevertheless, KRAS and p53 are often negative if structurally, the tumor is anaplastic or the sample amount is small. On the other hand, Maspin which is serine protease inhibitor, is recently attracted as a new gene marker of pancreatic cancer.
Aims and Methods: The aim of this study was to evaluate the usefulness of Maspin staining in histopathological diagnosis using EUS-FNA. 94 patients who performed both Maspin and p53 staining in specimen obtained by EUS-FNA were enrolled in this study. All patients were diagnosed as the pancreatic adenocarcinoma at Dokkyo medical university hospital using EUS-FNA in the period from April 2015 to December 2017. We evaluated positive rate of Maspin and/or p53, and the relationship between immunohistochemistry and clinical factors (sex, age, location, size, tissue differentiation, rate of metastasis, Maspin positive rate, and tumor biomarker).
Results: The positive rates were 72.4% (71/98) in p53, 98.0% (96/98) in Maspin. There was no statistically significant difference between p53 positive and negative cohorts, but Maspin was positive in all cases of the p53 negative cohort. On the other hand, there was statistically significant difference between Maspin positive cohort and the negative cohort in age (70.5 vs. 53.0, p = 0.026) and the revel of SUV (10 vs. 2.0, p = 0.023). In addition, p53 was positive in 2 cases where Maspin was negative.
Conclusion: The expression of Maspin was higher than p53 in pancreatic adenocarcinoma. Our study suggested that the immunostaining combined p53 and Maspin would contribute to the improvement of diagnostic yield for pancreatic tumor using EUS-FNA.
Disclosure: Nothing to disclose

P0119 DIAGNOSTIC USEFULNESS OF LOCALIZED STENOSIS OF THE MAIN PANCREATIC DUCT FOR DETECTION OF EARLY PANCREATIC CANCER
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Introduction: Although early detection of pancreatic cancer is associated with a better prognosis, it has been extremely difficult to detect. Localized stenosis of the main pancreatic duct (MPD) often indicates early pancreatic cancer, including intraductal cancer.
Aims and Methods: The aim of this study was to evaluate the predictive sensitivity of localized MPD stenosis for the detection of pancreatic cancer. Among 597 patients who underwent intentionendoscopic retrograde pancreatography (ERP) between January 2008 and December 2017 at Sendai City Medical Center, those in whom ERP was performed to evaluate abnormal findings on the MPD were extracted from the prospectively maintained database. Those with multiple MPD stenoses, diffuse MPD dilation, and a mass detectable on other imaging examination, were excluded. Those with other pancreatic diseases, such as intraductal papillary mucinous neoplasms (IPMN), autoimmune pancreatitis (AIP), and definite chronic pancreatitis were also excluded. Finally, 17 patients with a single, localized stenosis in the MPD without a mass (defined as the typical MPD findings for suspicious early pancreatic cancer [TF-EPC]) were included in this study.
Final diagnosis of the etiology causing the MPD stenosis was defined as being (1) malignant or benign by histological diagnosis with a surgically resected specimen when the tumor was resected, (2) malignant when an obviously malignant tumor appears at the site during follow-up if resection was not performed, or (3) benign when the abnormal findings improved or did not change on imaging examinations (EUS, CT, MRI or ERCP) after a 3-year follow-up without resection.
If the findings were difficult to define, whether they changed or not, the patients were excluded. The main outcome measurement was the predictive sensitivity of the TF-EPC for the presence of pancreatic cancer.
Results: Of the 9 patients who underwent surgical resection among the analyzed patients, the final diagnosis of the MPD stenosis was judged as pancreatic cancer in 8 patients and as a non-neoplastic change in 1 patient. In the remaining 8 patients, the MPD stenosis was judged as being non-neoplastic by performing clinical follow-up of > 5 years (mean follow-up period, 2186 ± 415 days). Overall, the final diagnosis of the MPD stenosis with the TF-EPC was pancreatic cancer in 8 patients (47%) and a non-neoplastic change in 9 patients. In other words, the predictive sensitivity of the TF-EPC for presence of pancreatic cancer was 47%. Of the 8 patients with pancreatic cancer, 3 were diagnosed as having primary pancreatic adenocarcinoma and the other 5 patients were diagnosed with ductal adenocarcinoma. The size of the invasive mass was less than 10 mm in all 5 patients with invasive cancer (mean diameter, 7.0 ± 0.9 mm). The specificity, sensitivity, and accuracy of cytology by using pancreatic juice obtained during ERP with cell-block preparation was 100%, 90%, and 88%, respectively.
Conclusion: MPD stenosis with typical findings for suspicious early pancreatic cancer, which was defined as a single, localized stenosis without other pancreatic diseases with no mass detectable on imaging examination, was derived from pancreatic cancer in half of the patients. Such findings were found to be useful for detecting early pancreatic cancer, although histological confirmation using pancreatic juice cytology would be necessary before surgical resection.
Disclosure: Nothing to disclose

P0120 APPROPRIATENESS OF PANCREATIC SURGERY IN HIGH-RISK INDIVIDUALS FOR FAMILIAL PANCREATIC DUCTAL ADENOCARCINOMA
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Introduction: About 5% of pancreatic ductal adenocarcinoma (PDAC) are inherited, with a deleterious germline mutation detected in ≥ 20% of families. Pancreatic screening in high-risk individuals (HRIs) is proposed to perform early surgical treatment of malignant lesions, such as pancreatic intraepithelial neoplasia [PanIN] or intraductal papillary mucinous neoplasms [IPMN] with high-grade dysplasia, or even invasive PDAC at an early stage. Performing surgery in HRI at the optimal time, i.e., neither too early (non-malignant lesions) nor too late (advanced PDAC), remains challenging. The outcomes of pancreatic surgery in HRI have never been properly explored.
Aims and Methods: We aimed to evaluate surgical appropriateness and explore predictive factors in screened HRI who underwent pancreatic surgery. A patient-level meta-analysis was performed on all studies reported since 1999 who included HRI defined by strict criteria and described individual screening, surgical and pathological data of operated HRI.
For each operated HRI, the highest risk pancreatic abnormality identified at screening was classified into low-risk abnormality [LRA] (cyst with benign features) or high-risk abnormality [HRA] (cyst with worrisome features or high-risk stigmata of malignancy, solid mass and/or sample positive for malignancy). The highest malignant pathological lesion was classified into no/malignant potential (branch-duct IPMN or PanIN with low-grade dysplasia) or potentially/frankly malignant (branch-duct IPMN or PanIN with high-grade dysplasia) or potentially/frankly malignant PDAC.
Surgical appropriateness was considered when potentially/frankly malignant lesions were resected. Univariate and multivariate logistic regression models of factors predictive of surgical appropriateness were performed. The variables of the multivariate model were used to establish a score and nomogram allowing the estimation of individual probability of surgical appropriateness.
Results: 13/24 studies were selected, which reported 90 HRI operated on. LRA and HRA were detected in 46.7% and 53.3% of HRI, respectively. Surgical appropriateness was consistent in 38 (42.2%) HRI operated, including 20 HRI (22.2%) with PDAC. Identification of HRA at screening was the only factor associated with surgical appropriateness at multivariate analysis (p = 0.001). We proposed the Beaujon score, including the identification of HRA, age ≥ 50 and the existence of deleterious germline mutation. The score was used to build a nomogram which predicted individual surgical appropriateness with an area under the curve of 0.81.
Survival data were available for 66 operated HRI. After a median postoperative follow-up of 29 months, 9 HRI died, including 8 who were operated on for invasive PDAC. HRI with invasive PDAC had a significantly lower overall survival (median, 35 months) compared to HRI with other pathological results (p < 0.0001).
Conclusion: Overall, 42.2% of HRI underwent appropriate surgery. Surgical appropriateness was higher in HRI with HRA identified at screening. We proposed the Beaujon score to help selecting the best candidates for pancreatic resection. This score requires prospective validation.
Disclosure: Pascal Hammel: Astra-Zeneca (investigator of POLO study)
P0122 PREDICTION OF LIVER METASTASIS AFTER SURGICAL RESSECTION OF ENDOCYTIC DUCTAL CARCINOMA OF THE PANCREAS BASED ON PREOPERATIVE ENDOCYTIC ULTRASOUNDOGRAPHY FINDINGS AND PATHOLOGICAL EXAMINATION

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Introduction: The poor prognosis after surgical resection of invasive ductal carcinoma of the pancreas (IDCP) is due to the high recurrence rate. IDCP usually recurs in the liver and at local sites, such as the pancreatic bed or adjacent structures. Notably, the survival duration among patients with liver metastasis (LM) is ≤3 years after R0 resection, even when the diameter of the IDCP is <2 cm (pTS1). We analysed patients with pTS1 IDCP and found that the median number of invading veins in the area of the IDCP was 5 and 2 in patients with and without LM [1], respectively. However, frequent venous invasion by the carcinoma and cancer cell migration into the bloodstream had already occurred at the time of surgical resection, particularly in patients with LM. Thus, measures should not only undergo surgical resection but also prepare for LM. Patients with IDCP with a vague periphery as demonstrated by EUS invasion and recurrence [2]. We analysed the correlations among LM, venous invasion, tumour growth patterns, and endoscopic ultrasonography (EUS) findings in patients with pTS1 IDCP.

Aims and Methods: Of 402 patients with IDCP, 21 (5.2%) had pTS1 tumours. The follow-up period among these 21 patients ranged from 6 months to 25 years. All patients underwent R0 resection. Handling of the surgical specimen and assessment of vascular permeation by the carcinoma were performed as previously described [1,3]. Clinicopathological factors were assessed according to the Classification of Pancreatic Carcinoma (4th English edition) by the Japan Pancreas Society. The tumour growth pattern of neoplasms infiltrating surrounding tissue (INFα, expanding growth; INFc, diffusely infiltrating pattern; INFb, in between INFα and INFc) was assessed by loupe findings of the maximum cut surface of the IDCP. EUS findings were evaluated with respect to morphology.

Results: The 21 patients comprised 12 men and 9 women aged 51 to 80 years. 5 patients died of liver metastasis. Among 14 patients who underwent EUS, 4 patients with LM exhibited worrisome imaging features of hepatocellular carcinoma on computed tomography and magnetic resonance imaging were recently shown to correlate with microvascular invasion and recurrence [2]. We analysed the correlations among LM, venous invasion, tumour growth patterns, and endoscopic ultrasonography (EUS) findings in patients with pTS1 IDCP.

Conclusion: Patients with IDCP with a vague periphery as demonstrated by EUS should not only undergo surgical resection but also prepare for LM.

Disclosure: Nothing to disclose

References


Abstract No: P0123

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P0123 ROLE OF RAPID ON SITE EVALUATION (ROSE) FOR ENDOCYTIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (FNA) OF SOLID PANCREATIC LESIONS: “ON SITE” MULTIDISCIPLINARY TEAM IS MORE IMPORTANT THAN TECHNIQUE FOR AN ACCURATE DIAGNOSIS

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Introduction: EUS-FNA is the first-line technique for sampling pancreatic lesions. It is regarded as safe procedure but many factors influence adequacy and accuracy, among the others presence of the cytopathologist and the real time evaluation and analysis of the specimens.

Aims and Methods: This is a retrospective analysis of patients who underwent EUS-FNA for known pancreatic solid lesions before and after ROSE adoption. All consecutive EUS-FNA procedures for pancreatic lesions performed during the first year of adoption (ROSE1 group) and the following year (ROSE2 group) were compared to those performed during the previous year (pre-ROSE group). EUS was performed using a linear echoendoscope. FNA was performed using fine needles 22 or 25 Gauge diameter. Demographics, lesion location and size, number of needle passes, final diagnosis were recorded. The gold standard for diagnosis was considered histological analysis of surgical specimen, when available, or clinical and radiologic follow up compatible with neoplasia (positive) or absence of deterioration/spontaneous resolution (negative). Specimen were categorized into diagnostic if a final diagnosis was reported and non diagnostic in case of no sufficient cells or when atypia was not further classified. Adequacy (samples providing sufficient material for evaluation), diagnostic yield (rate at which a diagnosis is made), diagnostic accuracy (correspondence between cases for which a diagnosis was rendered and the gold standard) were evaluated. Aim of the study was to compare the adequacy, diagnostic yield and accuracy of EUS-FNA for solid pancreatic lesions before and after introduction of ROSE.

Results: 94 pancreatic lesions in 92 patients were enrolled (26, 30 and 38 in pre-ROSE, ROSE1 and ROSE2 groups respectively). Adequacy rate was 96.2%, 93.3% and 100% in pre-ROSE, ROSE1 and ROSE2 groups, respectively (p = NS). Diagnostic yield was 76.9%, 86.7%, 92.1% and accuracy 65.4%, 76.7% and 86.8% in pre-ROSE, ROSE1 and ROSE2 groups, respectively, with significant difference between pre-ROSE and ROSE2 groups (p<0.05).

Conclusion: The routine use of ROSE during EUS-FNA for solid pancreatic lesions is associated with an improvement in terms of diagnostic yield and accuracy, but it does not seem to improve the adequacy of FNA. Lack of difference during the first year of adoption of ROSE was probably due to the learning curve of the multidisciplinary team.

Disclosure: Nothing to disclose
MONDAY, OCTOBER 22, 2018
09:00-17:00
Endoscopy and Imaging I - Hall X1.

P0124 WATER-POCKET ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL GASTRIC NEOPLASMS: A PROSPECTIVE RANDOMIZED STUDY
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Introduction: It is essential to obtain a clear view during the endoscopic submucosal dissection (ESD) to precisely dissect the appropriate submucosal layer. Several variations of underwater techniques for gastric ESD have been reported in comparison with gas insufflation method [1, 2]. We have developed a new ESD method with the creation of a local water-packet that provides a clear view in the dissection field. Therefore, we aimed to investigate the feasibility and safety of water-pocket ESD (WP-ESD) for superficial gastric neoplasms.

Aims and Methods: We prospectively recruited 50 patients with gastric neoplasms (early gastric cancer or gastric adenoma) between April 2017 and December 2017. Among them, 48 patients were treated with WP-ESD technique. The patients with WP-ESD were compared with 48 patients treated with standard ESD (S-ESD) who were selected by propensity score matching. The primary outcome was the ESD procedure time.

The rationale of the WP-ESD technique is that ESD procedure is carried out underneath the target lesion via a locally created water pool in the submucosal layer. First, to create a submucosal pocket, an initial incision is made approximately 2 cm proximal to the lesion. Second, the tip of the attached transparent ST hood is inserted into a small hole followed by injection of saline solution, and dissection of the submucosal layer is initiated in the water pool.

The study protocol was approved by the ethics committee of New Tokyo Hospital (IRB No. NTH 0112) and was registered in the University Hospital Medical Network Trials Registry (UMIN00030266).

Results: Total procedure time was significantly shorter in the WP-ESD group than in the S-ESD group (median [IQR], 27.5 [19–43] min vs. 41 [29.8–69] min; p < 0.001). Similarly, the dissection speed was significantly greater in the WP-ESD group than in the S-ESD group (median [IQR], 22.5 [16.8–35.3] mm²/min vs. 17.3 [12.7–22.1] mm²/min; p < 0.001). The rates of complete en bloc resection in the WP-ESD group and the S-ESD group were 97.9% and 95.8%, respectively (p = 0.36). The median maximum diameter of iatrogenic duodenal perforations ≥ 1 cm were retrospectively studied who were respectively treated by purse-string sutures using the novel LeCamp™ endoloops and the SureClip™ repositionable hemostasis clips with the single-channel endoscope at 4 institutes.

Conclusion: WP-ESD was associated with a shorter procedure time than S-ESD. WP-ESD may provide an alternative method for resection of superficial gastric neoplasms.

Disclosure: Nothing to disclose.

References

P0125 CLINICAL VALUES OF DENTAL FLOSS TRACTION ASSISTANCE IN ENDOSCOPIC FULL-THICKNESS RESECTION FOR SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA LAYER IN THE GASTRIC FUNDUS
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Introduction: With the development and maturation of endoscopic resection, endoscopic full-thickness resection (EFR) derived from endoscopic submucosal dissection (ESD) is gradually accepted and promoted to treat submucosal tumors (SMT) originating from muscularis propria (MP) layers. However, there are some difficulties when EFR is applied in the treatment of muscularis propria lesions in gastric fundus. This study intends to explore whether EFR can be more simple, safe and effective with the traction assistance of dental floss.

Aims and Methods: To assess modifications in anaesthesia practices for POEM. Preoperative Measures: Clear liquids and lukewarm water 24 hours before. Thorough pre anesthesia work up. Induction of anaesthesia and intraoperative management: POEM procedures were carried out under general anaesthesia with endotracheal intubation and positive pressure ventilation to reduce the risk of capno diastasis. One assistant is kept ready for Selliks manoeuvre and suctioning of the oral cavity if patient aspirates the fluid in the esophagus. Anesthesia in all the patients was induced by rapid sequence method (to prevent aspiration of esophageal content). Sedation and induction was achieved by (Inj. Glycopyrrolate 0.2 mg; Midazolam 0.02 mg/kg; Propofol-1-2mg/kg; Fentanyl 100mcg; Succinylcholine 1-2 mg/kg). Atraumatic endo-clip using the novel LeCamp™ endoloops and the SureClip™ repositionable hemostasis clips with the single-channel endoscope at 4 institutes.

Conclusion: None to disclose.

References

P0126 PURSE-STRING SUTURES USING NOVEL ENDOLOOPS AND REPOSITIONABLE CLIPS FOR THE CLOSURE OF LARGE IATROGENIC DUODENAL PERFORATIONS WITH SINGLE-CHANNEL ENDOSCOPY
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Introduction: Serious complications due to perforations restrict the development of duodenal endoscopic treatment. The key stage for remediation is the successful occlusion to prevent peritonitis and the need for surgical intervention. This report presents a new simple method for the closure of large iatrogenic duodenal perforations with purse-string sutures using the novel endoloops and repositionable clips through a single-channel endoscope.

Aims and Methods: A total of 23 patients with iatrogenic duodenal perforations ≥ 1 cm were retrospectively studied who were respectively treated by purse-string sutures using the novel LeCamp™ endoloops and the SureClip™ repositionable hemostasis clips with the single-channel endoscope at 4 institutes.

Results: The median maximum diameter of iatrogenic duodenal perforations was 1.65 cm (range 1.0–3.0 cm). Complete closure of all 23 perforations was achieved. No patient had severe complications such as peritonitis. The wounds were healed and no obvious duodenal stricture was observed in all cases at 4 months.

Conclusion: Purse-string sutures using the novel endoloops and the repositionable endoclips through single-channel endoscope were feasible, easy and effective methods for the closure of large duodenal iatrogenic perforations.

Disclosure: Nothing to disclose.

References
5. S. Huang, S. Zhu, J. Lin, M. Wang

P0127 TO ASSESS THE ANAESTHETIC REQUIREMENTS AND MODIFICATIONS REQUIRED IN PER ORAL ENDOSCOPIC MYOTOMY (POEM) FOR SAFE PROCEDURE AND PREVENTION OF COMPLICATIONS. A RETROSPECTIVE ANALYSIS OF PROTOCOL FOR ANAESTHESIA IN POEM DEvised AT OUR CENTRE. A STUDY OF 175 CASES
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Introduction: To assess modifications in anaesthesia practices for POEM.

Aims and Methods: To assess the anaesthetic requirements and modifications required in POEM for safe procedure and prevention of complications.

Preoperative Measures: Clear liquids and lukewarm water 24 hours before. Thorough pre anesthesia work up. Induction of anaesthesia and intraoperative management: POEM procedures were carried out under general anaesthesia with endotracheal intubation and positive pressure ventilation to reduce the risk of capno diastasis. One assistant is kept ready for Selliks manoeuvre and suctioning of the oral cavity if patient aspirates the fluid in the esophagus. Anesthesia in all the patients was induced by rapid sequence method (to prevent aspiration of esophageal content). Sedation and induction was achieved by (Inj. Glycopyrrolate 0.2 mg; Midazolam 0.02 mg/kg; Propofol-1-2mg/kg; Fentanyl 100mcg; Succinylcholine 1-2 mg/kg). Atraumatic endo-clip using the novel LeCamp™ endoloops and the SureClip™ repositionable hemostasis clips with the single-channel endoscope at 4 institutes.

Conclusion: Purse-string sutures using the novel endoloops and the repositionable endoclips through single-channel endoscope were feasible, easy and effective methods for the closure of large duodenal iatrogenic perforations.

Disclosure: Nothing to disclose.

References
SUBMUCOSAL DISSECTION IN THE ESOPHAGUS AND STOMACH
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Introduction: Endoscopic submucosal dissection (ESD) in the upper gastrointestinal tract is mostly performed in patients under general anesthesia with endotracheal intubation, especially when the estimated procedure time is likely to exceed two hours [1]. The advantage for using general anesthesia are control of body movements, protection, less respiratory problems or interruptions during the procedure and therefore lower complication rates [2]. However, general anesthesia leads to longer post-procedural hospital stay [3]. Anesthetic complications for general anesthesia reported in the literature are up to 18.9% [2]. Analgo-sedation in the upper gastrointestinal tract is mostly performed in patients under general anesthesia with endotracheal intubation instead of general anesthesia. The aim of this study is to report on the endoscopic and anesthetic complication rates of ESD with propofol sedation.

Aims and Methods: Retrospective cohort study of patients who underwent esophageal or gastric ESD in a tertiary referral center in the Netherlands between October 2013 and February 2018. All patients were sedated by intravenous administration of propofol until the required level of sedation was achieved according to the Ramsay Sedation Scale (score 4 to 5). Remifentanil infusion was started until the required level of analgesia was achieved. Vital signs were continuously monitored during the procedure in the endoscopy room. Primary endpoints were the rates of intra-procedural endoscopy and anesthesia related complications, secondary endpoints were 30-days post-procedural complication rates and the endotracheal intubation conversion rates.

Results: We included 86 patients with a median age of 70 years (range 24–91). 34 ESDs were carried out in the esophagus, 51 in the stomach and 1 in the duodenal bulb. Median lesion size was 25 mm (range 8–120). Median procedure time was 100 minutes (range 15–510). En bloc resection was performed in 77 patients (89.5%), piecemeal resection in 1 patient (1.2%). In 7 patients (8.1%), the procedure was discontinued and no histology was obtained due to muscular invasion (6 cases) or perforation in 1 patient (1.2%). ESD was converted to endoscopic mucosal resection due to bleeding. Early cancer was found in 72/79 patients (91.1%). In 2 patients (2.3%), an intra-procedural endoscopic complication occurred; both bleeding. In 14 patients (16.3%), a post-procedural complication occurred: 5 bleeding (5.8%), 6 retrosternal pain (7.0%), 2 dysphagia (2.3%), 1 stomach pain (1.2%). In 2 patients (2.3%) an intra-procedural anesthetic complication occurred; 1 coughing and in 1 patient hypotension and desaturation. In 2 patients (2.3%), a minor post-operative anesthetic complication occurred; 1 nausea and 1 atrial fibrillation. In 42 patients (48.8%) were discharged the same day, 38 patients (44.2%) were discharged the following day (29 logistic reasons). In 6 patients, hospital stay was > 2 days. Longer hospital stay was not related to anesthesia and no patients were readmitted for anesthesia-related complications.

Conclusion: Propofol-based analgo-sedation without endotracheal intubation is safe for ESD procedures in the esophagus and stomach with low complication rates and short hospital stay.

Disclosure: Nothing to disclose.
group and the Hp-infected group. Among 492 cases of early gastric cancer who underwent endoscopic resection in our hospital between April 2013 and February 2018, the following lesions were excluded: special type gastric carcinoma (gastric adenocarcinoma of the fundic gland type [n = 27], gastric adenocarcinoma with enteroblastic differentiation [n = 4]), and gastric carcinoma with lymphoid stroma [n = 2]). Remnant gastric carcinoma [n = 6], Hp-uninfected gastric carcinoma [n = 20], lesions in which M-NBI has not been performed [n = 2], and lesions without details of Hp eradication (190). The remaining lesions were classified into the Hp-eradicated group (n = 92) and the Hp-infected group (n = 149). Moreover, all cases of the 2 groups were classified into 3 histological subgroups according to Lauren classification: pure intestinal-type/pure diffuse-type/mixed-type. We compared the clinicopathological factors (age, sex, tumor location, tumor size, macroscopic type, invasion depth, lymphatic invasion, venous invasion, horizontal margin, vertical margin, non-neoplastic epithelium, adenocarcinoma with low-grade atypia) and endoscopic findings (the range of mucosal atrophy, demarcation line, microvascular pattern, microsurface pattern).

Results: The Hp-eradicated group was subclassified into 81 cases of pure intestinal-type and 11 cases of mixed-type. There was no case of pure diffuse-type in Hp-eradicated group. The Hp-infected group was subclassified into 131/5/12 cases of pure intestinal-type/pure diffuse-type/mixed type. In comparison between pure intestinal-type of the 2 groups, significantly smaller tumor size (12.5±8.8 mm vs. 16.4±11.4 mm, p<0.05), more depressed lesion (elavated/flat/depressed = 15/3/63 vs. 60/2/69, p<0.01), milder mucosal atrophy (C-1, C-2, 0-1/O-2, 3, 11/30/40 vs. 8/30/93, p<0.01), higher non-neoplastic epithelium covering rate (25/81, 30.9% vs. 19/131, 14.5%, p<0.01) were observed in Hp-eradicated group than in the Hp-infected group. Although DL (+) cases were significantly less in Hp-eradicated group than in the Hp-infected group, DL was detected in most cases in both groups (76/81, 93.8% vs. 130/131, 99.2%, p<0.05). Moreover, DL was detected in all cases of mixed-type in both groups. Whereas, there were no small number of DL (+) cases in pure diffuse-type in the Hp-infected group (2/5, 40%).

Conclusion: M-NBI with MESSDA-G can identify the DL in most patients with pure intestinal-type and mixed-type of early gastric cancer after Hp eradication. Disclosure: Nothing to disclose.

References
tubule-villus mucosal pattern in 80% (p = 0.01 versus other lesions); light blue-crest and regular vascular pattern, thickness and density were absent in all of them. The presence of a regular circular mucosal pattern was more frequently observed in HP and T1-GC compared to adenomas (p < 0.001). The presence of a central erosion with or without demarcation line was more frequently observed in T1-GC (p < 0.001 vs. HP).

[Table 1. *p< 0.012 versus adenoma; †p< 0.003 versus adenoma; ‡p< 0.01; ‡‡p< 0.001]

Conclusion: The NBI analysis of the mucosal pattern seems to be effective to endoscopically discriminate between adenomas and HP while the main characteristic of T1-GC is the presence of a central erosion sometimes with a clear demarcation line. Accordingly, NBI could be an important tool to endoscopically distinguish the histological nature of GPL.

Disclosure: Nothing to disclose

References


P0134 ELDERLY PATIENTS VS NON-ELDERLY PATIENTS IN CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION; PROPENSITY SCORE MATCHING ANALYSIS

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Introduction: Endoscopic submucosal dissection (ESD) for gastric neoplasms was accepted as a standard treatment even in elderly patients. However, it is difficult to obtain clinical outcomes and non-elderly patients because background characteristics are different. Therefore, this study aimed to compare the clinical outcomes between elderly and non-elderly patients by propensity score matching analysis.

Aims and Methods: Early gastric neoplasms treated by ESD between January 2013 and March 2018 at out hospital were retrospectively reviewed. Elderly patients were defined as those aged 75 years old or more. ESD in elderly (ESD-E, n = 58) and ESD in non-elderly (ESD-N, n = 58) were compared. Multivariate analyses and propensity score matching were used to compensate for the differences in age, gender, ASA-score, underlying disease, Anti-thrombotic agent use, tumor size, tumor location, tumor shape, presence of ulcer, differentiation and operator level, which included factors previously reported to affect the outcomes of ESD. Primary outcome was procedure time. Secondary outcomes were the rates of en-block/completion resection and the rates of complications (aspiration pneumonia/perforation/post-procedure bleeding).

Results: Propensity score matching analysis created 58 matched pairs. Adjusted comparison between 2 groups showed similar treatment outcomes (median procedure time: 61.5min vs. 77.5min; p = 0.342; en-block resection rate: 100% in both groups; complete resection rate: 86.8% vs. 97.4%, p = 0.200. However, the rates of complications were higher in ESD-E than those in ESD-N, but not significant. (Aspiration pneumonia: 10.5% vs. 7.9%, p = 1.00; Perforation: 5.3% vs. 0%, p = 0.493, post-procedure bleeding: 2.6% vs. 0%, p = 1.0).

Conclusion: ESD for gastric neoplasms in elderly patients achieved favorable outcomes as well as ESD in non-elderly patients. However, we should take care of complications in ESD for elderly patients.

Disclosure: Nothing to disclose

References


**P0136 ENDOSCOPIC MUCOSAL RESECTION OF DUODENAL ADENOMAS: SUCCESS, COMPLICATIONS, RECURRENTNESS, AND SURGERY-FREE OUTCOMES IN A UK TERTIARY CENTRE**

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**Introduction:** Duodenal adenomas consist of sporadic and familial adenomatous polyposis (FAP) associated adenomas. Endoscopic mucosal resection (EMR) is the recognised technique when considering endoscopic removal of these lesions, but outcomes from large studies are lacking. Leeds Teaching Hospitals (LTHT) is a large tertiary centre that has a local catchment area of more than 800,000 people, and to our knowledge this is the largest UK cohort assessing duodenal EMR outcomes.

**Aims and Methods:** Retrospective data collection was performed of all patients who underwent duodenal EMR over a 17-year period at LTHT. We collected data on patient demographics, lesion characteristics and outcomes including significant complications, recurrence and surgery-free survival. Procedures were performed by a single advanced therapeutic endoscopist or an endoscopy fellow under supervision.

**Results:** A total of 98 patients underwent EMR (sporadic n = 23, FAP n = 75). Median adenoma size was 12.5 mm (IQR 9.0–30.0 mm), with 46.9% removed en-bloc. Standard EMR was performed in 87 procedures, and pull-within snare technique in the remaining 11 procedures. Final lesion histology was TA/TVA with LGD (n = 80), TA/TVA with HGD (n = 12), intra-mucosal cancer (n = 3) and in 3 cases data was missing. Patients with FAP were significantly younger with a median age of 49 years (p < 0.001).

The overall complication rate was 12.4%. 1 (1.0%) patient had an intra-procedural bleed which could not be managed endoscopically, delayed bleeding occurred in 6 cases (5.2%) and perforation occurred in 5 cases (5.2%) of which could not be managed endoscopically. Following univariate analysis, “pull-within snare” technique (p = 0.03), piecemeal resection (p = 0.002), increasing polyp size (p = 0.003) were significantly associated with complications. Adenoma recurrence at first follow up was 25.0%.

**Conclusion:** This is the largest cohort in the UK pertaining to duodenal EMR outcomes, with success, recurrence and complications similar to other world-leading endoscopy centres. Adverse outcomes are associated with increasing lesion size, piecemeal resection and EMR technique.

**Disclosure:** No disclosures

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**P0137 A META-ANALYSIS OF SCLEROLIGATION VERSUS BAND LIGATION FOR ERADICATION OF ESOPHAGEAL VARICES:**

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**Introduction:** Esophageal band ligation (EVL) for esophageal varices has significantly less bleeding rates and complications, and needs a lower number of sessions to achieve eradication of the varices than sclerosis therapy yet has a higher recurrence rate. This is because EVL does not obliterate the deeper varices or perforating veins, whereas the chemical effect of sclerosis therapy does Scleroligation (combined sclerosis and band ligation) has been used successfully for management of esophageal varices and has been recently evaluated in management of gastroesophageal varices.

**Aims and Methods:** We aimed to determine therapeutic efficacy and safety of endoscopic scleroligation and endoscopic band-ligation of esophageal varices. A literature search was conducted in the following medical electronic databases: PubMed, CENTRAL, SCOPUS and Web of Science on the 23rd of December 2017 using the following strategy: scleroligation OR (sclerotherapy AND plus AND ligation) AND (Esophageal varices OR varices). 8 randomized controlled trials from 1996 to 2017 were included in the meta-analysis after tight full text screening. The included studies were analyzed by using RevMan 4.2 software to calculate odds ratio and 95% confidence interval.

**Results:** Of 97 citations discovered by initial search, 8 parallel RCTs were finally included in this meta-analysis. We found that there were significantly less bands used in EVL than in ESL (Chu = 46.80; 95% CI: −3.13 to −1.30; df = 6 (p < 0.0001); F = 87.6%). Compared to ESL, the overall number of sessions to variceal obliteration in ESL was significantly lower (Chu = 571.90; 95% CI: −0.54 to 1.12; F = 99%; p < 0.00001). ESL required fewer weeks of treatment than EVL, further confirming its positive therapeutic effect. Variceal recurrence following ESL was significantly lower than with EVL (Chu = 17.35; 95% CI: 0.97 to 1.09; F = 54%; p < 0.03). Both procedures had the same adverse effects with no significant difference regarding frequency.

**Conclusion:** Endoscopic Scleroligation (ESL) shows high efficacy and safety in management of varices with a low incidence of recurrence.

**Disclosure:** Nothing to disclose

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**P0138 CAP-ASSISTED REMOVAL OF IMPACTED ESOPHAGEAL FOOD BOLUS: “THE EASY WAY”**


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**Introduction:** The commonest foreign body impacted in the esophagus in adults is a food bolus [1]. The European Society of Gastrointestinal Endoscopy issued clinical guidelines to deal with this problem in 2016 [2]. It recommends either pushing technique or retrieval methods using one of several accessories. However, pushing technique could be associated with adverse events. Also, during retrieval, with the conventional methods, the food bolus tends to fragment into small pieces making extraction both time and effort consuming. Cap-assisted endoscopic extraction of food bolus is an easier method. In this method, a cap is fixed to the tip of the scope and the bolus is removed by applying suction. However, data comparing it to other methods is scarce.

**Aims and Methods:** We aimed to compare two methods for extraction of an impacted esophageal food bolus; the cap-assisted suction method and the conventional methods. We retrospectively reviewed data from 253 patients who underwent endoscopy for food bolus extraction in the period between 2014 and 2017. We compared the two groups for the rate of en bloc removal, total procedure time, and procedure-related complications.

**Results:** 253 patients had endoscopy for food bolus extraction. In 76 patients (30%) the push-technique was used. 177 patients (70%) had one of the retrieval methods. The cap-assisted method was used in 84 patients while 93 patients had retrieval with the conventional methods. The application of cap-assisted technique achieved a higher rate of en bloc removal 82.1% compared to 11.8% with the conventional method (p < 0.001), a shorter procedure time (6.6 ± 3.2 minutes versus 15.3 ± 4.6 minutes, p < 0.0001), and less adverse events (0/84 versus 5/93, p = 0.01).

**Conclusion:** Cap-assisted removal of impacted esophageal food bolus is associated with more en bloc removal, shorter procedure duration, and less adverse effects compared to conventional methods. We encourage including this method in the options to remove an impacted esophageal food bolus.

**Disclosure:** Nothing to disclose

**References**


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**P0139 A META-ANALYSIS OF SCLEROLIGATION VERSUS BAND LIGATION FOR ERADICATION OF ESOPHAGEAL VARICES:**

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**Introduction:** Endoscopic band ligation (EVL) for esophageal varices has significantly less bleeding rates and complications, and needs a lower number of sessions to achieve eradication of the varices than sclerotherapy yet has a higher recurrence rate. This is because EVL does not obliterate the deeper varices or perforating veins, whereas the chemical effect of sclerosis therapy does Scleroligation (combined sclerosis and band ligation) has been used successfully for management of esophageal varices and has been recently evaluated in management of gastroesophageal varices.

**Aims and Methods:** We aimed to determine therapeutic efficacy and safety of endoscopic scleroligation and endoscopic band-ligation of esophageal varices. A literature search was conducted in the following medical electronic databases: PubMed, CENTRAL, SCOPUS and Web of Science on the 23rd of December 2017 using the following strategy: scleroligation OR (sclerotherapy AND plus AND ligation) AND (Esophageal varices OR varices). 8 randomized controlled trials from 1996 to 2017 were included in the meta-analysis after tight full text screening. The included studies were analyzed by using RevMan 4.2 software to calculate odds ratio and 95% confidence interval.

**Results:** Of 97 citations discovered by initial search, 8 parallel RCTs were finally included in this meta-analysis. We found that there were significantly less bands used in ESL than in EVL (Chu = 46.80; 95% CI: −3.13 to −1.30; df = 6 (p < 0.0001); F = 87.6%). Compared to ESL, the overall number of sessions to variceal obliteration in ESL was significantly lower (Chu = 571.90; 95% CI: −0.54 to 1.12; F = 99%; p < 0.00001). ESL required fewer weeks of treatment than EVL, further confirming its positive therapeutic effect. Variceal recurrence following ESL was significantly lower than with EVL (Chu = 17.35; 95% CI: 0.97 to 1.09; F = 54%; p < 0.03). Both procedures had the same adverse effects with no significant difference regarding frequency.

**Conclusion:** Endoscopic Scleroligation (ESL) shows high efficacy and safety in management of varices with a low incidence of recurrence.

**Disclosure:** Nothing to disclose
References


Introduction:
Among 1280 patients with EGC, 663 patients were followed-up for over 5 years, in whom metachronous gastric neoplasm developed in 65 patients (10.0%). Rates of technical and clinical success were 100% rates of technical and clinical success. However, relapse of symptoms may occur in the mid term requiring additional treatment strategies. In the present study, we evaluated the correlation of the new technique of gastric poem (G-POEM). The question arises whether G-POEM may be a helpful tool for the treatment of gastric cancer after endoscopic resection discovered throughout previous studies.

Aims and Methods:
Patients with clinically and endoscopically and histopathologically diagnosis of gastric cancer by endoscopic resection were eligible for the study. Patients were randomized to G-POEM or BoTox injection with symptom relief thereafter. Finally, 34 patients were included in the G-POEM group, 32 patients in the BoTox group. G-POEM were performed with integrated injection function were used (Flush knife, Fujifilm; Dual Knife J, Olympus; Hybrid Knife, Erbe). All procedures were carried out under general anaesthesia using CO2 insufflation and periinterventional application of i.v. antibiotics.

Conclusion:
Metachronous gastric neoplasm had developed in 9.8% of patients with early gastric cancer (EGC) and the risk factors of metachronous tumor development in long-term follow-up.

Disclosure: Nothing to disclose

P0142 EFFICACY AND SAFETY OF GASTRIC POEM (G-POEM): RESULTS OF A PILOT SERIES

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Introduction: In contrast to POEM for achalasia, there is only limited data available on the new technique of gastric poem (G-POEM). The question arises whether G-POEM may be a helpful tool for the treatment of gastric cancer after endoscopic resection.

Aims and Methods: Patients with clinically, endoscopically and histopathologically confirmed diagnosis of gastric cancer after resection with pylorospasm and who had undergone repeated endoscopic resection sessions, e.g. by balloon dilation and/or BoTox injection with short-term relief were treated by G-POEM. ESD knives with integrated injection function were used (Flush knife, Fujifilm; Dual Knife J, Olympus; Hybrid Knife, Erbe). All procedures were carried out under general anaesthesia using CO2 insufflation and periinterventional application of i.v. antibiotics.

Conclusion: G-POEM was shown to be effective and safe in the short term with 100% rates of technical and clinical success. However, relapse of symptoms may occur in the mid term requiring additional treatment strategies.

Disclosure: Nothing to disclose

P0143 RISK FACTORS OF METACHRONOUS GASTRIC NEOPLASM BEYOND 5 YEARS AFTER ENDOSCOPIC RESECTION FOR EARLY GASTRIC CANCER

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Introduction: High-grade dysplasia or invasive cancer successful endoscopic mucosal resection (EMR) is recommended on the new technique of gastric poem (G-POEM). The question arises whether G-POEM may be a helpful tool for the treatment of gastric cancer after endoscopic resection.

Aims and Methods: This study included patients with FAP followed-up in our hospital. We excluded individuals with a history of upper gastrointestinal surgery. EGD was performed using FUSE by qualified endoscopists of the Japanese Gastroenterological Endoscopy Society and visibility of the ampulla of Vater was evaluated. The visibility of the ampulla of Vater was classified according to Woo et al., as follows: Type 1, the whole area of the papilla; Type 2, the upper part of the papilla including the orifice; Type 3, the upper part of the papilla excluding the orifice; Type 4, the lower part of the papilla including the orifice; or Type 5, no visualization of the papilla. The primary endpoint was the proportion of Type 1 in off-line review of the videos, and the secondary endpoint was that of Type 1 on in-site diagnosis.

Results: 49 FAP patients were enrolled in this study between July 2016 and December 2017. Patients were randomized to FUSE group (Type 1/ Type 2-4/ Type 5) or the conventional group (Type 1/ 2-4/ 5). In the FUSE group, the ampulla of Vater was visualized in 8/49 (16.3%) patients compared to 1/49 (2.0%) patients in the conventional group (p=0.012). Intrales correlation coefficients were 1.0 (FUSE group) and 0.85 (conventional group).

Conclusion: FUSE EGD is recommended for screening and surveillance endoscopy for patients with FAP.

Disclosure: Nothing to disclose

P0144 EFFICACY OF FULL-SPECTRUM ENDOSCOPY (FUSE) TO VISUALIZE THE AMPULLA OF VATER IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS (FAP): A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Duodenal cancer is one of the extracolonic malignancies which causes death in patients with familial adenomatous polyposis (FAP). However, the visualization of the ampulla of Vater is not always sufficient with standard esophagogastroduodenoscopy (EGD) because of a limited field of view. Full-spectrum endoscopy (FUSE) provides a wider 240° field of view with images on the front and left side of the lip of the endoscope. The aim of this prospective study was to evaluate the improvement of visualization of the ampulla of Vater in FAP using FUSE compared to standard EGD.

Aims and Methods: This study included patients with FAP followed-up in our hospital. We excluded individuals with a history of upper gastrointestinal surgery. EGD was performed using FUSE by qualified endoscopists of the Japanese Gastroenterological Endoscopy Society and visibility of the ampulla of Vater was evaluated. The visibility of the ampulla of Vater was classified according to Woo et al., as follows: Type 1, the whole area of the papilla; Type 2, the upper part of the papilla including the orifice; Type 3, the upper part of the papilla excluding the orifice; Type 4, the lower part of the papilla including the orifice; or Type 5, no visualization of the papilla. The primary endpoint was the proportion of Type 1 in off-line review of the videos, and the secondary endpoint was that of Type 1 on in-site diagnosis.

Results: 49 FAP patients were enrolled in this study between July 2016 and December 2017. Patients were randomized to FUSE group (Type 1/ Type 2-4/ Type 5) or the conventional group (Type 1/ 2-4/ 5). In the FUSE group, the ampulla of Vater was visualized in 8/49 (16.3%) patients compared to 1/49 (2.0%) patients in the conventional group (p=0.012). Intrales correlation coefficients were 1.0 (FUSE group) and 0.85 (conventional group).

Conclusion: FUSE EGD is recommended for screening and surveillance endoscopy for patients with FAP.

Disclosure: Nothing to disclose

P0145 ENDOCOSCOPIC SCORING SYSTEM FOR PREDICTING THE ANASTOMOTIC COMPLICATIONS AFTER ESOPHAGECTOMY: A PROSPECTIVE COHORT STUDY

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Introduction: The postoperative complications related to gastric conduit reconstruction after esophagectomy are still common issues after esophagectomy. We previously reported that the objective of the novel endoscopic scoring system which is significantly better in the FUSE group in both on-site diagnosis and off-line review (p<0.001). Intrales correlation coefficients were 1.0 (FUSE group) and 0.85 (conventional group).

Conclusion: FUSE EGD is recommended for screening and surveillance endoscopy for patients with FAP.

Disclosure: Nothing to disclose
Score 1: normal mucosa or erosion, score 2: less than 67% circumferential ischemic tissue formation, score 3: more than 67% circumferential ischemic mucosa or ulcer, or full-circumferential ischemic mucosa or ulcer formation with lesion length less than 20mm, score 4: full-circumferential ischemic mucosa or ulcer formation with lesion length more than 20mm. The highest score was then calculated for each patient.

The primary outcome measure was the predicting rate of the anastomotic complications using the scoring system within 2 months after esophagectomy. Clinical Trials.gov Registry, ID:NCT02973789.

Results: A total of 49 patients were enrolled in this study. 47 patients underwent esophagectomy to esophageal cancer. 2 patients underwent esophagectomy to benign strictures due to corrosive esophagitis and achalasia. 16 patients (33.3%) developed anastomotic complications after esophagectomy. Anastomotic leakage occurred in 4 patients. A stricture occurred in 13 patients. 1 patient had gastric conduit necrosis. All patients safely underwent endoscopic examinations without any complications. The incidence rates of each patients score 1, 2, 3, and 4 were 47.9%, 20.8%, 16.7%, and 14.6%, respectively. p < 0.05.

Next, the patients with a maximum score 3 or 4 were defined as the high-risk groups of anastomotic complications. The patients with maximum score 1 or 2 was defined as the low-risk groups of anastomotic complications. The sensitivity and the specificity of predicting the complications in high-risk groups were 62.5% and 100% at 1POD. The sensitivity and the specificity of predicting anastomotic complications in high-risk groups were 81.3% and 93.8% at 1POD.

Conclusion: Endoscopic examinations after esophagectomy were safely performed. The application of the endoscopic classification to mucosal ischemia after esophagectomy resulted in suboptimal accuracy to predict the anastomosis complications.

Disclosure: Nothing to disclose

Reference

PI0146 A COMPARISON OF THE STRENGTH OF ENDOSCOPIC SUTURE: PARTIAL-THICKNESS SUTURE AND FULL-THICKNESS SUTURE

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Introduction: Conventional surgery requires full-thickness suture in order to avoid leakage. Full-thickness suture has shown to be more effective than superficial suture, but full-thickness suture has been controversial in endoluminal surgery because it can cause external organs damage or bleeding. Partial-thickness suture has been attempted to ensure the stability, but its effect is questioned as the lack of support after endoluminal surgery. To evaluate the difference between both suture methods, it is necessary to consider widening the width when performing the partial-thickness suture to have similar strength. Further studies on endoscopic suture method in gastrointestinal tract are needed.

Disclosure: Nothing to disclose

PI0147 AND WHEN NBI DOESN'T SHOW GASTRIC INTESTINAL METAPLASIA DO WE STILL NEED TO SEPARATE BIOPSY SAMPLES INTO DIFFERENT VIALS?

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Introduction: For the correct staging and classification of chronic atrophic gastritis (CAG) it is necessary to perform at least 4 biopsies (2 from the antrum/incisure and 2 from the body) with the biopsy samples being placed in different vials according to the current recommendations. Virtual Chromoendoscopy with Narrow-Band-Imaging (NBI) assists the diagnosis and vigilance of CAG.

Aims and Methods: We aimed to evaluate if, in the absence of a typical endoscopic pattern of GIM with NBI, biopsy samples can be placed in the same vial without implications in the diagnosis and follow-up of the patient. The aim of the prospective study was to perform an upper endoscopy with biopsies of both antrum/incisure and body. In every patient, upper endoscopy was performed with NBI. Patients with gastric lesions and/or suggestive areas of CAG were excluded. Patients included were submitted to ≥ 4 biopsies (2 from the antrum/incisure and 2 from the body) with the samples being placed in the same vial for histologic assessment (n = 182). Finally, histologic staging systems OLG and OLGIM were calculated.

Results: OLG and OLGIM calculation was possible for every patient. It was possible to distinguish samples from antrum/incisure from those of gastric body. In total, 178 (97.8%) presented OLGIM 0 and only 4 (2.2%) presented OLGIM 1. 149 (81.9%) presented OLG 0, 23 (12.6%) presented OLG1 and 5 (5.5%) presented OLG2. The placement of biopsy samples in the same vial had no implications in the diagnosis and follow-up in none of the patients since no one was diagnosed with severe gastric atrophy/intestinal metaplasia (negative predictive value of 100%).

Conclusion: In the absence of a typical endoscopic pattern of CAG with NBI, biopsy samples can be placed in the same vial if it is desired to determine the presence of Helicobacter pylori or even to abstain from biopsies if this is not the case. This change in clinical practice can have a significant financial impact on endoscopy costs.

Disclosure: Nothing to disclose

References

PI0148 ENDOSCOPIC DIAGNOSIS OF HELICOBACTER PYLORI ERADICATION HISTORY USING LINKED COLOR IMAGING AND DEEP LEARNING: A SINGLE-CENTER PROSPECTIVE STUDY

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Introduction: Helicobacter pylori (HP) eradication is an effective therapeutic approach to reduce gastric cancer mortality. In Japan, 1.5 million people annually undergo HP eradication; meanwhile, it has been revealed that despite successful eradication, the risk of gastric cancer persists for patients who already had precancerous lesions or progressed mucosal atypia. The aim of the present study was to create a novel computer aided endoscopic diagnosis (CAED) system for HP eradication history using linked color imaging (LCI) and deep learning (DL). CAED is a new image enhanced endoscopy (IEE) that enhances slight differences in mucosal color, while DL is a type of machine learning technology that imitates neural network in the brain.

Aims and Methods: The aim of this prospective study was to create a CAED system to distinguish between HP uninfected people and patients who have history of HP eradication therapy, using LCI and DL. In this study, we included patients who underwent EGD and were tested for serum HP antibodies (HPab) or urea breath test (UBT) at our medical clinic. Patients with active HP infection in the absence of eradication history, were excluded from the study. As a gold standard for HP infection status, we used HPab titer for uninfected subjects (≤ 5 U/ml, n = 148), and UBT value for eradicated patients (< 2.5%, n = 81). Patients underwent HP eradication out at our hospital. In total, 229 subjects were enrolled in this study. In order to evaluate the diagnostic accuracy of the CAED system patients were subdivided in 2 groups: a training group (n = 189, HP uninfected = 128, eradicated = 61); and a test group (n = 40, HP uninfected = 24, eradicated = 16). Comparing the output data from the test group with the actual data on HP infection status allowed us to assess the accuracy of the CAED system. During the course of the EGD an endoscopist took 3 LCI pictures of the lesser curvature, greater curvature, and antrum of the stomach using EG-L580NW (Fujifilm Co., Japan). The LCI images were subsequently augmented by rotation and right-left flip. We generated 2,508 training images and 480 testing images. An original DL model was designed, which has 18 deep convolutional layers for the CAED system. R (version 3.3.2) was used for statistical analyses.
Results: Area under the curve (AUC) of the receiver operating characteristics (ROC) for the lesser curvature, greater curvature, and antrum was 0.95 (95% CI 0.914–0.981), 0.93 (95% CI 0.882–0.969), and 0.89 (95% CI 0.843–0.944), respectively.

Conclusion: Patients with an HP infection are easy to diagnose without using EGD because noninvasive infection reaction is positive. In contrast, EGD is the only examination capable of distinguishing between HP-infected patients with low gastric cancer risk and patients with a history of eradication. The CAED system demonstrated excellent accuracy in distinguishing between the 2 groups using LGI. Our next step is to apply our findings to clinical practice.

Disclosure: Nothing to disclose

Reference

PO151 THE CLINICAL IMPACT OF CLOSURE OF THE MUCOSAL DEFECT AFTER DUODENAL ESD
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Introduction: Delayed complications (bleeding or perforation) are major concerns of duodenal ESD. Recently, we conducted a retrospective study including about 170 cases of duodenal ESD and found both perforation and bleeding was much lower than those reported by previous reported (presented at DDW 2018). We have routine closed the post-ESD mucosal defect as far as possible, and we hypothesized the discrepancy of the outcomes between ours and previous studies was come from the difference in the proportion of complete closure of post ESD mucosal defect.

Aims and Methods: The aim of this study was to assess the efficacy of prophylactic closure of mucosal defect after ESD. This is a retrospective study from a university hospital. We collected the outcomes of duodenal ESD in 169 patients with duodenal epithelial neoplasia (174 lesions) treated by ESD at our department between July 2010 and January 2017. Study subjects were divided into 3 subgroups according to the degree of closure of post-ESD mucosal defect; complete group, incomplete group, and not attempted group. The proportion of delayed complications (including delayed bleeding and delayed perforation), the maximum serum level of C-reactive protein (CRP), and the total hospital stay were compared among these subgroups. Moreover, a multivariate logistic regression model to find risk factors for delayed complications.

Results: The proportion of delayed complications of patients in complete group, incomplete group and not attempted group were 1.7%, 23% and 15.6%, respectively. The difference between complete group and the others was significant (p < 0.01). Maximum serum CRP level was much lower in complete group (1.51 ± 2.18 vs. 6.28 ± 10.0 mg/dl, p < 0.01) and hospital stay was significantly shorter in complete group than in incomplete/none group (median [range] 4 [4–13] vs. 7 [3–58] days, p < 0.01). Multivariate analysis revealed complete closure was an only independent predictor to reduce delayed complications and it revealed about 95% significant decrease of delayed complications.

Conclusion: The present study revealed that complete closure of the mucosal defect after duodenal ESD significantly decreased delayed complications and improved other outcomes such as inflammatory reaction or duration of hospital stay.

Disclosure: Nothing to disclose

PO152 GASTRIC DYSPLASIA IN FAMILIAL ADENOMATOUS POLYPSIS - WHAT IS THE RELEVANCE?
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Introduction: Familial adenomatous polyposis (FAP) is an inherited autosomal-dominant disease characterized by the development of polyps both in the upper and lower gastrointestinal tract. With the implementation of prophylactic colectomy, the incidence of colorectal cancer has declined and extracolonic manifestations have become more relevant.

In what gastric lesions are concerned, FAP patients are known to have an increased risk for gastric dysplasia, although it is unclear if these lesions confer an increased risk of gastric cancer.

Aims and Methods: The aim of our study was to characterize gastric dysplastic lesions in patients with FAP. We enrolled 144 patients with germline mutation in the APC gene from 63 FAP families and we retrospectively reviewed 366 Upper Gastrointestinal Endoscopies (UGE) performed during regular surveillance at the Familial Cancer Clinic.

Statistical tests: Chi-square, Fisher’s Exact Test, Student T test, Mann-Whitney U test, Cox Regression Model

Results: From the 144 patients included in the study, 94 (Men: 49 Women: 45, mean age 48.3 ± 14.8 years) underwent UGE at least once during a median follow-up period of 12.7 ± 5.7 years. The dysplastic lesions were detected in 16 patients (17%) at 37 endoscopically visible lesions (Paris classification: 0-Ip: 10, 0-IIa: 7, 0-IIa+C0: 10, 0-IIc: 10). The proportion of delayed complications (including delayed bleeding and delayed perforation), the maximum serum level of C-reactive protein (CRP), and the total hospital stay were compared among these subgroups. Moreover, a multivariate logistic regression model to find risk factors for delayed complications.

Conclusion: The present study revealed that complete closure of the mucosal defect after duodenal ESD significantly decreased delayed complications and improved other outcomes such as inflammatory reaction or duration of hospital stay.

Disclosure: Nothing to disclose

PO150 COMPARISON BETWEEN ENDOSCOPIC SUBMUCOSAL DISSECTION AND SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION FOR ESOPHAGEAL SUBMUCOSAL TUMORS ORIGINATING FROM THE MUSCULARIS PROPRIA LAYER
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Introduction: Endoscopic submucosal dissection (ESD) or submucosal tunneling endoscopic resection (STER) is widely acknowledged as an important treatment option for esophageal submucosal tumors from the muscularis propria layer. However, the clinical outcomes of ESD or STER for esophageal submucosal tumor have not been completely evaluated.

Aims and Methods: The aim of this study is to compare the 2 different treatments. We retrospectively collected the data of 876 patients who had undergone ESD or STER for esophageal submucosal tumors from January 2011 to September 2015 in the Endoscopy Center of Zhongshan Hospital. Gender, age, tumor size, depth and shape, procedure time, complications, postoperative length of stay, and follow-up duration between ESD and STER groups were compared.

Results: 424 patients received ESD, while 452 patients received STER. There was no significant differences in age, gender, tumor size, depth and shape, or procedure time, complications, postoperative length of stay, and follow-up duration between ESD and STER groups. Moreover, the patients receiving STER had a longer procedure time due to closing the tunnel entrance (ESD vs STER, 23.2 ± 16.5 min vs. 44.0 ± 25.8 min, p < 0.001). No recurrence and death was occurred in the STER and ESD groups during a mean follow-up of 50.0 and 51.8 months, respectively.

Conclusion: Both ESD and STER would likely be effective and safe alternatives for resecting SMTs < 10mm. Accounting for safety and preventing perforation, we are inclined to STER for SMTs > 10mm. Additionally, the choice between the 2 procedures would also depend on the depth and shape of submucosal tumors.

Disclosure: Nothing to disclose
Histopathologic findings revealed 28 lesions with low-grade dysplasia (LGD), 8 with high-grade dysplasia (HGD) and 2 adenocarcinomas, both diagnosed in the first UGE performed. In regard to the evolution of dysplasia, 7 patients maintained LGD in the subsequent EGDS; only one patient had progression from LGD to HGD, in a 1 year period. This case involved multifocal dysplasia of the antrum and the patient underwent subtotal gastrectomy. The majority (70.3%) of gastric dysplastic lesions were treated endoscopically (endoscopic mucosal resection: 16; polypectomy: 9; endoscopic submucosal dissection: 1) and surgery was conducted in 2 cases.

Gastric dysplasia was positively associated with the presence of gastric polyps and flat lesions (p = 0.014 and < 0.001, respectively) and with atrophic gastritis and/or intestinal metaplasia (p = 0.001). Gastric dysplasia was not associated with FAP phenotype, Helicobacter pylori infection or the presence/number of FGP.

Conclusion: Despite the high prevalence of gastric dysplasia in FAP patients, its course is indolent. This may allow endoscopic surveillance and validate a conservative treatment strategy in the majority of cases.

Disclosure: Nothing to disclose

References

P0153 CLINICAL SCORE TO PREDICT THE CHANCE OF SUCCESSFUL ENDOSCOPIC APPROACH OF ESOPHAGEAL LEAKS: CAN WE APPLY OUR CLINICAL PRACTICE?

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Introduction: The endoscopic approach of esophageal perforations poses a therapeutic challenge. Recently, a predictive score has been proposed to predict the chance of endoscopic stenting in patients with esophageal leaks. This score consists of 4 clinical variables that proved to be effective in discriminating the probability of success, especially when the probability of success is >70% or ≤50%, with lower discriminatory power in case of intermediate probabilities (50-70%).

Aims and Methods: We aimed to evaluate the applicability of the clinical score in a cohort of patients with anastomotic leaks managed with fully/partially covered stents in FAP.

Conclusion: The application of this predictive model proves to be useful in clinical practice, favoring management with endoscopic stenting in patients with probability of success ≥50%. It is cautious to consider other therapeutic options in patients with a lower probability of success.

Disclosure: Nothing to disclose

Reference

P0154 CLINICAL MANAGEMENT OF ENDOSCOPICALLY RESECTED PT1-CRC IN A HEREDITARY SETTING

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Introduction: Implementation of colorectal cancer (CRC) screening programs and the improvement of endoscopic techniques increases the endoscopic resection of polyps with early invasive CRC (pT1 Nx M0). The risk of lymph-node metastasis often leads to additional surgery, but despite guidelines, correct management remains unclear.

Aims and Methods: Aim of this study was to assess factors affecting the decision-making process in endoscopically resected pT1-CRCs in an academic centre. We retrospectively reviewed patients undergoing endoscopic resection of pT1-CRC from 2006 to 2016. Clinical, endoscopic, surgical treatment and follow up data were collected and analysed. Such lesions were categorized according to endoscopic/histological risk-factors in low- and high-risk groups. In detail, low-medium grade of differentiation, no lymphovascular invasion, no tumour budding, Haggi 1-3 and Kikuchi sm1, and en bloc resection was considered as low-risk pT1-CRC. Comorbidities were classified according to Charlson index (CCI). Surgical referral for each group was computed, and dissociation from current European CRC screening guidelines recorded. Multivariate analysis for factors affecting the post-endoscopic surgery referral was performed.

Results: 72 patients with endoscopically resected pT1-CRC were included. Overall, 20 (27.7%) and 52 (72.3%) were classified as low- and high-risk, respectively. In the low-risk group, 11 (55%) were referred to surgery, representing an over-treatment as compared with current guidelines. In the high-risk group, a non-surgical endoscopic surveillance was performed in 20 (38.5%) cases, representing a potential under-treatment. After median follow up of 30 (6-130) months, no patients developed tumour recurrence. At multivariate analysis, age (OR 1.21; 95% CI 1.02-1.42; p = 0.02) and co-morbidities (CCI ≥ 1.67, 95% CI 1.12-3.14; p = 0.04) were independent predictors for subsequent surgery.

Conclusion: A substantial rate of inappropriate post-endoscopic treatment of pT1-CRC was observed, when compared with current guidelines. This was apparently related with an over-estimation of patient-related factors rather than endoscopically or histological-related factors.

Disclosure: Nothing to disclose

P0155 PINE-CONE AND VILLI PATTERNS ARE ENDOSCOPIC SIGNS SUGGESTIVE OF ULCERATIVE COLITIS-ASSOCIATED COLORECTAL CANCER AND DYSPLASIA

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Introduction: Patients with ulcerative colitis (UC) are at high risk for the development of colorectal neoplasia: colitis-associated cancer or dysplasia. We recently performed a randomized controlled trial comparing targeted vs. random biopsy and demonstrated that targeted biopsies were almost comparable to random biopsies in terms of the neoplasia detection rate when performed by experienced colonoscopists; however, the appropriate site for targeted biopsy is still unclear. Therefore, endoscopic findings of neoplastic lesions for targeted biopsy are necessary for the further effective surveillance colonooscopy.

Aims and Methods: We aimed to elucidate key endoscopic findings suggestive of colitis-associated cancer or dysplasia. We retrospectively evaluated patients with UC-associated neoplasia. Surgical procedures were performed between April 2016 and October 2017 at a single referral centre (Department of Surgical Oncology, the University of Tokyo, Japan). Two gastrointetinal (GI) surgeons/endoscopists, who were blinded to the pathological diagnosis, independently assessed the images and classified them according to Kudo’s pit pattern and surface morphology, such as pine-cone/villi patterns. GI pathologists independently made pathological findings. The correlation between stereoscopic and pathological findings (neoplastic vs. non-neoplastic) for each image was investigated. The interobserver agreement was assessed using kappa statistics.

Results: Kudo’s neoplastic pit patterns (type III-V) were significantly correlated with the presence of neoplasia (sensitivity 77.4%, specificity 89.5%, positive
predictive value 92.8%), with a substantial concordance rate (kappa value 0.677). A hundred regions presented with pine-cone/villi patterns, which showed high specificity (96.8%) and positive predictive value (92.0%) for neoplasia, although sensitivity was low (21.4%). Concordance rate was also substantial (kappa value 0.625). A revision of the endoscopic findings of flat dysplasia with non-neoplastic pit patterns (9 lesions in 6 patients) revealed that 7 of 9 lesions had a reddish area with a demarcation line in each neoplastic lesion.

Conclusion: Targeted biopsies in surveillance colonoscopy for patients with UC must focus on lesions showing pine-cone/villi patterns in addition to Kudo’s non-neoplastic pit patterns such as type III, IV or V. For some flat neoplastic lesions with non-neoplastic pit patterns such as type I or II, a reddish area with a demarcation line may be one of the effective clues for targeted biopsy.

Disclosure: Nothing to disclose
P0159 Superior High-Quality Colon Cleansing with 1L NER1006 versus Sodium Polysulfate + Magnesium Citrate, 2L Polyethylene Glycol + Ascorbate, or Oral Sulfate Solution: Post-Hoc Pooled Analysis of Three Randomised Phase 3 Clinical Trials

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Introduction: High-quality colon cleansing is associated with improved lesion detection during colonoscopy (1-3). The cleansing efficacy and safety of NER1006, a novel 1L polyethylene glycol (PEG)-based bowel preparation, was evaluated in 3 randomised phase 3 trials DAYB1, MORA2, and NOCT3.

Aims and Methods: For each trial, this post hoc analysis compared the level of high-quality, segmental cleansing attained by NER1006 versus its comparator: Sodium Polysulfate + Mg Citrate (SPMC; DAYB), 2L PEG + Ascorbate (2LPEG; MORA) and Oral Sulfate Solution (OSS; NOCT). Dosing regimens varied by trial. All trials used treatment-blinded central reader-assessed cleansing scores and similar recruitment criteria. Alternative primary endpoints were overall and right colon cleansing using the validated Harefield Cleansing Scale (HCS). The number and share of high-quality segments (HCS score 3-4) assessed by a 3-image comparator were analysed in 3 primary analysis populations: The full analysis set (FAS; all randomised patients), the modified FAS (mFAS; FAS excluding any patient who failed lab screening after randomisation and who also did not take their study treatment), and the Per-protocol set (PP; FAS with fulfilled entry criteria, who took ≥75% of both study preparations doses, had data for at least 1 of the primary endpoints, and no major protocol deviations).

Results: A total of 1,985 patients were included in this analysis (Table 1). In each of the 3 primary analysis populations (FAS, mFAS, PP), day before dosing with NER1006 attained significantly more high-quality segments than with SPMC (16.9% vs. 10.4%, p < 0.001, 17.4% vs. 10.7%, p < 0.001, 18.4% vs. 10.7%, p < 0.001). Overnight split dosing with NER1006 showed more high-quality segments than with 2LPEG (46.1% vs. 29.0%, p < 0.001, 47.5% vs. 30.2%, p < 0.001, 48.7% vs. 32.5%, p < 0.001). Morning only dosing with NER1006 in AM also achieved more high-quality segments than overnight split dosing with 2LPEG PM/AM (46.8% vs. 29.0%, p < 0.001, 48.1% vs. 30.2%, p < 0.001, 50.6% vs. 32.5%, p < 0.001). Finally, overnight split dosing with NER1006 PM/AM delivered more high-quality segments than with OSS (40.1% vs. 36.2%, p = 0.013, 45.0% vs. 40.2%, p = 0.005). No serious adverse events were reported in the entire population in this post hoc pooled analysis.

Disclosure: Nothing to disclose

References:

P0160 R0 Resection Margin, a New Quality Measure in Era of National Bowel Screening?

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Introduction: Colorectal cancer is the second most commonly diagnosed cancer in Ireland. (1) Complete polypectomy is common among Endoscopists(2) NCCLS (National Colon Cancer Screening) colonoscopies are offered to bowel cancer screening patients after a positive Faecal Immunochromatographic Testing (FIT). These anecdotally have larger polyps. The goal of polypctomy is to achieve an R0 margin meaning that the margin is free of abnormal tissue.

Aims and Methods: To determine whether there is an association of R0 resection margin with Endoscopist, histopathologist, size, location and technique of polypectomy in an NCCS cohort. It was a retrospective observational study on 3 primary analyses between October 2013 and June 2017. These procedures were conducted in a single centre at Louth county hospital (LCH). SPSS software was used for statistical analysis. Statistical significance was set a priori at 0.05.

Results: In this ongoing study a total 542 colonoscopies were performed with no polyps in 19%. Here we present a subanalysis of 186 colonoscopies on which 707 polyps were identified. The average age was 66 years (SD 2.8) with 190 (27%) females. The polyp distribution was 255 (36%), 85(12%) and 365 (52%) in right, transverse and left colon respectively. Most of the polyps were less than 5 mm (59%) with 11.5% more than a cm in size. 152 (22%) had an R0 margin histologically, and 30 (5%) had involvement of the margin. In 373 (67%) polyps histopathologist were unable to assess the margin and (33%) polyps were not retrieved. Polypectomy technique in the form of hot snare had a direct relation with R0
Our study is the largest study comparing UEMR with conventional EMR. Accessibility of margins also had a linear relation with the size of the polyp, resection technique, statistically significant difference between hot snare and biopsy to cold biopsy and snare (p<0.02) and the reporting pathologist. Achieving an R0 margin was not statistically significant with endoscopic (experienced endoscopist on average do more than 300 colonic polyps per year), size and location of the polyp.

Conclusion: Only 25% of the polyps retrieved achieved an R0 margin while in 71% cases pathologist were unable to assess the margin. A multidisciplinary approach has to be developed between the endoscopist and pathologist achieving R0 margin. Polypometry requires significant focused training and experience to maximize success. In future, this could be included as a key performance indicator for polypectomy. We also recommend more studies on margin analysis.

Disclosure: Nothing to disclose.

Reference

P0161 COMPARING THE EFFICACY AND SAFETY BETWEEN UNDERWATER ENDOSCOPIC MUCOSAL RESECTION AND CONVENTIONAL ENDOSCOPIC MUCOSAL RESECTION IN RESECTING SESSILE COLORECTAL NEOPLASMS: A PROPENSITY SCORE-MATCHED COHORT STUDY

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Introduction: Colonoscopy resection of colorectal polyps has been shown to reduce colorectal cancer related death.1 For sessile colorectal polyps, endoscopic mucosal resection (EMR) is an established method for the removal of.2 However, recurrence after EMR is a major limitation. Piecemeal resection and intraprocedural bleeding are reported to be risk factors of recurrence after EMR.3,4 Underwater EMR (UEMR) was proposed as an alternative method for removal of colorectal polyps.5 There is no large-scale dataset directly comparing the efficacy and safety of UEMR with conventional EMR in resecting average sized lesions.

Aim of Study: The aim of our study is to compare efficacy and safety of UEMR with conventional EMR in average sized colorectal sessile polyps using a large retrospective cohort with propensity score matched design.

A retrospective observational study was conducted on all adult patients referred to us for endoscopic resection of sessile colorectal polyps between August 2012 and November 2017. During this period, conventional EMR was performed until August 2015, when UEMR was introduced to our hospital, and UEMR was performed for all lesions after August 2015. Follow-up of the patients was by a clinic visit around 7–14 days after the procedure to monitor adverse events. Surveillance colonoscopy was scheduled according to MSTF guidelines. The outcome measures included en bloc resection rate, procedure time, bleeding, and margin status. We match and control the baseline differences of both groups in a 1:1 ratio by calculating propensity scores using a multivariable regression model.

Results: 462 lesions in 407 consecutive patients were treated. In the first study period between August 2012 and August 2015, all of the 256 lesions in 222 patients were resected by conventional EMR. In the second study period between August 2015 and November 2017, all of the 206 lesions in 183 patients were resected by underwater EMR.

- The propensity score matching created 170 matched pairs (totally 340 patients).
- The mean age was 64 years old.
- With highest ADR in the 6 months immediately after intervention.
- The Sydney EMR recurrence tool.

Conclusion: The aim of this study is to compare individual ADR before and after intervention, and determine factors associated with response in a multi-centre study in Singapore. We also recommend more studies on margin analysis.

Disclosure: Nothing to disclose.

References

P0162 INCREASED WITHDRAWAL TIME ALONE MAY NOT IMPROVE ADENOMA DETECTION RATE: A MULTI-CENTRE STUDY ON IMPACT OF INDIVIDUAL QUALITY SCORES

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Introduction: Adenoma detection rate (ADR) is a key indicator of colonscopy quality. Previous studies have shown that performance feedback can improve ADR, but these were mostly based in the West and lack examination of factors associated with response.

Aims and Methods: The aim of this study is to compare individual ADR before and after intervention, and determine factors associated with response in a multi-centre study in Singapore. We also recommend more studies on margin analysis.

Aim of Study: The aim of this study is to compare individual ADR before and after intervention, and determine factors associated with response in a multi-centre study in Singapore. We also recommend more studies on margin analysis.

Results: 33 endoscopists who performed 21,760 scopes met the inclusion criteria. Overall adjusted baseline ADR was 27.3%(±1.3%) and increased to 31.8%(±0.9%) after intervention (p<0.01). At baseline, 12 endoscopists had ADR < 25%. Their ADR increased from 17.0%(±2.0%) to 27.3%(±1.3%) after intervention (p<0.01), with highest ADR in the 6 months immediately after intervention. APC, proximal ADR, proportion of cases with large poly<5mm also increased after intervention (0.25 to 0.50, 8.8% to 16.3%, 14.7% to 22.8% respectively, all p<0.01). 6 responders and 6 non-responders were identified. Responders had higher mean patient age (66.6 vs. 56.3 years), performed more scopes with BBPS>5 (94.9% vs. 92.0%, p<0.01) and more screening scopes (33.4% vs. 25.3%, p<0.01) than non-responders. Non-responders had shorter WT, but this difference was not significant after intervention (0.01). 5(94.9%) responders had higher quality scores in ADR after intervention.

Conclusion: Quality scorecards were successful in improving ADR in a multi-centre study in Asia. Response to feedback is multi-factorial. Increased WT alone without improving other modifiable factors may not result in improved ADR after feedback.

Disclosure: Nothing to disclose.

References

P0163 USEFULNESS OF JNET CLASSIFICATION WITH DOUBLE-FOCUS Magnification FOR DIAGNOSIS OF COLORECTAL TUMORS: SINGLE CENTER RETROSPECTIVE STUDY

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Introduction: Narrow-band imaging (NBI) magnifying endoscopy has been reported to be useful for qualitative and quantitative diagnosis of colorectal lesions. Recently, Japan NBI Expert Team (JNET) classification was advocated which is the first universal narrow-band imaging magnifying endoscopic classification for colorectal tumors. The method, magnifying endoscopy requires high experience and skill. On the other hand, dual-focus NBI with electronic zoom (DF-NBI) can easily provide almost the same image of optical zoom magnifying images only by button push.

Aims and Methods: The aim of study is to clarify the usefulness of JNET classification with DF-NBI for colorectal tumors. We analyzed consecutive 290 colorectal lesions, which were diagnosed by JNET classification with DF-NBI observation before endoscopic treatment or surgery between April 2017 and
March 2018. The instrument used in this study was a dual focus endoscope (CF- HD160, Olympus). The lesions were diagnosed in accordance with the criteria of the World Health Organization. Using these cases, we examined the relationship between each type of the JNET classification with DF-NBI and histopathological findings. We calculated sensitivity, specificity, positive and negative predictive value (PPV and NPV), and accuracy for each category of the classification. The JNET classification; the colorectal NBI magnifying classification consists of 4 types that are classified based on vessel pattern and surface pattern. The characteristics of Type 1 are invisible vessel pattern and having regular dark or white spots as surface pattern. The characteristics of Type 2A are regular vessel pattern. Polyp size over 25mm was a risk factor of intra-procedural bleeding (p=0.015). Polyp size over 25mm was a risk factor of intra-procedural bleeding after EMR without detachable snare.

**Conclusion:** 1:20000 epinephrine injection should be performed for over 25mm colon polyp to prevent intra-procedural bleeding after EMR without detachable snare.

**Disclosure:** Nothing to disclose

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**P0165 THE EFFECT OF PROPHYLACTIC CLIP PLACEMENT ON DELAYED BLEEDING FOLLOWING ENDOSCOPIC MUCOSAL RESECTION OF LARGE COLORECTAL LESIONS: A META-ANALYSIS**

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**Introduction:** The main aim of this study was to conduct a meta-analysis on the effect of clipping on DPB following endoscopic mucosal resection (EMR) of colorectal lesions ≥ 20 mm.

**Aims and Methods:** The main aim of this study was to conduct a meta-analysis on the effect of clipping on DPB following endoscopic mucosal resection (EMR) of colorectal lesions ≥ 20 mm. We performed a search of PubMed and the Cochrane library for studies comparing the effect of clipping vs. no clipping on DPB following endoscopic resection. The Cochran Q test and I2 were used to test heterogeneity. Pooling was conducted using a random-effects model.

**Results:** 13 studies with a total of 7794 polyps were included. Overall, when lesions of all sizes and types of endoscopic resection (conventional polypectomy, EMR or endoscopic submucosal dissection [ESD]) were included, DPB was observed less frequently with clipping (1.3%) as compared to no clipping (2.7%) (pooled OR 0.50, 95% CI: 0.25–0.91, p=0.02). In the subgroup analyses, clipping was also associated with a decrease in the rate of DPB after (1) resection of lesions ≥20 mm (pooled OR: 0.33; 95% CI: 0.18–0.62; p=0.001) and for lesions <20 mm removed by EMR (pooled OR 0.24, 95% CI: 0.12–0.50, p<0.001).

**Conclusion:** Prophylactic clipping may reduce DPB following EMR of large colorectal lesions. Future trials are needed to further identify risk factors and stratify high risk cases in order to implement a cost-effective preventive strategy.

**Disclosure:** Nothing to disclose
significant difference in age, sex, current medication, reason for colonoscopy, colonoscopic findings and polyp detection rate between the 2 groups. Constipation and past history of abdominal surgery was found to be predictive of a failed repeated preparation (Odd ratio = 1.54, 95% CI (1.14-2.07), p = 0.004).

Conclusion: Second colonoscopy on next day with NaP 45 mL was more effective than after 7 days with PEG 4L in colonic preparation failure. Constipation and past history of abdominal surgery were significant risk factors of repeated preparation failure.

Disclosure: Nothing to disclose.

P0167 1L NER1006 ACHIEVES HIGH-QUALITY BOWEL CLEANSING WITH LOWER TOTAL FLUID VOLUME INTAKE THAN STANDARD POLYETHYLENE GLYCOL + ASCORBATE: A POST-HOC ANALYSIS

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Introduction: Successful bowel cleansing is required for effective colonoscopy. Polyethylene glycol (PEG)-based bowel preparations are widely used for this, despite many still requiring high fluid volume intake. To enhance the patient experience, the phase 2 study OPT2 assessed the clinical proof of concept of NER1006, a novel 1L PEG-based bowel preparation, versus standard 2L PEG + ascorbate (2LPEG). Here we report the cumulative segmental cleansing score versus total fluid intake for NER1006 and the Control.

Aims and Methods: The OPT2 study had 2 parts and evaluated 5 different low volume PEGs vs the control. This post-hoc analysis assessed the lead phase 3 candidate, NER1006, from Part 2 of the study vs the Control. Treatment-blinded colonoscopists assessed the bowel cleansing quality using the Harefield Cleansing Scale (HCS). For each patient, the sum of observed segmental cleansing scores (0-4) for each of the 5 segments (cumulative maximum total = 20), and the total fluid volume intake (i.e. preparation volume + mandatory additional clear fluid volume + voluntary ad libitum clear fluid volume) were assessed. The number and share of patients who attained high-quality cleansing (segmental HCS scores 3 or 4) in all segments (cumulative HCS score of 15 or higher) were calculated.

Results: 60 patients underwent screening colonoscopy (Table 1). They were either 40 to 70 years old with a known personal or familial risk of contracting colorectal cancer, or 55 to 70 years old. 30 patients per group had their bowels prepared within less than 5mm in diameter, that was 10.4%, 0% and 0%, respectively. Most of the flat-type (91.9%) and protruded-type (94.3%) lesion showed type III or IV pit pattern corresponding to adenomas, whereas 91.7% of the depressed-type lesions were characterized by type III, VI or VN pit patterns corresponding to carcinomas. For endoscopists, most of the flat- and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3 (59.0%) and EC3b (53.5%) corresponding to invasive carcinomas.

Conclusion: This study revealed the diagnostic characteristics of depressed-type lesions. They show typically type III, VI or VN pit patterns in magnifying endoscopy and type EC3a or EC3b in endoscopy. These lesions tend to invade the submucosal layer even when they are small. It is important to diagnose colorectal neoplasms according to their morphology.

Disclosure: Nothing to disclose.

P0169 ENDOCYTOSCOPY FEATURE OF DEPRESSED TYPE COLORECTAL NEOPLASMS IN MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY

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Introduction: Colorectal cancers are generally recognized to develop from polyps. This adenoma-carcinoma sequence theory has been in the mainstream of development of colorectal cancers. However, recently the existence of many depressed-type lesions has been revealed, which are considered to emerge directly from normal epithelium, not through the adenomatous stage. This theory is called de novo pathway.

Now, it is possible to presume the histology of colorectal lesions using magnifying endoscopy (pit pattern classification) and endocytoscopy (EC classification). We can observe not only the structural atypia but also the cellular atypia in vivo.

Aims and Methods: The aim is to clarify the endoscopic characteristics of depressed-type colorectal neoplasms, demonstrating the validity of pit pattern and EC classification.

A total of 30021 colorectal neoplasms excluding advanced cancers were resected endoscopically or surgically in our unit from April 2001 to May 2017. Of these, 22958 lesions were low-grade dysplasia, 5913 were high-grade dysplasia and 1150 were submucosally invasive (T1) carcinomas. According to the developmental morphology classification, they were divided into 3 types: depressed, flat and protruded-type. We investigated the rate of T1 carcinomas and the characteristics of depressed-type neoplasms concerning pit pattern and EC classification.

Results: The rate of T1 carcinomas in depressed-type lesions reached to 62.1%, meanwhile that in flat-type and protruded-type lesions was 3.4% and 2.9%, respectively. Within less than 3mm in diameter, that was 10.4%, 0% and 0%, respectively. Most of the flat-type (91.9%) and protruded-type (94.3%) lesion showed type III or IV pit pattern corresponding to adenomas, whereas 91.7% of the depressed-type lesions were characterized by type IIIS, VI or VN pit patterns corresponding to carcinomas. For endoscopists, most of the flat- and protruded-type lesions showed EC2 corresponding to adenomas. In contrast, the depressed-type lesions were observed as EC3a (59.0%) and EC3b (53.5%) corresponding to invasive carcinomas.

Conclusion: This study revealed the diagnostic characteristics of depressed-type lesions. They show typically type III, VI or VN pit patterns in magnifying endoscopy and type EC3a or EC3b in endocytoscopy. These lesions tend to invade the submucosal layer even when they are small. It is important to diagnose colorectal neoplasms according to their morphology.

Disclosure: Nothing to disclose.
**P0171 PERIOPERATIVE HEPARIN BRIDGING FOR ENDOSCOPIC RESECTION OF THE COLORECTAL TUMOR FOR PATIENTS RECEIVING ANTICOAGULATION RESULTED IN A HIGHER INCIDENCE OF BLEEDING COMPLICATION THAN OTHER HIGH-RISK ENDOSCOPIC PROCEDURES**

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**Introduction:** In the ESGE and Japanese guidelines, perioperative heparin bridging is recommended for high thrombotic risk patients who are receiving anticoagulation before endoscopic procedures. We retrospectively investigated clinical outcomes of patients with atrial fibrillation who had been applied perioperative bridging anticoagulation by intravenous unfractionated heparin for high-risk endoscopic procedures at our institution between April 2006 to June 2017.

**Aims and Methods:** We retrospectively investigated clinical outcomes of patients with atrial fibrillation who had been applied perioperative bridging anticoagulation by intravenous unfractionated heparin for high-risk endoscopic procedures at our institution between April 2006 to June 2017. (1) Warfarin was discontinued 5 days before the procedure and intravenous unfractionated heparin was started with 5000 unit bolus followed by 500 unit per kilogram of body weight per day continuous intravenous injection. (2) Activated partial thromboplastin time (APTT) was evaluated to adjust the dose of heparin to raise APPT to 45 to 70 seconds. (3) Heparin was discontinued 4-6 hours before the endoscopic procedure and resumed from the next morning. (4) Warfarin was also resumed along with heparin with a loading dose of 5mg for 3 days followed by a preoperative dose of the patient. (5) Heparin was discontinued when INR reached 1.6 or higher. The primary outcomes were arterial thromboembolic events within 30 days of the endoscopic procedures, and postoperative bleeding events that needed endoscopic hemostasis or blood transfusions were treated as complications. Results: During the study period, 76 cases received high-risk endoscopic procedures among them, 2 cases refused heparin bridging, thus we assessed 74 (19 females) cases with a mean age of 73.8 years old in the study. The endoscopic procedures were colorectal EMR or ESD (29 cases), gastric ESD (23 cases), colorectal sphincterotomy (15 cases), esophageal ESD (15 cases), and duodenal EMD (2 cases). There was no arterial thromboembolic event within 30 days of the endoscopic procedures, and postoperative bleeding events that needed endoscopic hemostasis or blood transfusions were treated as complications. Discussion: Nothing to disclose

**References**


**P0172 1L NER1006 EVENING/MORNING DOSE SUSTAINS SUCCESSFUL COLON CLEANSING IN 7 OUT OF 8 PATIENTS EVEN 7+ HOURS AFTER THE SECOND DOSE: POST-HOC ANALYSIS OF OVERNIGHT SPLIT-DOSING REGIMENS OF 1L NER1006 VERSUS 2L POLYETHYLENE GLYCOL + ASCORBATE OR ORAL SULFATE SOLUTION**

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**Introduction:** In colorectal EMR/ESD, perioperative heparin bridging should be applied for high thrombotic risk patients who are receiving anticoagulation before endoscopic procedures. Aims and Methods: To retrospectively investigate clinical outcomes of patients with atrial fibrillation who had been applied perioperative bridging anticoagulation by intravenous unfractionated heparin for high-risk endoscopic procedures at our institution between April 2006 to June 2017.

**Results:** During the study period, 76 cases received high-risk endoscopic procedures, among them, 2 cases refused heparin bridging, thus we assessed 74 (19 females) cases with a mean age of 73.8 years old in the study. The endoscopic procedures were colorectal EMR or ESD (29 cases), gastric ESD (23 cases), colorectal sphincterotomy (15 cases), esophageal ESD (15 cases), and duodenal EMD (2 cases). There was no arterial thromboembolic event within 30 days of the endoscopic procedures, and postoperative bleeding events that needed endoscopic hemostasis or blood transfusions were treated as complications. Discussion: Nothing to disclose

**References**


This post hoc analysis assessed the duration of the cleansing efficacy so treatments with sustained high efficacy would be valuable.4

High-quality bowel cleansing facilitates effective colonoscopy.1–3

Aims and Methods: Patients aged 18–85 years were randomized to receive a split-dosing regimen of either evening/ morning (PM/AM) NER1006, or 2LPEG or OSS. Overnight split dosing started at ~6:00 pm (± 2 h) with dose 2 at ~6:00 am (± 2 h). The percentage of patients with overall bowel cleansing success (Harefield Cleansing Scale grades A and B) was analysed by duration between the end of the second dose of the bowel prep plus mandatory fluids and the start of colonoscopy (1-h intervals: ≤ 3, > 3–4, > 4–5, > 5–6, > 6–7, or > 7 h). Data were analysed in the modified full analysis set (mFAS) population, which comprised all patients who received at least 1 dose of study drug and who had documented primary colonoscopy data from a central reader. Patients included in the analysis of variance (ANOVA) between time intervals and colon cleansing success also needed calculable time intervals after dose 2.

Results: Data from 1037 patients were included in the analysis (Table 1). In time intervals from up to 3 h to over 7 h after dose 2, successful bowel cleansing was attained in at least 88% (7 out of 8) patients with NER1006 PM/AM regimen. At >7 hours NER1006 PM/AM attained at least 89.3% HCS cleansing success whereas this level of cleansing efficacy was not attained by either 2LPEG or by OSS (p < 0.001). Data showed reduced success rates after 7 hours (81.3% and 77.4%, respectively). The ANOVA revealed a significant decline in efficacy over time for OSS (p = 0.033). No such differences were observed for NER1006 PM/AM (p = 0.32, MORA, p = 0.36, NOCT) or 2LPEG (p = 0.15).

Conclusion: Split dosing with NER1006 evening morning dosing can, in a reproducible fashion, deliver overall cleansing success in 7 out of 8 patients even after 7 or more hours post dose 2. This sustained efficacy may become particularly useful for afternoon or delayed colonoscopies.

Disclosure: Bharat Amlani and Lucy Clayton, employees of Norgine Ltd. Cesare Hassan was an investigator in the DAYB study and received honoraria from Norgine Ltd or investigator advisory board attendance.

References
Introduction: Computer-aided diagnosis (CAD) for colonscopy is drawing attention as an attractive tool to identify neoplastic polyps requiring resection from non-neoplastic polyps that can be left in situ [1]. However, its role has not been established because of the lack of high-quality clinical trials.

Aims and Methods: We aimed to clarify the efficacy of “real-time” use of CAD with 500-fold ultra-magnifying endoscopes [2] with a single arm, open-label, prospective trial. This trial included 821 patients undergoing colonoscopy with use of CAD in a tertiary university hospital between June and December 2017. CAD predicted pathology (neoplastic or non-neoplastic) of the diagnosis of diminutive polyps (≤5 mm) based on real-time outputs. CAD performance was evaluated, with the actual pathology of the resected specimen as the gold standard. The CAD system had been trained with 61925 endoscopic images acquired from a total of 5 universities hospitals and cancer center hospitals in Japan, where we established the diagnostic strategy of using CAD in the field. The primary aim of this study was to assess the cost and benefits of endoscopic submucosal dissection. The secondary aims of the study are to assess the part of sterile medical devices (SMD) in the overall cost of the procedure, to determine predictive factors for a positive cost/benefit balance and to do a medicoeconomic comparative with surgery for superficial colonic neoplasms.

Results: Overall, 466 diminutive polyps (including 250 in the rectosigmoid colon) from 325 patients were assessed by CAD using both the narrow-band imaging (NBI) mode and the methylene blue-stained mode. CAD was able to analyze 95.1% (457/486) of the polyps. Intention-to-treat analysis, in which non-analyzable polyps were treated as misdiagnosed ones, revealed mean NPsVs for CAD regarding diminutive, rectosigmoid polyps of 95.2% (95% confidence interval, 90.3–98.0) for the NBI mode and 93.7% (88.3–97.1) with the stained mode. The diagnostic sensitivity, specificity, and accuracy of CAD were as follows; 83% (95% confidence interval, 64%–94%), 97% (94%–99%), and 93% (89%–96%) in the segment-based analysis, 77% (64%–87%), 97% (94%–99%), and 93% (89%–96%) in the patient-based analysis, respectively. The difference between the overall cost and the revenue provide the medicoeconomic study with core information. We have selected in the same center patients who had surgery from 2009 to 2017 for superficial colonic neoplasms in our hospital. After the etiologic factor analysis by Stepwise logistic regression analyses, the predictive factor for a positive budgetary balance which was a severity level of DRG higher than 1 (OR 9.91; IC95% 11.3–214.25; p < 0.0001). We compared colonic surgery and ESD for superficial lesions in the same center/hospital. 69 patients were in surgery and 71 in ESD. There is no significant difference between the 2 groups in terms of age, localization, anatomopathology or ASA score. The size of lesions was twice higher in ESD than in surgery (50 mm vs. 25 mm; p < 0.0001). The average length of hospitalization was superior in surgery (11 days vs. 2 days in ESD; p < 0.0001). Morbidity at 30 days was not significantly superior in surgery (28 vs. 14% in ESD; 0.061). At country level, the cost of surgery was 5 times higher if we consider revenue related to the stay (€8,960 vs. €1,770; p < 0.0001). But at the hospital scale, the budgetary balance was positive for surgery patients (€2,400 vs. -€8,800 in the dissipation of cost).

Conclusion: As of today, the ESD benefit/deficit balance is negative in 80% of cases. Overcharge is due to a lack of act ranking. Specific dissection equipment accounts for the largest share of expenditures. It is clearly less morbid and expensive than classic surgery.

Disclosure: Nothing to disclose.
pathological diagnoses (non-neoplastic, adenoma, SSA/P, invasive cancer). The high diagnostic ability of EC-CAD to distinguish between adenoma and invasive cancer has already revealed in previous report [2]. As a next step, we conducted a prospective study to evaluate the real-time use of the current system.

Aims and Methods: The primary endpoint of this study was to verify the positive predictive value (PPV) in distinguishing invasive cancer from other lesions was 90% or higher when EC-CAD was applied for examination. This prospective study was conducted at Showa University Northern Yokohama Hospital from June 2017 to December 2017. In this study, we used the software constructed based on EC images obtained by staining cell nuclei with 1.0% methylene blue. At the start of the study, we used software that let the system learn 16000 images. During the study period, we made an update 3 times (the number of learning images for the system: 1st 18966 images, 2nd 32265 images, 3rd 36586). The subjects were colorectal lesions of 2mm or more in diameter which histological evaluation was performed after EC observation. Regarding the diagnostic results given by the EC-CAD, since a plurality of endoscopic images were acquired from one lesion, the majority decision method adopting the most frequent diagnostic result was used as a first diagnosis of the system. As a sub analysis, the endoscopists were divided into experts and trainee based on the difference in experience, and it was examined whether procedure time and diagnostic accuracy using EC-CAD were affected by the expertise.

Results: A total of 106 colorectal lesions (4 non-neoplasms, 34 adenomas, 68 invasive cancers (10 T1 cancers, 58 T2-T4 cancers)) from 99 patients were included. 77% (6434/8313) of the acquired EC images were able to be diagnosed by EC-CAD. Regarding the diagnostic performance of EC-CAD to distinguish invasive cancers from other lesions, sensitivity, specificity, accuracy, PPV and negative predictive value (NPV) were 93%, 97%, 94%, 98% and 88%, respectively. Considering experts and trainees separately, the sensitivity, specificity, accuracy, PPV, NPV were 93% vs. 93%, 97% vs. 100%, 94% vs. 94%, 98% vs. 100% and 89% vs. 67%, respectively. The time taken for EC image acquisition was 5.6 seconds on average. There was no significant difference in image acquisition time between experts (5.5 sec) and trainees (6.3 sec).

Conclusion: It suggested that EC-CAD will provide a reliable diagnosis with PPV 90% or higher in distinguishing invasive cancer from other lesions, regardless of the experience of endoscopists.

Disclosure: Nothing to disclose

References

P0178 TRAINEES’ INFLUENCE ON ADENOMA DETECTION AND FOLLOW-UP RECOMMENDATIONS AT SCREENING AND SURVEILLANCE COLONOSCOPES

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Introduction: Colorectal cancer has emerged as the main diagnostic and therapeutic tool in the detection of colonic adenomas. Training future endoscopists is essential to meet future demands.

Aims and Methods: In this study we have shown somewhat conflicting results regarding the influence of trainee-participation on adenoma detection rates (ADR), mostly showing positive or indifferent effects of trainee participation. A previous prospective study by our group showed no adverse effect of trainee participation on ADR. This study did not include first year trainees or subsequent surveillance exams. The aim of the current investigation was to see, whether the inclusion of first year trainees magnifies the noted difference and whether trainee participation affects ADRs or the timing of subsequent surveillance exams. A retrospective analysis of average-risk screening colonoscopies over a 3-year interval was performed. Patients with poor preparation were excluded. The final analysis included 4922 screening colonoscopies between the years 2004-2006, as well as 2184 subsequent surveillance exams. Data were collected from pathologic and endoscopic electronic data bases. The primary outcome was the ADR at colorectal polyps with and without early-stage colorectal cancers.

Results: Trainees participated in 1131 (23%) screening exams and in 232 (11%) surveillance exams. ADR did not significantly differ (p = 0.19) for screening exams with trainee participation (19.5%) or those without (21.4%). ADRs were generally higher at surveillance exams, both with (22.4%) and without (27.5%) trainee participation. The noted difference of ADRs at surveillance colonoscopies with or without trainee participation did not reach statistical significance (p = 0.1). Multivariate analysis showed no influence of first year fellow participation on the outcome. When surveillance recommendations differed from guidelines, shorter surveillance intervals were given more frequently if trainees participated during the initial screening procedure (p = 0.001).

Limitations: Single-center, retrospective study.

Conclusions: ADR did not significantly differ at screening or surveillance colonoscopies with or without trainee participation. There was a trend towards higher ADR at surveillance exams in both groups. The inclusion of first year trainees had no adverse effect on the outcome. However, trainee participation may result in shortened surveillance recommendations after initial screening exams.

Disclosure: Nothing to disclose

P0179 DEVELOPMENT OF A REAL-TIME ENDOSCOPIC IMAGE DIAGNOSIS SUPPORT SYSTEM USING DEEP LEARNING TECHNOLOGY IN COLONOSCOPY

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Introduction: The development of a real-time robust detection system for colorectal neoplasms will significantly reduce the risk of missed lesions during colonoscopy. However, gaps in colonoscopy skills among endoscopists, primarily due to experience, have been identified, and solutions are critically needed.

Aims and Methods: To overcome this experience gap, we aimed to develop an artificial intelligence (AI) system that automatically detects early signs of colorectal cancer during colonoscopy.

Patients with and without colorectal polyps and those with colorectal cancer were included. A training data set of 5,000 images of 2,116 early-staged colorectal cancers or precursor lesions and 134,983 images of noncancerous tissue were provided. Using this training set, Deep Learning algorithms were provided to learn the colonoscopic features of the disease. The diagnostic accuracies and area under the receiver-operating characteristic curve of this algorithm as well as the processing speed of this AI system were measured by using validation set of 4,840 images (705 images with 752 lesions and 4135 images without lesions) from consecutive patients with and without early-staged colorectal cancers or precursor lesions.

Results: The sensitivity and specificity of the system were 97.3% (95% confidence interval [CI] = 95.9%-98.3%) and 99.0% (95% CI = 98.6%-99.2%), respectively, and the area under the curve was 0.975 (95% CI = 0.964-0.986) in the validation set. The sensitivities were 98.0% (95% CI = 96.6%-98.8%) in the polyoid subgroup and 93.7% (95% CI = 87.6%-96.9%) in the nonpolyoid subgroup. A supplementary human observational study demonstrated that the AI system had a superior diagnostic yield as endoscopists, including experienced, fellows, and beginners (Figure 1). The system analyzed all 4,840 images in 106.0 seconds (average, 21.9 ms/image), whereas endoscopists required median 725.2 seconds (IQR = 655-914) to analyze the 309 images. In addition, this system achieved in real-time detecting and displaying results of each video frame within 33 milliseconds (30 frames per second).

Conclusion: We have developed a real-time endoscopic image diagnosis support system using deep learning technology that automatically detects early signs of colorectal cancer during colonoscopy. This AI system can alert endoscopists in real time to avoid missing abnormalities such as polyps during colonoscopy, improving the early detection of this disease.

Disclosure: Nothing to disclose

Abstract No: P0179

<table>
<thead>
<tr>
<th>Sensitivity* (n) (95% CIs)</th>
<th>Specificity** (n) (95% CIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All lesions (752 lesions)</td>
<td>97.3% (732/752) (95.9-98.3)</td>
</tr>
<tr>
<td>Polypoid lesions (641 lesions)</td>
<td>98.0% (628/641) (96.6-98.8)</td>
</tr>
<tr>
<td>Flat and depressed lesions (111 lesions)</td>
<td>93.7% (104/111) (87.6-96.9)</td>
</tr>
</tbody>
</table>

*Sensitivity was defined as AI correctly detected lesion number/number of all lesions; **Specificity was defined as AI negative image number/true lesion negative image number (images without lesions); Correct answer was defined when AI detect and display loci of lesion by flag.
PO1080 GRADING OF DYSPLASIA FOR DIAGNOSING COLORECTAL ADENOMAS USING ENDOCYTOSCOPY (EC)

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Introduction: Recent opinions have expressed that if an endoscopic diagnosis of adenomas can be made with high accuracy, then the omission of a pathological diagnosis following endoscopic resection is acceptable. Currently, there is no clear consensus regarding whether endoscopic treatment is required for all adenomas. Colonoendoscopy-based grading of dysplasia can be clinically effective for diagnostic purposes, if such a diagnosis of adenomas, particularly of low-grade adenomas, can be made with high accuracy.

Aims and Methods: In this study, we focused on the existence of mixed-pit pattern type I lesions in slit-like lumens, which is an endoscopiccytoscopic (EC) finding characteristic of adenomas, and investigated pathological findings that were correlated with this observation. We retrospectively examined 700 lesions among the neoplastic lesions that could be observed by EC between May 2005 and May 2017 and that were classified as EC2 according to the EC classification system and could be pathologically examined after endoscopic resection. Lesions characterized by mixed-pit pattern type I lesions were classified as EC2 normal pit (NP) sign (+), while those characterized by slit-like lumens only were classified as EC2 NP sign (−). We investigated the final pathological diagnosis results. In addition, we investigated the concordance rate of surveillance interval recommendation in EC diagnosis and pathological diagnosis based on USA guideline, and also examined the location, diameter, and morphological type of lesions to elucidate their clinical traits. In order to evaluate the concordance rate of EC 2 NP sign, 3 experts (T.K., Y.M. and M.M) and 3 trainees (T.W., T.K and K.M) reviewed digitally recorded EC images of the lesions.

Results: A total of 466 lesions were classified as EC2 NP sign (+). Of these, low-grade adenomas accounted for 450 lesions and advanced lesions (high-grade dysplasia, tubulovillous adenoma, invasive cancer) accounted for 16. NP sign (+) as an indicator of low-grade adenomas had a sensitivity of 85.4%, specificity of 90.8%, positive predictive value of 96.6%, negative predictive value of 67.1%, accuracy of 86.7%, and positive likelihood ratio of 9.23. It was 95.5% that the concordance rate of surveillance interval recommendation based on USA Guideline compared with EC and pathological diagnosis. Furthermore, an examination of the EC 2 NP sign (+) rate by location, diameter, and morphological type of lesions revealed that 75.7% were located in the proximal colon (p < 0.001), 81.4% of the lesions were ≤ 10 mm in diameter (p < 0.001). Further, 75.8% were of the flat/depressed type (p < 0.001). The interobserver agreement for the EC2 diagnosis following endoscopic resection is acceptable. Currently, there is no clear consensus regarding whether endoscopic treatment is required for all adenomas. Colonoendoscopy-based grading of dysplasia can be clinically effective for diagnostic purposes, if such a diagnosis of adenomas, particularly of low-grade adenomas, can be made with high accuracy.

References

PO1081 DEVELOPMENT OF A MODIFIED SMSA SCORING SYSTEM WITH IMPROVED ACCURACY IN THE PREDICTION OF COMPLICATIONS OF ENDOCYTOSCOPIC MUCOSAL RESECTION IN THE COLON

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Introduction: ADR (adenoma detection rate) is generally accepted quality indicator. For possible gaming with ADR other indicators are needed. MAP (mean adenoma per colonoscopy) reflects the quality of examination of entire colon and is considered to be the most objective quality indicator.

Aims and Methods: The aim of our study was to compare MAP with ADR and PDR (polyp detection rate) of all colonoscopists in our department. We retrospectively assessed the quality indicators of all colonoscopies performed in non-university hospital Frydek-Mistek from January 2013 to December 2017. We counted ADR, PDR and MAP for all colonoscopies in patients over 50 years of age excluding therapeutic, IBD, management of complications and sigmoidoscopy screening (screening, surveillance, diagnostic) and separately only for screening colonoscopies. Correlations between MAP, ADR and PDR were performed using Pearson’s correlation coefficient, p<0.05 was considered significant.

Results: The group for statistics comprised 6925 patients (3620 men, 3305 women, mean age 66.2 years). There were positive correlations between ADR of screening and pathological diagnosis. Furthermore, an examination of the EC2 NP sign among the 3 experts was 0.82, 0.90, and 0.94 and among the 3 trainees were 0.84 (T.K., Y.M.), 0.78 (T.K.-M.M.) and 0.82 (Y.M.-M.M.), respectively. The intraobserver agreement for the 3 experts agreed 0.84 (T.W.-T.K.), 0.86 (T.W.-M.K.) and 0.98 (T.K.-M.M.), and the 3 trainees were 0.80, 0.80 and 0.86, respectively.

Conclusion: These results suggest that when using EC for diagnosing colorectal neoplastic lesions, NP sign is a good indicator of low-grade adenomas with the EC2 classification. It was suggested that EC diagnosis could make it easier to determine whether endoscopic treatment is needed or not. Furthermore, the NP sign (+) rate tended to be high in lesions located in the proximal colon, that were ≤ 10 mm in diameter, and that were of the flat/depressed type.

Disclosure: Nothing to disclose

References
colono-scopies performed in non-university hospital Frydek-Mistek from January 2011 to October 2017 were counted ADR in all colonoscopies over 50 years of age excluding therapeutic, IBD, management of complications and sig-moido-scopies (screening, surveillance, diagnostic) and separately only for screening colonoscopies. Correlation analysis was performed using Pearson’s correlation coefficient, multiple chi square test was used to compare patients’ age and one anoVA was used to compare proportion of men and women among endoscopists, p < 0.05 was considered significant.

Results: In study period, 10472 colonoscopies and sigmoido-scopies were done in total. The number of polyps in the left colon becomes < 1 (F = 39.82 p < 0.001).

Conclusion: Right-sided colon polyps more likely to have dysplasia compared with left-sided polyps. Therefore, missing a polyp in the right colon is likely more significant than missing one in the left colon and guidelines should focus a stratification on the proximal colon and provide feedback to endoscopists regarding their proximal adenoma detection rates.

Differences in proportion of men and women (p = 0.048) and age of patients (p = 0.002). This should be taken into consideration when comparing various endoscopists but it does not affect the correlation analysis of ADR from all and screening colonoscopies. ADR for screening and surveillance were higher than for diagnostic colonoscopies in all endoscopists, ADR for all colonoscopies were lower than for screening but sufficiently by over 25 %, see the table. There was positive correlation between ADR of screening and all colonoscopies (r = 0.008 p < 0.005).

N ADR N ADR N ADR
Endoscopist N all ADR all screening surveillance ADR diagnostic
1 1467 39.1 567 41.3 380 45.3 520 32.1
2 419 47.0 146 49.3 186 52.7 87 31.0
3 815 37.7 170 40.0 226 48.7 419 30.3
4 1394 41.7 430 49.3 379 44.6 585 39.4
5 2466 45.0 700 48.5 597 52.8 1117 38.9
6 424 48.6 86 57.0 115 47.0 223 46.2

Conclusion: Calculation of ADR for all colonoscopies was possible in our department and there was positive correlation with ADR for screening colonoscopies. Because of inclusion of diagnostic examinations, ADR for all colonoscopies was lower than for screening but still over recommended values.

Disclosure: Nothing to disclose

PO198 LAPAROSCOPIC ENDOSCOPY COOPERATIVE SURGERY (LECS) TO OVERCOME THE LIMITATIONS OF ENDOSCOPIC RESECTION FOR COLORECTAL TUMOURS
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Introduction: We established a new procedure, laparoscopic endoscopy cooperative surgery (LECS) procedure to overcome the limitations of endoscopic resection (ER) for colorectal tumors. This procedure involves full thickness resection using a combination of laparoscopic assisted colectomy (LAC) and endoscopic submucosal dissection (ESD), which is quite different from the conventional method. In this report, we clarify the feasibility of performing a safe full-thickness resection with an adequate surgical margin by LECS with ESD.

Aims and Methods: The aim of this study is to clarify the feasibility of performing a full-thickness resection with an adequate surgical margin by LECS with ESD. We performed full-thickness resection for 17 colorectal tumors in 17 patients (male: female 10:7; mean age, 66.5 years) by LECS. The clinicopathological outcomes of these 17 cases and the feasibility of full-thickness resection were evaluated retrospectively.

The indications for LECS in patients with colorectal tumors were as follows: 1) intra-mucosal carcinoma (Tis) and adenoma with high-grade atypia (Vienna Classification, Category 3, 4) accompanied by wide and severe fibrosis in the submucosal layer (tumor recurrence after endoscopic or surgical resection), 2) intra-mucosal carcinoma (Tis) and adenoma with high-grade atypia involving the diverticulum or appendix, and 3) involving intraluminal or intramural growth-type submucosal tumors.

Results: We successfully performed full-thickness resection using LECS in 17 cases (Tis cancer [n = 6], adenoma [n = 9], schwannoma [n = 1], and gastro-intestinal stromal tumor [GIST] [n = 1]). The average tumor diameter was 22.4mm (range, 8-41mm). LECS was successfully performed in 17 all cases without conversion to open surgery: the R0 rate was 100%. The indications for LECS were as follows: involvement of the mucosa of the appendix (n = 6), tumor accompanied by severe fibrosis (n = 5), involvement of a diverticulum (n = 3), submucosal tumor (n = 2), and poor endoscopic operability (n = 1). We experienced no complications (e.g., leakage or gastrointestinal stenosis), and the median hospital stay was 6.4 days (range, 4 to 12 days). All 17 patients who were followed for ≥3 months (average, 30.8 months; range, 3-72 months) showed no residual or local recurrence. Thus, the use of the ESD technique in LECS, can achieve a safe oncological margin in cases involving colorectal tumors. Furthermore, a high complete resection rate, with an adequate surgical margin and a lower local recurrence rate can be expected.

We developed a LECS procedure to overcome the limitations of colorectal ESD, and completed the full-thickness resection of tumors that were considered to have a high risk of perforation. LECS was a safe, feasible, minimally-invasive procedure that achieved the full-thickness resection of colorectal tumors and which showed excellent clinical outcomes.

Disclosure: Nothing to disclose

PO199 RATIO OF RIGHT-SIDED TO LEFT-SIDED DysPLastic COLOReCTAL POLYPS IS A VALID KEY PERFORMANCE INDICATOR
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Introduction: Quality improvement in performance of colonoscopy, with special attention to the detection of proximally located precursors, has the potential to prevent postcolonoscopy colorectal cancer [1].

Aims: In this study we aimed to test hypothesis that the prevalence of dysplastic polyps (nDP) but with inflammatory and postinflammatory polyps exclusion.

Disclosure: Nothing to disclose

PO200 FEASIBILITY AND SAFETY OF WATCH AND WAIT STRATEGY OF DELAYED BLEEDING AFTER COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION: IS EMERGENCY COLONOSCOPY REALLY NEEDED?
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Introduction: Colorectal cancer (CRC) is one of the most common causes of cancer-related death worldwide, colorectal endoscopic submucosal dissection (ESD) has spread rapidly as an effective treatment strategy for early-stage CRC. However, there is major concern about bleeding as a complication of this procedure. While some reports have been published on the management of delayed bleeding after colorectal ESD, there is no consensus on the optimal treatment protocol for situations where emergency colonoscopy is deemed necessary for delayed bleeding after ESD. The criteria for judgement for emergency
colonoScope remains unclear. In this study, we attempted to extract the risk factors. Aims and Methods: The data of 454 consecutive patients who underwent ESD at Chiba University Hospital from April 2017 to December 2018 were reviewed in this study. The watch and wait strategy is a protocol of delayed bleeding after colorectal ESD. The location of rectum, and lesion size \( \geq 40 \) mm were identified by multivariate analysis as being significantly and independently associated with bleeding after ESD (OR: 5.547, and/or moderate amount of hematochezia more than 5 times. If there were no cases which require emergency colonoscopy, blood transfusion, or serious condition caused by delayed bleeding under our watch and wait strategy".

Conclusion: Our results suggest that the location of rectum, and lesion size \( \geq 40 \) mm are independent factors of delayed bleeding after colorectal ESD, but there were no cases which require emergency colonoscopy, blood transfusion, or serious condition caused by delayed bleeding under our watch and wait strategy.

Disclosure: Nothing to disclose

References

P0188 COMPUTER-AIDED DETECTION FOR COLONOSCOPY USING DEEP LEARNING

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Introduction: Colonoscopy and endoscopic eradication of neoplastic lesions are effective for the reduction of colorectal cancer incidence. However, 26% of colorectal diminutive neoplasms were reported to be missed in one colonoscopy (1). To reduce the number of missed cases, we developed a prototype computer-aided detection (CADe) system for colonoscopy (2).

Aims and Methods: The aim of this study was to evaluate the performance of the developed CADe system for colorectal polyps by using recorded video data. To develop the CADe system, we collected 84 full high-definition colonoscopy videos from study participants who underwent total colonoscopy from April 2015 to October 2015 at Showa University Northern Yokohama Hospital. Each colonoscopy video recorded from coaxial injection to withdrawal was visually analyzed across the anus. Therefore, these videos included polypos-negative and polyph-negative frames. Regarding the machine learning process, 2 expert endoscopists annotated all the frames regarding the presence or absence of a polyp. These videos included 166 polypos. The video data of 105 polypos were randomly selected, and 80-min polypos-negative videos were used for machine learning. If the system detects a polyp in the frame, it outputs an alert. To evaluate the performance of the system, we extracted 61 polypos-positive videos and 20-min polypos-negative videos from the study materials as validation sample. The percentage of correctly detected polyph and false-positive detection rate for the negative frames were calculated using the validation sample. Correct detection by the system was defined as a system output of an alert for more than half the length of each polyph-positive video.

Results: The system correctly detected 92% (56/61) of the polyps. Regarding morphological assessment, 92% (36/39) of flat lesions and 91% (20/22) of prolapsed lesions were identified as true-positive. The false-positive detection rate was 59% (19,680/33,088 frames). The system correctly detected 92% (56/61) of the polyps. Regarding morphological assessment, 92% (36/39) of flat lesions and 91% (20/22) of prolapsed lesions were identified as true-positive. The false-positive detection rate was 59% (19,680/33,088 frames).

Conclusion: The results showed that artificial intelligence has the potential of developing a CADe system for colorectal polyps by using recorded video data. To develop the CADe system, we collected 84 full high-definition colonoscopy videos from study participants who underwent total colonoscopy from April 2017 to December 2018. If the system detected more than half of the polyps, it was defined as a true positive. The polyph-negative videos were divided into 2 groups: bleeding group (27 neoplasms), and no-bleeding group (377 neoplasms). In bleeding group, there are no cases which require emergency colonoscopy for hemostasis after delayed bleeding under this watch and wait strategy. The location of rectum, and lesion size \( \geq 40 \) mm were identified by multivariate analysis as being significantly and independently associated with bleeding after ESD (OR: 5.547, respectively; p<0.05 for all).

Conclusion: Our results suggest that the location of rectum, and lesion size \( \geq 40 \) mm are independent factors of delayed bleeding after colorectal ESD, but there were no cases which require emergency colonoscopy, blood transfusion, or serious condition caused by delayed bleeding under our watch and wait strategy.

Disclosure: Nothing to disclose

References
1. Ajioka S, Noma Y, Sato T, et al. Artificial intelligence-assisted polyp detection during colonoscopy: clinical performance for recognizing anatomical locations of colonoscopic images, which may be useful to acquire such skills is overcoming the difficulty in recognizing anatomical locations during colonoscopy. Recently, various computer-aided diagnosis (CAD) systems with deep convolutional neural networks (CNN) have achieved remarkable performance in many medical fields including the diagnosis of colorectal diseases. A CNN system that can recognize anatomical locations during colonoscopy may assist undertrained practitioners efficiently.

Aims and Methods: We constructed a CAD system with CNN based on GoogLeNet architecture to categorize colonoscopic images according to anatomical locations. 7 anatomical categories were used; terminal ileum, cecum, ascending colon to transverse colon, descending colon to sigmoid colon, rectum, anus and indistinguishable image. We retrospectively obtained images that were taken during total colonoscopy performed from January, 2017, to November, 2017, at single center in Japan. We used 9995 images of 409 cases for training the CNN system, and independent 5121 images of 118 cases for validating its performance. For each validation process of an image, the CNN system provided a probability score ranging from 0 to 100%, which indicates the probability for which category an image would belong to. We drew receiver operating characteristic (ROC) curve and calculated the area under the curves (AUC) by each category.

Results: In the validation process, the CNN system correctly recognized 66.6% of images (3410/5121). The rates of correct recognition by each anatomical category were 69% (145/209) for terminal ileum, 30% (211/683) for cecum, 51% (891/1715) for ascending to transverse colon, 99% (182/183) for descending to sigmoid colon, 23% (199/867) for rectum, and 91% (182/199) for anus, respectively. The specificity for each category were 99% for terminal ileum, 98.2% for cecum, 93.8% for ascending to transverse colon, 60% for descending to sigmoid colon, 98.1% for rectum, and 97.8% for anus. The calculated AUCs by the ROC curves were more than 0.8 for each anatomical category; 0.979 for terminal ileum, 0.940 for cecum, 0.875 for ascending to transverse colon, 0.846 for descending to sigmoid colon, 0.835 for rectum, and 0.992 for anus. The CNN system showed 97% images with a probability score of more than 99% that showed 91.7% accuracy in total.

Conclusion: We constructed the new CNN system with clinically relevant performance for recognizing anatomical locations of colonoscopic images, which may reduce the burden and time of acquiring the colonoscopic technique for beginners.

Disclosure: Nothing to disclose

References
1. Ajioka S, Noma Y, Sato T, et al. Artificial intelligence-assisted polyp detection during colonoscopy: clinical performance for recognizing anatomical locations of colonoscopic images, which may be useful...
relationship between histology and pit pattern (p<0.01). According to LSTs, all 182 LST-Gs with a non VN pit pattern were intraepithelial neoplasias and SM-minute Ca cases. In 22 SM-deep Ca cases of LSTs, all 11 LST-Gs showed a type VN pit pattern, while only 2 cases in 11 LST-NGs showed a type VN pit pattern. There was significant relationship between subtypes and pit pattern in submucosal deep invasion of LSTs (p<0.01).

Conclusion: We suggest that the treatment for early-stage colorectal tumors greater than 20mm should be determined on the basis of the morphology and pit pattern by magnification colonoscopy. It is necessary to consider surgical resection for most of depressed and sessile polypoid-types because of the high rates of submucosal deep invasion. According to LSTs, LST-Gs with a type VN pit pattern are possible to allow of endoscopic piecemeal mucosal resection because of absence of SM-deep Ca cases, while LST-NGs should be considered a definite indication for ESD. Furthermore, it is necessary to obtain en-block specimens for precise histological assessment, because a few SM-deep Ca cases with a type VN pit pattern cannot be correctly diagnosed despite of using magnification endoscopy.

Disclosure: Nothing to disclose

P0191 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION FOR NOVICE ENDOSCOPISTS: THE UTILITY OF SUBMUCOSAL POCKET CREATION USING A TRACTION DEVICE

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Introduction: Endoscopic submucosal dissection (ESD) evolved as a method for en bloc resection of large early-stage gastrointestinal tumours for accurate histopathologic evaluation in Japan. colorectal endoscopic submucosal dissection (ESD) can be technically difficult for various reasons, such as submucosal fibrosis. A thin muscular layer can lead to increased perforation rates and longer procedure times. Novel strategies, such as the submucosal pocket formation method, have been reported to overcome these difficulties. Additionally, we recently introduced a new technique, submucosal pocket creation using a traction device (TD). This device is designed to be fixed with clips on the free edges of a mucosal overlay to deflect the diseased mucosa away from the dissection plane during submucosal dissection. When colorectal ESDs are initially performed, we use this technique to facilitate a safe and efficient procedure.

Aims and Methods: We aimed to evaluate the utility of submucosal pocket creation using the TD during colorectal ESD as required by trainee endoscopists. At the Cancer Institute Hospital of Japanese Foundation for Cancer Research from January to March 2018, we retrospectively investigated outcomes of 82 colorectal ESDs performed by 2 groups of endoscopists (A and B). Group A comprised 5 endoscopists with less than 50 cases of colorectal ESD experience and group B comprised 5 endoscopists with more than 500 cases of colorectal ESD experience. ESDs were performed using a novel second-generation endoscopy that allows diagnostic imaging at 520× magnification. In the EC classifications, lesions diagnosed as EC3a vary extensively from adenoma to SM-m, including some lesions that are not suitable for endoscopic treatment. Therefore, to improve the accuracy of the depth of invasion using the EC classification, we investigated the presence or absence of 2 factors; high degree of nuclear enlargement (HNE) and multilayered nuclei (MNs), that are indicators of SM-m.

Aims and Methods: Between May 2005 and March 2018, we retrospectively evaluated 117 EC3a lesions diagnosed as EC2 or EC3, according to the EC classification. We subclassified EC3a into 2 grades (low grade and high grade) and defined low grade as not recognizing both HNE and MNs, and high grade as for any of the 2 factors. We examined the diagnostic accuracy of SM-m based on this ECa subclassification. In addition, we compared the diagnostic ability of EC for SM-m with that of other modalities; narrow-band imaging (NBI) and pit pattern.

Results: The sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and positive likelihood ratio for the diagnostic accuracy of the ECa subclassifications were 90.4%, 91.5%, 81.0%, 96.0%, 91.2%, and 10.7 (p<0.001). Diagnostic performance for predicting SM-m or worse among EC, NBI and pit pattern is as follows: The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy about EC were 96.8%, 92.4%, 96.6%, 92.8%, 95.4% respectively. On the other hand, those of NBI were 98.6%, 52.2%, 83.7%, 93.9%, and 84.6%, and pit pattern were 96.1%, 83.3%, 93.4%, 95.7%, 92.4%, respectively.

Conclusion: From the EC findings, the presence of HNE, and MNs are important risk factors for SM-m or worse outcomes. Furthermore, the ECa subclassification taking account of these findings could be effective for the diagnosis of SM-m or worse.

Disclosure: Nothing to disclose

References

P0193 EARLY-STAGE COLORECTAL PROTRUDED TUMOR WITH DEPRESSION MAY ORIGINATE FROM “DE NOVO” CANCER


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Introduction: It is widely accepted that the majority of colorectal cancers develop through polypoid growth. However, recent studies have shown that depressed tumors also contribute to the development of colorectal cancers. According to careful observation during colonoscopy, a protruded tumor with depressed morphology sometimes develops into a depressed-type tumor, which suggests that the bases are covered with normal mucosa. On the other hand, all 81 tumors without depression showed type III, IV or V pit patterns, which suggests that the bases are covered with neoplastic glands. There was significant relationship between the presence of depression and histology of the bases of protruded SM-Cas.

Conclusion: Our findings suggest that the treatment for early-stage colorectal protruded sessile tumors should be determined on the basis of the detection of depressed morphology and pit pattern diagnosis by magnification colonoscopy. It is necessary to consider surgical resection for the protruded tumors with depression, because they are all submucosal invasive carcinoma cases. Also, they may originate from what we call de novo cancers, depressed-type tumors, because all their cases are submucosal invasive carcinomas regardless of their size and have no adenomatous glands and moreover their bases are covered with normal mucosa. Therefore, we should always pay attention to protruded tumors with depression during colonoscopy.

Disclosure: Nothing to disclose

References
P0194 CLINICOPATHOLOGICAL FEATURES OF LOCAL RECURRENCE AFTER ENDOCUFF BIOPSY USING NARROW BAND IMAGING ENDOSCOPY IN PATIENTS WITH DIMINUTIVE POLYPS

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Introduction: Cold forceps polypectomy (CFP) is often used to remove diminutive polyps. It does not induce thermal damage to tissue, and therefore has few complications such as postoperative bleeding and perforation. Other advantages are that it can be implemented using routine biopsi techniques, and the resected tissue can be recovered easily and reliably after resection. In addition, jumbo biopsy forceps are considered superior to standard forceps for removing colorectal polyps. The observation to check the margin of resected resections are enhanced with narrow band imaging (NBI)-enhanced endoscopy can also improve complete resection rate. However, in such cases, we sometimes experience local recurrence cases, the issue of features of them have not been clarified in detail.

Aims and Methods: In this study, we examined the clinicopathological features of local recurrence after jumbo forceps assisted by NBI endoscopy for patients with diminutive polyps. This multicentre, prospective, single-arm observational study was conducted at 11 institutes of the National Hospital Organization in Japan between January 2015 and September 2016. Patients aged 20–75 years with diminutive polyps were enrolled. A total of 504 patients were prospectively assessed, and 1015 polyps were resected. In addition, a total of 955 lesions were resected in the 471 patients who followed up 1 year after CFP to examine the polypectomy sites for local recurrence (follow-up rate, 94.1%). We analysed the local recurrence rate, clinicopathological characteristics of primary polyps and local recurrent polyps, as well as resection rates and adverse events.

Results: Local recurrence occurred in 20 (2.1%) cases of the 955 lesions subjected to flattening-assisted colonoscopy to standard colonoscopy. Improving ADR is the central focus of the current quality movement in colonoscopy. The fold flattening devices could ameliorate the ADR.

Aims and Methods: The aim of the study was to compare the efficacy of mucosal flattening assisted colonoscopy vs standard colonoscopy to improve the adenoma detection rate in patients undergoing colonoscopy. Secondary outcomes evaluated were: adenoma detection, procedure-related complications, patient satisfaction, and costs. The fold flattening devices could ameliorate the ADR.

Disclosure: Nothing to disclose

P0195 LONG-TERM OUTCOMES AFTER ENDOCUFF SUBMUCOSAL DISSECTION WITH THE STAG BEETLE KNIFE JR FOR EARLY COLONIC NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is one of the most useful methods for treating early colorectal neoplasms, and an insulation-tipped knife, hook knife, flush knife, or dual knife is conventionally used to perform ESD. However, because these devices are used without fixation to the target tissue, there is the potential risk of adverse events due to an unexpected incision or perforation. To reduce the risk of adverse events associated with a conventional knife when performing ESD, we used a scissors-type stag beetle (SB) knife Jr, which has a stretcher and an adequate dissection layer and prevents unexpected muscular layer injury. We previously reported that performing colorectal ESD with the SB knife Jr is easy, safe, and technically efficient. However, there is a need for more long-term clinical data to establish the full advantages of colorectal ESD with the SB knife Jr, with respect to favorable survival rates and very low recurrence rates.

Aims and Methods: The aim was to evaluate the long-term outcomes of ESD performed with the SB knife Jr for early colorectal neoplasms. ESD was performed for 163 lesions in 151 patients (male:female ratio = 78:73; mean age = 69 years) between October 2010 and March 2015. Data for 137 lesions in 126 patients (81%) who were followed up for more than 3 years were identified and analyzed. The en bloc resection rate, complete resection rate, curative resection rate, resected tumor size, procedural time, complications, and long-term outcomes, including local and distant recurrence rates, and survival rates were analyzed. 5-year overall survival rate was 97.5% (95% CI 95.3–99.7%), 3-year disease-specific survival rate (DSS) was 97.5%. The survival rates were analyzed for the entire study cohort, and the local and distant recurrence rates were analyzed for the cohort that underwent curative resection or those who were observationally managed through conservative treatment.

Results: The patients’ mean age was 68 ± 10 years, and the male:female ratio was 67:59. On histopathology, the prevalence rate for tubular adenoma was 29.9% (41/137), with Tis in 46.7% (64/137), T1a in 10.2% (14/137), and T1b in 13.1% (18/137). The mean resected tumor size was 32.1±16.5 mm, and the median procedure time was 80 (range, 15 - 420) min. The en bloc resection rate, complete resection rate, and curative resection rate were 97.8% (134/137), 94.2% (129/137), and 83.9% (115/137), respectively. No perforations occurred during the procedure. The delayed bleeding rate was 3.6% (5/137), rectal stricture occurred in one patient (0.7%) and was treated conservatively.

Conclusion: For long-term outcomes, the local recurrence rate was 1.6% (2/123), and no distant recurrence was observed in the recurrence analysis cohort. On survival curve, the 5-year overall survival rate was 97.5% (95% CI 95.3–99.7%), 3-year OS and DSS rates were 94.2%/92.1% and 99.0%/99.0%, respectively. 1 patient (0.7%, 1/137) died of colorectal cancer, and 9 (6.6%, 9/137) died of other diseases.

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Introduction: The adenoma detection rate (ADR) has emerged as the most important quality measure in colonoscopy, as it predicts the interval cancer after colonoscopy. Improving ADR is the central focus of the current quality movement in colonoscopy. The fold flattening devices could ameliorate the ADR.

Aims and Methods: The aim of the study was to compare the efficacy of mucosal flattening assisted colonoscopy vs standard colonoscopy to improve the adenoma detection rate in patients undergoing colonoscopy. Secondary outcomes evaluated were: adenoma detection, procedure-related complications, patient satisfaction, and costs. The fold flattening devices could ameliorate the ADR.

Disclosure: Nothing to disclose

P0196 MUCOSAL FLATTENING-ASSISTED COLONOSCOPY (FAC) FOR IMPROVING ADENOMA DETECTION RATE: A SYSTEMATIC REVIEW WITH PAIRWISE AND NETWORK META-ANALYSIS

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Introduction: The adenoma detection rate (ADR) has emerged as the most important quality measure in colonoscopy, as it predicts the interval cancer after colonoscopy. Improving ADR is the central focus of the current quality movement in colonoscopy. The fold flattening devices could ameliorate the ADR.

Aims and Methods: The aim of the study was to compare the efficacy of mucosal flattening assisted colonoscopy vs standard colonoscopy to improve the adenoma detection rate in patients undergoing colonoscopy. Secondary outcomes evaluated were: adenoma detection, procedure-related complications, patient satisfaction, and costs. The fold flattening devices could ameliorate the ADR.

Disclosure: Nothing to disclose
when the ADR was greater than 40% using standard colonoscopy. Endocuff was clinically and statistically relevant when ADR with standard colonoscopy is lower than 25%, (O.R. 1.87 ITT analysis). About Ending no definitive conclusion could be drawn due to the scarce literature available, although the preliminary analysis did not show an advantage when compared to standard colonoscopy. Direct and indirect comparison between Ending vs Endocuff did not provide definitive conclusions.

Disclosure: Nothing to disclose

P0197 FORWARD-VIEWING ENDSCOPE FOR ERCP IN PATIENTS WITH BILLROTH II GASTRECTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS


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Introduction: The forward-viewing endoscope has been increasingly used to perform endoscopic retrograde cholangiopancreatography (ERCP) in patients who underwent Billroth II gastrectomy.

Aims and Methods: This study intended to assess efficacy and safety of the forward-viewing endoscope for ERCP in Billroth II gastrectomy patients compared with standard side-viewing endoscope using a systematic review and meta-analysis. A systematic review was conducted for studies that evaluated the outcomes of ERCP for patients with Billroth II gastrectomy. Random-effect model meta-analyses with subgroup analyses were conducted. The methodological quality of the included publications was evaluated using the risk of bias assessment tool for non-randomized studies. The publication bias was assessed.

Results: In total, 25 studies (1 randomized, 18 retrospective, 1 prospective, and 5 case series studies) with 2446 patients (499 forward-viewing and 1947 side-viewing endoscopes) were analyzed. The pooled afferent loop intubation rate was higher with the forward-viewing endoscope (90.3%, 95% confidence interval (CI):85.6-95.3% vs. 86.8%, 95% CI:82.8-89.9%). The pooled selective cannulation rate was higher with the side-viewing endoscope (92.3%, 95% CI:88.0-95.2% vs. 91.1%, 95% CI:87.2-93.8%). The pooled bowel perforation rate was higher with the side-viewing endoscope (3.6%, 95% CI:2.3-5.7% vs. 3.0%, 95% CI:1.7-5.3%). The pooled pancreatitis rate was higher with the forward-viewing endoscope (5.4%, 95% CI:3.6-8.0% vs. 2.5%, 95% CI:2.3-5.7%). The pooled afferent loop intubation rate was higher with the forward-viewing endoscope (3.0%, 95% CI:1.6-5.5% vs. 2.0%, 95% CI:1.4-3.0%). The heterogeneity among the studies was not significant. The publication bias was minimal.

Conclusion: This meta-analysis indicates that the forward-viewing endoscope is as safe and effective as conventional side-viewing endoscope for ERCP in patients with Billroth II gastrectomy.

Disclosure: Nothing to disclose

References


P0198 LIVER HYDATID CYST - WHEN DO WE NEED BILIARY STENTING IN MANAGEMENT PROTOCOL. A STUDY OF 56 CASES

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Introduction: Hydatidosis, a zoonotic infection, is due to the larval stage of the tapeworm Echinococcus (E.). The outer lamina of a cyst, the acotyl or peri- cyst, is formed by compressed and fibrotic host tissue and may become calcified, whereas inner layers are of parasitic origin and act as a germinal centre. A cyst may or may not contain daughter cyst(s). Secondary echinococcosis can develop where cyst contents are released. The cyst, is formed by compressed and fibrotic host tissue and may become calcified, than large peripheral cysts.

Cyst which is near to hilum has more chances of biliary communication rather due to cyst internal rupture. None of the patients had recurrence in our present series, in average follow up of 3 months. 1 patient had fluid collection which was treated with percutaneous drainage.

Conclusion: Cystectomy - a non radical alternative of hydatid disease is practical and feasible approach.

Disclosure: Nothing to disclose

References


P0199 COMPARISON OF DEXMEDETOMIDINE WITH MIDAZOLAM VERSUS MIDAZOLAM ALONE FOR SEDATION DURING ERCP: A PROSPECTIVE OBSERVATIONAL STUDY

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Introduction: Dexmedetomidine (DEX) is a highly selective α2-adrenergic agonist that elicits sedative and analgesic effects in humans. Recently, DEX has been used for endoscopic sedation. However, the usefulness and safety of DEX for sedation during endoscopic procedure has not been fully evaluated.

Aims and Methods: The aim of this study was to compare the efficacy and safety of standard sedation using midazolam (midazolam group) with combination sedation using DEX and midazolam (midazolam+DEX group). A prospective, observational study was conducted in 89 patients who underwent ERCP. Written informed consents were obtained from all patients before enrollment. Satisfaction score among patients were evaluated with Visual Analogue Scale. Body motion during sedation (1–5 represents discontinuance of procedure), vital signs, and recovery time were assessed.

Results: 46 patients were administered with midazolam alone (midazolam group) and 43 patients were administered with DEX and midazolam (midazolam+DEX group). The baseline characteristics and procedure time were similar between the 2 groups. Body motion was significantly lower in midazolam+DEX group than in midazolam group (1.5 vs. 2.58, p<0.0001). Satisfaction score, recovery time, respiratory depression, hypotension and bradycardia were not significantly different between the 2 groups.

Conclusion: The present study suggests that a combination of DEX and midazolam is as safe as midazolam alone for sedation during ERCP. This combination has less body motion than midazolam alone without extending recovery time.

Disclosure: Nothing to disclose

References


P0200 UTILITY OF ENDOSCOPIC RETROGRADE CHOLANGIPANCREATOGRAPHY FOR THE MANAGEMENT OF SYMPTOMATIC Pancreas Divisum IN CHILDREN: EXPERIENCE FROM A SINGLE CENTER IN CHINA

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Introduction: Pancreas divisum (PD) is the most common congenital anomaly of the pancreas. Most PD individuals are asymptomatic, but a few may present symptoms in the form of recurrent acute pancreatitis (RAP), chronic pancreatitis (CP) or pancreatic-type pain. Currently, most PD-related studies published in the literature have been limited to adults. Clinical data in pediatric PD are relatively insufficient. However, it is important to early diagnose and timely treat symptomatic PD, especially in children for the better clinical outcomes.
Aims and Methods: To estimate the safety and efficacy of endoscopic retrograde cholangiopancreatography (ERCP) for the treatment of symptomatic PD in children. We retrospectively analyzed patients of symptomatic PD(PD-P) who were younger than 18 years old from January 2011 to December 2017 in our institute. The PD-P included PD with RAP (RAP group) and PD with CP (CP group). All children were under 18 years of age as a main therapy. During an ERCP, minor endoscopic sphincterotomy combined with dorsal duct stenting(Mi-ESCS) was performed for complete PD (CPD) patients, and Bi-papilla ESCS (Bi-ESCS) was performed for incomplete PD (IPD) patients. ERCP-related data, complications, cholangiographic data were collected and analyzed. Long-term follow up was carried out to observe occurrence of developing CP in RAP group, children’s recovery, as well as their weight, growth and intelligence.

Results: A total of 312 pediatric ERCPs were performed for 157 children during this period. Of which 34 were PD-P cases, among which 30 were s-PD. The endoscopic detection rate of PD was 21.7%. Of the 30 s-PD patients, 19 were PD with RAP, among which 17 were CPD and 2 were IPD. The other 11 were PD with CP, among which CPD and IPD were 7 and 4 respectively. A total of 84 attempted ERCPs were performed among which 44 were for RAP group and 40 for CP group. The success rate of cannulating the minor papilla was 97.6% (82/84). The total response rate to endorhesis was 93.3%, with that of 100% (19/19) in RAP group and 81.8% (9/11) in CP group. The 2 patients with no response to endorhesis in CP group underwent surgery. The mean interval of changing pancreatic dorsal duct stent is 3 months (from 2 to 6 months). The mean number of changing dorsal duct stent was 2.3 in RAP group and 3.6 in CP group. ERCP-related complications were mild with a rate 7.1% (23/325), all of which were managed conservatively. During follow up from 3 to 84 months (mean 38.1 months), all patients had patent relief. In RAP group, 2 patients developed CP with a rate of 10.5%, others showed no more dilation of dorsal ducts. In CP group, 1 patient had pain relief within few months of acute pancreatitis, however, they demanded multiple repeated changing dorsal stents with no obvious improvement in pancreatic duct. In both groups, children presented normal in weight, growth and intelligence.

Conclusion: Mi-ESCS and Bi-ESCS with ERCP are safe and effective methods to manage s-PD in pediatric patients. It seems very important for such children to undergo endoscopic interventions as early as possible in order to avoid developing CP. Children of PD with CP may present asymptomatic with long term ERCP therapy.

Disclosure: Nothing to disclose.

P0201 PANCREATIC DUCT PERFORATION DURING GUIDEWIRE CANNULATION FOR THERAPEUTIC BILIARY ERCP
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Introduction: Guidewire (GW) cannulation of the common bile duct (CBD) in ERCP is becoming increasingly widespread. Inadvertent GW passage into the main pancreatic duct (MPD) is relatively common. As a consequence, sometimes it happens that MPD perforation occurs. The techniques of Mi-ESCS and Bi-ESCS with ERCP are safe and effective methods to manage s-PD in pediatric patients. It seems very important for such children to undergo endoscopic interventions as early as possible in order to avoid developing CP. Children of PD with CP may present asymptomatic with long term ERCP therapy.

Disclosure: Nothing to disclose.

P0202 EUS-GUIDED PANCREATIC DRAINAGE: A STEEP LEARNING CURVE
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Introduction: Endoscopic ultrasound guided biliary drainage (EUS-PD) is an efficacious, safe option for patients with pancreatic duct obstruction who fail conventional endoscopic retrograde cholangiopancreatography (ERCP). The procedure involves accessing the pancreatic duct using EUS, creating a fistulous tract, and deploying a decompressing stent across the tract. It is a technically challenging procedure, requiring advanced skills in EUS and ERCP. The aim of this study was to define the learning curve for EUS-PD.

Aims and Methods: Consecutive patients undergoing EUS-PD by a single operator with training in therapeutic endosonography, were included from a dedicated registry from May 2003 to September 2017. Demographics, procedure info, adverse events, and follow-up data were collected. Non-linear regression and CUSUM analyses was conducted for the learning curve. Technical success was defined as successful stent placement. Clinical success was defined as resolution of procedure indication.

Results: 55 patients were included (54%M, mean age 58 years). The majority of patients had benign disease (n = 51, 91%): chronic pancreatitis n = 26, anasto- motic leak n = 14, and s-PD n = 2. The remaining 4 patients had malignant obstruction. 25 patients (44%) had altered anatomy. Technical success was achieved in 47 patients (84%). Stent placement was transluminal in 43 patients (92%) and transpapillary in 4 (9%), antegrade in 36 patients (77%) and retro- grade in 4 patients (8%). Successful pancreatic stenting was achieved in 46/47 (98%) patients who achieved technical success. Adverse events were seen in 13 patients (6 of whom did not achieve technical success) and included bleeding requiring embolization (n = 5), bleeding treated with angiography, perforation requiring surgery (n = 1), pancreatitis (n = 5), and a pancreatic fluid collection drained via EUS (n = 2). Median procedure time was 80 mins (range 49–159 mins). CUSUM chart shows 80 minute procedure time was achieved at the 27th procedure indicating efficiency. Apart from 2 outliers, procedure durations further reduced with consequent procedures from 40ths onwards reaching a plateau which could be the plateau indicating mastery (nonlinear regression p < 0.0001)

Conclusion: Endoscopists experienced in EUS-PD are expected to achieve a repeatable, efficient procedure time of < 80 mins, in 95% of cases, when the procedure takes < 80 minutes and a learning rate of 27 cases. Continued improvement is demonstrated with additional experience, with plateau indicating mastery suggested at the 40th case. EUS-PD is probably one of the hardest therapeutic endosonographic procedure to learn and master.

Disclosure: Michel Kahaleh MD: has received grant support from Boston Scientific, Fujinon, EMcision, Xlumena Inc., W.L. Gore, MaunaKea, Apollo Endosurgery, Cook Endoscopy, ASPIRE Bariatrics, GI Dynamics, NinePoint Medical, Merit Medical, Olympus and Mi Tech. He is a consultant for Boston Scientific, Xlumena Inc., Concordia Laboratories Inc, ABBvie, and MaunaKea Tech. - Amy Tyberg MD is a consultant for EndoGastric Solutions. - Prashant Kedia MD is a consultant for Boston Scientific, Endogastric solutions and Apollo Endosurgery. All other authors have nothing to disclose.

P0203 EUS-GUIDED GALLBLADDER DRAINAGE: A LEARNING CURVE MODIFIED BY TECHNICAL PROGRESS
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Introduction: Endoscopic ultrasound-guided gallbladder drainage (EUS-GBLB) is an efficacious, safe option for patients with cholecystitis who cannot undergo cholecystectomy. The procedure involves accessing the gallbladder using EUS, creating a fistulous tract, and deploying a stent across the tract. It is a technically challenging procedure, requiring skills in EUS, fluoroscopy, and stent deployment. The aim of this study was to define the learning curve for EUS-GBLB.

Aims and Methods: Consecutive patients undergoing EUS-GBLB by a single operator were included from a prospective registry from January 2012 to July 2017. Demographics, procedure info, post-procedure follow-up data, and adverse events were collected. Non-linear regression and CUSUM analyses was conducted for the learning curve. Clinical success was defined as resolution of cholecystitis post-procedure.

Results: 84 patients were included (58%M, mean age 76 years). 20 patients (42%) had malignant cholecystitis, the remaining had benign disease. Technical success was 100%. Most patients had lumen-apposing metal stents (LAMS) (15mm, n = 29, 60%; 10mm, n = 51, 17%), 25 of which were cautery-enhanced. The remaining patients had FCSEMS (n = 9, 19%) or plastic stents alone (n = 2, 4%). 1 patient required bridging stents placement. The majority of stents were transduodenal (n = 28, 38%), the remaining transgastric (n = 15; 31%) or trans- jejunial (n = 4, 8%), and 1 patient had 2 stents placed from transgastric and...
transudosal duct position during the same procedure. Clinical success was achieved in 97% of the remaining patients between 2008 and 2012, 7 were lost to follow-up and 3 had persistent cholecystitis. 9 patients (19%) had adverse events including bleeding (n = 4), liver abscesses (n = 2), and hypotension post procedure. 2 patients passed away post-procedure due to respiratory failure and peritonitis secondary to ruptured gallbladder wall. 6 patients required re-intervention for stent occlusion with repeat endoscopy or surgical cholecystectomy. The median procedure time was 41 minutes (range 16–121 mins). CUSUM chart shows 41 minute procedure was achieved at the 19th procedure hence indicating efficiency. Procedure durations following 10 procedures being between 90 minutes and undertow interquartile regression p < 0.0001 indicating continued improvement with experience. This also may be due to the introduction of cautery-enhanced LAMS.

**Conclusion:** Endoscopists experienced in EUS-GLB are expected to achieve a reduction in procedure time over successive cases, with efficiency reached at 41 minutes and a learning rate of 19 cases. Continued improvement is demonstrated with additional experience and the introduction of cautery-enhanced LAMS.

**Disclosure:** Michel Kaehler MD has received grant support from Boston Scientific, Fujionix, Emcision, Xlumena Inc., W.L. Gore, MaunaKea, Apollo Endosurgery, Cook Endoscopy, ASPBARIATRICS, GI Dynamics, NinePoint Medical, Merit Medical, Olympus and MI Tech. He is a consultant for Boston Scientific, Xlumena Inc., Concordia Laboratories Inc, AB&Bie, and MaunaKea Tech. Amy Tyberg MD is a consultant for EndoGastric Solutions. Prashant holds patents with additional experience and the introduction of cautery-enhanced LAMS.

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**Introduction:** Endoscopy is the preferred approach for the diagnosis and treatment of bile duct stones. However, endoscopic retrograde cholangiopancreatography (ERCP) may be unnecessary. We conducted a retrospective, unicentric analysis of elective ERCP procedures (OR = 209.1, 95% CI 2.18–2050.8), normal total bilirubin (OR = 138.9, 95% CI 1.19–1627.2), ERCP performed in ≤7 days (OR = 32.9, 95% CI 1.08–1004.8) and removal of the stent in ≤12 weeks (OR = 40.7, 95% CI 1.11–160.9) were associated with resolution of the biliary leak and absence of another pathology (p < 0.005; r² = 0.71). The area under the ROC curve of these criteria for outcome prediction was 0.93 (p < 0.001). When ≥3 criteria were present (42.9%, of patients), the model presented specificity of 100% and predictive value of 45.8% in outcome prediction.

**Conclusion:** We identified criteria that allow selection of 43% of patients in whom repetition of ERCP after treatment of biliary leaks may be unnecessary. These patients can have their biliary stents removed by esophagogastroendoscopy, increasing safety and efficiency of healthcare resources utilization.

**Disclosure:** Nothing to disclose.

**References**


**P0204 SINGLE-OPERATOR CHOLANGIOSCOPY REDUCES PATIENT RADIATION EXPOSURE IN THE MANAGEMENT OF DIFFICULT BILE DUCT STONES AND INDETERMINATE BILE DUCT STRICTURES: A SINGLE-CENTRE, HISTORICAL COMPARISON STUDY**

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**Introduction:** Single-operator cholangioscopy (D-SOC) was developed as a novel approach to enable direct and increased number of images, patient radiation doses can be high, especially in complex cases. A new digital single-operator cholangioscopy (D-SOC) system (SpyGlass Digital System, Boston Scientific) allows direct visualization of the ducts, targeted biopsies, visual wire manipulation and difficult stone lithotripsy in a radiation-free manner. We investigated whether the Spyglass platform used adjunctively to ERCP may actually reduce patient radiation exposure.

**Aims and Methods:** We retrospectively analyzed a prospective database of consecutive patients undergoing D-SOC following failure of ERCP either difficult-to-treat biliary stones or indeterminate strictures. The overall patient radiation exposure outcomes in terms of Kerma Area Product (KAP), Fluoroscopy time (T) and the total number of films (F) were compared to a control subgroup of patients who had their stents removed by esophagogastroduodenoscopy, and Apollo Endosurgery. - All other authors have nothing to disclose.

**Results:** A total of 43 patients were included, 62.8% (n = 27) female, mean age 58.2 ± 17.2 years. The most common etiology of biliary leaks was laparoscopic cholecystectomy (56.8%) and the most common location the cystic duct stump (33.5%). Technical success was 93.5%, with resolution of the biliary leak in 100% of patients. On multivariate analysis, elective ERCP procedure (OR = 209.1, 95% CI 2.18–2050.8), normal total bilirubin (OR = 138.9, 95% CI 1.19–1627.2), ERCP performed in ≤7 days (OR = 32.9, 95% CI 1.08–1004.8) and removal of the stent in ≤12 weeks (OR = 40.7, 95% CI 1.11–160.9) were associated with resolution of the biliary leak and absence of another pathology (p < 0.005; r² = 0.71). The area under the ROC curve of these criteria for outcome prediction was 0.93 (p < 0.001). When ≥3 criteria were present (42.9%, of patients), the model presented specificity of 100% and predictive value of 45.8% in outcome prediction.

**Conclusion:** We identified criteria that allow selection of 43% of patients in whom repetition of ERCP after treatment of biliary leaks may be unnecessary. These patients can have their biliary stents removed by esophagogastroendoscopy, increasing safety and efficiency of healthcare resources utilization.

**Disclosure:** Nothing to disclose.

**References**


Aims and Methods: The study aim was to assess if the terminal bile duct diameter can be determined by inspecting the major papilla morphology/width during duodenoscopy. Between July 2017 and January 2018, in 3 hospitals, all consecutive patients with naive papilla referred for ERCP were eligible for enrollment. The transverse diameter (tD) of the papilla was measured using a comparative measurement technique (biopsy forceps) and a novel software (validity and reliability tested). The papilla morphology was classified into 1 of 4 groups: non-proeminent, prominent, bulging, distorted. The tBD’s diameter was measured in the distal 1 cm (cholediagram acquired in supine/prone) in a workstation, by an independent researcher. Main outcome was evaluated using a Pearson correlation.

Results: Between July 2017 and January 2018, in 3 hospitals, all consecutive patients with naive papilla referred for ERCP were eligible for enrollment. The transverse diameter (tD) of the papilla was measured using a comparative measurement technique (biopsy forceps) and a novel software (validity and reliability tested). The papilla morphology was classified into 1 of 4 groups: non-proeminent, prominent, bulging, distorted. The tBD’s diameter was measured in the distal 1 cm (cholediagram acquired in supine/prone) in a workstation, by an independent researcher. Main outcome was evaluated using a Pearson correlation.

Conclusion: Despite what is suggested in the literature, the morphology and the width of the major papilla do not have any association with the diameter of the tBD, and consequently these 2 dimensions should not be taken into account when designing for a cannulation technique.

Disclosure: Nothing to disclose.

Reference

P0208 FEASIBILITY OF A NEW SHORT-TYPE DOUBLE-BALLOON ENDOCOSCOPE WITH ADVANCED FORCE TRANSMISSION AND ADAPTIVE BENDING FOR PANCREATOBILIARY INTERVENTION IN PATIENTS WITH SURGICALLY ALTERED ANATOMY: A PROPENSITY-MATCHED ANALYSIS

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Introduction: Recently, short-type double-balloon endoscopes (DBEs) for pancreaticobiliary interventions in patients with surgically altered anatomy have become available in many institutions. However, we previously demonstrated in a multicenter study that endoscopic retrograde cholangiopancreatography (ERC) using a conventional short-type DBE is a lengthy procedure, requiring approximately 22 minutes to reach the target site and 56 minutes to complete ERCP-related interventions. A new short-type DBE has been developed with a major focus on facilitating scope insertion to the target site for pancreaticobiliary interventions in patients with surgically altered anatomy. Aims and Methods: We investigated the feasibility of this new short-type DBE by comparing it with a conventional DBE. Data from 885 ERCP procedures using balloon endoscopy were analyzed. We used propensity score matching to adjust for differences between patients who underwent the new DBE procedure and the new short-type DBE versus the conventional short-type DBE. The outcomes of interest were the success rate of reaching the target site, the success rate of the pancreaticobiliary intervention, the insertion time required to reach the target site, the overall procedure time, the success rate of cannulation of the papilla of Vater, the time to cannulation of the papilla of Vater, and adverse events during or after the ERCP procedure.

Results: A total of 163 pairs of patients were selected on the basis of propensity score matching. The success rate of reaching the target site was 100% in both the new DBE group and the conventional DBE group (p = 0.10). The new DBE group had a significantly shorter insertion time required to reach the target site than the conventional DBE group (10 min vs. 14 min, p = 0.01). The success rate of the pancreaticobiliary interventions in the new DBE group was as high as that in the conventional DBE group (92% vs. 89% p = 0.35). The overall procedure time decreased from 62 min in the conventional DBE group to 55 min in the new DBE group (p = 0.26). Apart from cholecystocholedochusintumus and pancreatojejuno-ostomy, the success rate of cannulation of the papilla of Vater in the new DBE group was higher than that in the conventional DBE group (96% vs. 87%, p = 0.10). No significant difference in the rate of adverse events was observed between the 2 groups.

Conclusion: A new short-type DBE allows faster insertion to the target site for pancreaticobiliary intervention in patients with surgically altered anatomy.

Disclosure: Nothing to disclose.

References

P0209 POSITIVE CORRELATION BETWEEN PANCREATIC PARENCHYMAL VOLUME AND PEP


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Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) remains a common and serious adverse event associated with ERCP. PEP after initial ERCP was reported to have an incidence ranging from 10% to 15% in various studies, and the mortality rate was 0.11%. PEP is considered a high-priority adverse event. Recently, preventative measures for PEP such as high-dose rectal diclofenac and pancreatic stent placement have been proposed as useful approaches. However, they may not be appropriate for all patients, given the risks involved. Therefore, in order to use these preventive methods more effectively, it is necessary to be able to easily stratify patients into the high- and low-risk groups for PEP.

The three major causes of PEP are patient-related factors, operator-related factors, and technique-related factors. It is difficult to predict the incidence of PEP because there are many potential factors in each category. We considered the importance of predicting PEP based on pre-ERCP findings because it may be possible to increase the safety of the endoscopic procedure. In a previous study, the degree of pancreatic exocrine function showed a significant positive correlation (p < 0.001) when determined using the 131I-labeled Breath Test and ancin cell area ratio. However, the risk associated with pancreatic parenchymal volume has never been examined as a risk factor for PEP. We hypothesized that a large pancreatic parenchymal volume would increase the risk of PEP. The pancreatic parenchymal volume of the pancreas was quantified using the volume analyzer SYNAPSE VINCENT® (Fujifilm Medical Co, Tokyo, Japan) in pre-ERC images and used to evaluate whether it could be a risk factor for PEP.

Aims and Methods: The aim of this study was to investigate the risk factors for PEP by quantification of pancreatic parenchymal volume using pre-ERC images. Overall, 800 patients were recruited from April 2012 to February 2015 for this study. There were 240 patients who satisfied the inclusion criteria. Measurement of pancreatic parenchymal volume was achieved using the volume analyzer SYNAPSE VINCENT® in all cases and was used to evaluate the risk factors for PEP.

Results: According to the criteria established by the consensus guidelines (Cotton classification), 23 patients (9.6%) were classified as having mild disease, 4 (1.7%) as having moderate disease, and 5 (2.1%) as having severe disease. Multivariate model analysis adjusted for age, female sex, pancreatic duct guidewire cannulation, precut sphincterotomy, and pancreatic injection showed that a large pancreatic parenchymal volume was a significant risk factor for PEP (odds ratio 1.12, 95% confidence interval 1.07–1.17; p < 0.01). In addition, a larger pancreatic parenchymal volume was significantly associated with a higher incidence of PEP (p < 0.001).

Conclusion: A large pancreatic parenchymal volume was identified as a risk factor for PEP. The results of this study suggest that pre-ERC images might be useful for predicting PEP. Additional caution should be required for patients with larger pancreatic parenchymal volumes to prevent PEP.

Disclosure: Nothing to disclose.

References

P0210 INITIAL MULTICENTRE DATA FROM THE HUNGARIAN ERCP REGISTRY

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Introduction: The continuous monitoring of quality indicators in gastrointestinal endoscopy became an essential requirement nowadays. Most of these data cannot be extracted from the currently used free-text reports, therefore a...
web-based data collecting system, the Hungarian ERCP Registry was developed. Here we present the first multicentre data from the registry.

**Aims and Methods:** Data collection started in January 2017 at University of Pécs, and a further 4 centres (Szeged, Debrecen, Budapest and Szombathely) started to use the registry from a later date.

Regarding the ERCP data, 884 patients were recorded in the database until March 2018 in the 5 participating centres. 30-day follow up data was collected to detect all procedure related late complications, this data is available in 73.5% of the procedures. Native papilla (NP) was detected in 698 ERCPs (62.5% of all procedures). The success rate of biliary cannulation was 90.5% in these patients. Post-ERCP pancreatitis (PPE) developed in 22 cases (3.2% of procedures with NP), clinically significant bleeding was reported in 14 patients (2.0% of cases with NP). Cholangitis was observed in 18 cases (1.6% of all procedures), and pancreatitis in 16 cases (1.4%). Endoclips suppository was placed in 43.8% of the cases, while prophylactic pancreas stent was applied in 9.5% of the procedures to prevent PEP. The data of the participating centres are shown below. Center/ERCP number/36 f/U (%)/NP in ERCP (%)/Success in NP (%)/Comp. rate (%)/PPE/Bleed/Cholang. /Perf.: Pécs/692/75.1/62.6/89.6/3.2/1.4/0.7/1.9; Szeged/207/67.6/66.2/94.2/3.9/3.1/1.0; Budapest/151/69.5/55.6/89.3/3.1/2/1.2/3.3/0.0; Debrecen/35/85.7/57.1/100/11/0.0/0.0/0/0; Szombathely/32/81.5/73.3/4.2/2/0/0.0/0/0.

**Conclusion:** These are the first prospectively collected multicentre key performance indicators from the Hungarian ERCP Registry. This web-based registry is a suitable tool to detect the quality of patient care and also be used for clinical research. Further centres are encouraged and welcome to join this project.

**Disclosure:** Nothing to disclose.

**P0211 USE OF THE FORWARD-VIEWING ENDOSCOPE CAN BE A RISK FACTOR FOR POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOSCOPY PANCREATITIS: A PROSPECTIVE MULTICENTRE OBSERVATIONAL STUDY**

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**Aims and Methods:** A forward-viewing endoscope is used for endoscopic retrograde cholangiopancreatography (ERCP) in patients with surgically altered anatomy such as Billroth II type or Roux-en Y type reconstruction. Difficulty in performing cholangiopancreatography (ERCP) in patients with surgically altered anatomy is often encountered. The forward-viewing endoscope has been used in such cases. In the present study, the diagnosis of post-ERCP pancreatitis (PPE) was performed in patients with altered anatomy who underwent ERCP with the forward-viewing endoscope. A total of 1877 patients were analysed, from 7 high-volume hospitals in Japan were enrolled (SOSUI study). We excluded patients with acute pancreatitis, biliary-enteric anastomosis, failure to reach the ampulla, altered anatomy other than Billroth II or Roux-en Y reconstruction, and the use of rescue techniques (rT) can be conditioned, among other factors, by the papillary morphology.

**Results:** Use of the forward-viewing endoscope in ERCP is a risk factor for PEP. Some authors suggest that the difficulty of biliary cannulation and the use of rescue techniques (rT) can be conditioned, among other factors, by the papillary morphology.

**Conclusion:** The success rate of biliary cannulation (tbc), difficult cannulation and rT. The influence of papillary morphology on the performance of the 2 lithotripsy modalities.

**Disclosure:** Nothing to disclose.

**P0212 SINGLE-OPERATOR HEBRAL CHOLANGIOPANCREATOSCOPY-GUIDED LITHOTRIPSY FOR DIFFICULT BILIARY AND PANCREATIC STONES - A PROSPECTIVE MULTICENTER STUDY**

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**Aims and Methods:** We intended to evaluate if the duration of biliary cannulation, the existence of a difficult cannulation and the use of rT are influenced by the papillary morphology.

**Conclusion:** This was a multicenter (3) prospective cohort study, including consecutive patients referred for ERCP with naïve papilla between August 2017 and January 2018, performed by experienced endoscopists (~ 4000 CPRE). The prevalence of biliary stones is very effective and is associated with transient and mild complications. There is a clear need for comparative studies between EHL and rT.

**Disclosure:** Nothing to disclose.

**P0213 DOES THE MORPHOLOGY OF THE MAJOR PAPILLA INFLUENCE BILIARY CANNULATION? - A MULTICENTER PROSPECTIVE STUDY**

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**Introduction:** Recent, the availability of single-operator cholangiopancreatoscopy (SOCP) turned these techniques more accessible and easier to perform. The success rate of biliary cannulation (tbc), difficult cannulation and rT.

**Conclusion:** The success rate of biliary cannulation, the existence of a difficult cannulation and the use of rT are influenced by the papillary morphology.

**Disclosure:** Nothing to disclose.
and 16.67% of the distorted ones. In patients with non-prominent papillae (5 cases) the mean tbc was 2,025 mins (iqr=8.53); in the bulging papilla (12.26%), the tbc was 2.25 mins (iqr=5.66); in the distorted (5.66%), tbc=2,025 mins (iqr=7.51). In the multivariate analyzes the papilla type/dimensions did not show to be a predictor of the 3 outcomes evaluated.

Conclusion: Contrary to what is stated in the literature, the type and dimensions of the papilla do not correlate with the difficulty of cannulation nor condition the techniques used.

Disclosure: Nothing to disclose.

P0214 THERAPEUTIC ENDOCOSCOPIC RETROGRADE CHOLANGIOGRAPHY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY
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Introduction: Endoscopic retrograde cholangiography (ERC) is an endoscopic procedure that is globally used for the treatment of biliary disease. However, ERC in patients with surgically altered gastrointestinal (GI) anatomy remains a challenging procedure due to the difficulty of reaching the target site. Consequently, percutaneous interventions or operations have been selected in these patients in spite of being more invasive procedures. Today the progression of techniques and devices like a Double-balloon endoscope (DBE) enables us to perform ERC in these patients. The aim of this study is to evaluate the utility and safety of therapeutic ERC in patients with surgically altered GI anatomy (except for Billroth-I reconstruction).

Aims and Methods: A total of 2341 consecutive ERCP procedures were performed at our hospital during a 5-year period (2012 to 2016). 105 ERC procedures for biliary disease on 67 separate patients with altered GI anatomy were included in this study. We retrospectively investigated: (1) the success rate of reaching the target site; (2) the success rate of cholangiography; (3) the therapeutic success rate (the success rate of ERC-related interventions); (4) the occurrence of adverse events.

Results: The mean age was 69.7 years, ranging from 37 to 87 years; 43 were male and 24 were female. The most common reconstruction technique was Roux-en-Y formation, which was performed in 54 cases, followed by biliopancreatic diversion in 48 cases, Billroth-II reconstruction in 12 cases, and bilioduodenal anastomosis in 5 cases. Bile duct stone 59% (n=2), benign bile duct stenosis 19% (n=20), pancreatic cancer 9.5% (n=10), hepatocellular carcinoma 3.8% (n=4), bili duct cancer 2.9% (n=3) were major indications. Bile duct stone extraction was performed in 46.7% (n=49), plastic stent and self-expanding metal stent (SEMS) was positioned for biliary drainage in 42.9% (n=45) and 1.9% (n=2), respectively. The results of the above investigations were: (1) 92.4% (97/103), 2) 97.9% (95/97), 3) 83.8% (88/105). Adverse events occurred in 9 cases (8.6%) with perforation 3.8% (n=4), pancreatitis 19.1% (n=2), aspiration pneumonia 1.9% (n=2), and cholangitis 1% (n=1). They were successfully treated conservatively in all patients with the exception of 1 in whom a perforation developed, requiring emergency surgery. Procedure-related mortality did not occur.

Conclusion: ERC in patients with surgically altered GI anatomy remains a challenging procedure. But today, the number of the successful therapeutic ERC is increasing in these patients by using DBE or PCF. Successful therapeutic ERC was achieved in 83.8%, a relatively high figure and the rate of adverse events were relatively low in this study. Therapeutic ERC should be performed positively for biliary disease, even if it’s a case of altered GI anatomy.

Disclosure: Nothing to disclose.

P0215 A MULTICENTER RANDOMIZED TRIAL COMPARING A 25G EUS FINE NEEDLE ASPIRATION DEVICE WITH A NOVEL 20G EUS FINE NEEDLE BIOPSY DEVICE

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Introduction: Several studies have compared Endoscopic Ultrasound (EUS) fine needle aspiration (FNA) to biopsy (FNB) needles, but none has proven the superiority of 1 needle over the other.

Aims and Methods: As studies were either underpowered or confined to 1 geographical region, we performed an investigator-initiated global randomized controlled trial, to compare the performance of a novel 20G FNB to a 25G FNA needle. 13 EUS-centers from 5 continents randomized consecutive patients with a solid lesion for FNB (ProCore) or FNA (EchoTip Ultra). Primary endpoint was diagnostic accuracy for malignancy and for the Bethesda classification (non-neoplastic, benign, atypical, malignant). Secondary, technical success, safety, and sample quality were assessed. Multivariable and supplementary analyses were performed to adjust for confounders.

Results: 608 patients were allocated to FNA (n=306) or FNB (n=302), enrolling 312 pancreatic lesions (51.5%), 147 lymph nodes (24%), and 149 other lesions (25%). Technical success rate was 100% for FNA and 99% for FNB (p=0.043), without differences in adverse events. FNB outperformed FNA in terms of histological yield (77% vs. 44%, p<0.001), accuracy for malignancy (87% vs. 78%, p=0.002) and Bethesda classification (82% vs. 72%, p=0.002). This was robust to correction for indication, lesion size, number of passes, and an on-site pathologist (OR 3.35, 95% CI 1.51-8.26, p=0.004), and did not differ between centers (p=0.836).

Conclusion: The 20G FNB needle outperforms the 25G FNA needle in terms of histological yield and diagnostic accuracy. This diagnostic benefit was irrespective of lesion type and consistent amongst participating centers, supporting general applicability of our findings.

Disclosure: This investigator-initiated study was supported by means of an unrestricted grant from Cook Medical.

P0216 CHOLANGITIS AFTER ENDOCOSCOPIC ULTRASOUND IN PATIENTS WITH BILLIARY STRictures AND ASSOCIATED RISK FACTORS
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Introduction: Endoscopic ultrasound (EUS) and EUS-guided fine needle aspiration (FNA) have emerged as an efficient diagnostic tool for pancreatobiliary diseases and have been considered to be a safe modality because of low risk of complications such as bleeding, perforation and pancreatitis. However, the risk of cholangitis after EUS/EUS-FNA in patients with biliary strictures has not been systematically evaluated so far.
been fully examined. In this study, we examined the rate and the risk factors of cholangitis after EUS-FNA in these patients.

Aims and Methods: We retrospectively reviewed the data of 138 inpatients with biliary strictures who underwent EUS/EUS-FNA at our institution between April 2012 and September 2017. We excluded 8 patients with percutaneous biliary drainage, 5 patients with difficulty in reaching duodenum and 1 patient who underwent EUS/EUS-FNA and ERCP at the same day. Cholangitis and its severity were diagnosed based on Tokyo Guidelines 2013.

Results: 125 patients (147 cases in total) were included; 59.2% were male; median age was 71; 46.4% of them were malignant (149 patients); pancreatic cancer: 13 patients, distal cholangiocarcinoma: 18 patients, hilar cholangiocarcinoma: 2 patients, intrahepatic cholangiocarcinoma: 3 patients, gallbladder cancer: 7 patients, the others) and 33 patients were benign (13 patients, IgG4-related disease, 1 patient, primary sclerosing cholangitis; 2 patients, tumor-forming pan-creatitis; 17 patients, others). The location of biliary strictures was 106 cases in distal (72.1%), 30 in hilar (20.4%), 4 in intrahepatic (2.7%) and 7 in spreading (4.8%). Endoscopic biliary stenting (EBS) had been already performed before EUS/EUS-FNA in 86 cases (58.5%). Median time from EBS to EUS/EUS-FNA was 21 days (range: 1–125 days). EUS-FNA was performed in 57 cases (38.8%). Cholangitis was observed in 4.1% (6/147). The severity was mild in 2, moderate in 3 and severe in 1 case. The patient who suffered from severe cholangitis underwent urgent endoscopic nasobiliary drainage at the day of EUS. The incidence of cholangitis in the cases with EBS was significantly higher than those without EBS (7.0% vs. 0% ; p = 0.042). Other statistically significant risk factors of cholangitis were gamma-GTP levels (> 1.5 upper limit of normal (ULN) (7.2%), < 1.5 ULN (0%, 0.64); p = 0.030) and ALP levels (> 1.5 ULN (10.7%, 5/6) vs. < 1.5 ULN (0%, 0.91); p = 0.003). Age, gender, malignant/benign disease, the location of biliary strictures, endoscopic sphincterotomy, examination time, examination with/without EUS, WBC, CRP, AST and ALT were not significant risk factors. In the cases with higher ALP levels, cholangitis occurred in 16.7% of the cases with EBS (6/36), while no cholangitis occurred in the cases without EBS (0/20).

Conclusion: The rate of cholangitis after EUS/EUS-FNA was 4.1% in the cases with biliary strictures. The use of prophylactic antibiotics might be beneficial in these cases, especially the cases with EBS and biliary elevation.

Disclosure: Nothing to disclose.
This is a pilot study that included 16 subjects with obesity (BMI 35.2 ± 5.3). The average length of hospital stay after ICU open lavage done but succumbed. More mortality in open and MAN groups. Open surgical techniques - More risk of fistula formation than minimal access \( \text{vs} \) open.

Portal vein thrombosis (PVT) is being increasingly diagnosed. Patients with PVT which don't fulfill the criteria of malignancy by imaging techniques; Presence of neoplastic thrombus serves as an important determinant of tumor \( \text{vs} \) endoscopy respectively. Technical success by FNA \( \text{vs} \) endoscopy was defined as successful tissue acquisition of a specimen adequate for cytohistopathological evaluation. Technical success was significantly higher with TTBNB (77.6%) \( \text{vs} \) EUS-FNA (36.7%) \( p < 0.001 \). In all, there were 2 cases of self-limiting intracystic bleeding (4.1%) which did not require additional interventions. There was 1 case (2%) of mild acute pancreatitis reported 48 hours after the procedure. This interim analysis of our multicenter prospective study suggests that EUS-TTNB is safe and effective for the evaluation of PCLs. EUS-TTNB represents an additional tissue acquisition method that may help increase the diagnostic yield of pancreatic cystic mucinous cysts during EUS.

Conclusion: Nothing to disclose

P0223 PROSPECTIVE MULTICENTER STUDY OF EUS-GUIDED THROUGH-THE-NEEDLE BIOPSY FOR SOLID LESIONS: AN INTERIM ANALYSIS

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Introduction: The primary aim was to evaluate the safety and feasibility of EUS-TTNB of PCLs. The secondary aim was to assess the potential incremental diagnostic yield of TTBNB of mucinous cysts. Aims and Methods: The primary aim was to evaluate the safety and feasibility of EUS-TTNB of PCLs. The secondary aim was to assess the potential incremental diagnostic yield of TTBNB of mucinous cysts. Prospective multicenter study of consecutive patients undergoing EUS fine-needle aspiration (FNA) and TTNB for PCLs \( > 15 \text{ mm} \) in size between June 2016 to November 2017. Technical success by FNA \( \text{vs} \) TTBNB was defined as successful tissue acquisition of a specimen adequate for cytohistopathological evaluation. Cyst fluid CEA was used to initially categorize cysts as neoplastic (CEA < 192 ng/mL) \( \text{vs} \) mucinous (CEA \( \geq 192 \text{ ng/mL} \)). A cyst was determined to be mucinous on cytolysis or histology by the presence of mucinous pancreatic cystic epithelium.

Results: A total of 49 patients (mean age 64.4 ± 15.2 years; 51% women) were included in the interim analysis. Mean PCL size was 56.2 mm, range 15–200 mm. Technical success was significantly higher with TTBNB (77.6%) \( p < 0.001 \) for PCL sampling. For cysts with insufficient amount of fluid for CEA (n = 14) \( \text{vs} \) CEA < 192 ng/mL (n = 24), the cumulative incremental diagnostic yield of a mucinous cyst was significantly higher with EUS-TTNB (44.7%) \( p = 0.0001 \) compared to EUS-FNA (2.6%) \( p < 0.001 \). In all, there were 2 cases of self-limiting intracystic bleeding (4.1%) which did not require additional interventions. There was 1 case (2%) of mild acute pancreatitis reported 48 hours after the procedure. This interim analysis of our multicenter prospective study suggests that EUS-TTNB is safe and effective for the evaluation of PCLs. EUS-TTNB represents an additional tissue acquisition method that may help increase the diagnostic yield of pancreatic mucinous cysts during EUS.

Conclusion: Nothing to disclose

P0224 PROSPECTIVE MULTICENTER STUDY OF EUS-GUIDED THROUGH-THE-NEEDLE BIOPSY FOR THE EVALUATION OF PANCREATIC CYST: AN INTERIM ANALYSIS

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Introduction: EUS-FNA is standard practice for tissue acquisition of solid lesions adjacent to the gastrointestinal tract. An EUS-guided through-the-needle microforceps is a novel tissue acquisition device. Aims and Methods: The aim of our study was to evaluate the safety and feasibility of EUS through-the-needle biopsy (TTBNB) of solid lesions using the microforceps. Prospective multicenter study of consecutive patients undergoing EUS fine-needle aspiration (FNA) and TTBNB of solid lesions \( > 15 \text{ mm} \) in size between June 2016 to November 2017. Technical success by FNA \( \text{vs} \) TTBNB was defined as successful tissue acquisition of a specimen adequate for cytohistopathological evaluation.

Disclosure: Nothing to disclose

P0220 ROLE OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION OF PORTAL VEIN THROMBUS IN THE DIAGNOSIS AND STAGING OF HEPATOCELLULAR CARCINOMA

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Introduction: Portal vein thrombosis (PVT) is being increasingly diagnosed. Presence of neoplastic thrombus serves as an important determinant of tumor staging, as well as prognosis, and influences treatment selection. In some cases, it may be the initial sign of an undetected HCC. Therefore, accurate differentiation of bland from neoplastic thrombus is crucial for patient treatment. Aims and Methods: This is a prospective study that included 11 cirrhotic patients with PVT who don’t fulfill the criteria of malignancy by imaging techniques; either with or without hepatic mass or undergone local treatment following a diagnosis of HCC and develop PVT during their follow-up. Under EUS guidance, the main, left and right portal veins were identified and a 22-gauge EUS-FNA needle was advanced from the duodenum into the portal vein, 1–2 passes through portal vein thrombus were taken. The puncture site was monitored under EUS for complications. To assess the ease, safety, and efficacy of EUS-FNA in characterizing the nature of the PVT which don’t fulfill the criteria of malignancy via imaging techniques; Results: Out of 11 patients; 7 patients (64%) were males. 6/11 were cirrhotic without liver masses, 4/11 HCC and 1/11 developed PVT during their follow-up after EUS-guidance. Technical success by FNA or TTNB was defined as successful tissue acquisition of a specimen adequate for cytohistopathological evaluation. Conclusion: EUS-FNA is an effective and safe method in characterizing the nature of PVT which don’t fulfill the criteria of malignancy via imaging techniques. We believe that EUS-FNA should be utilized more frequently in the diagnosis and staging of HCC.

Disclosure: Nothing to disclose

P0221 EVALUATION OF THE ROLE OF ENDOSCOPIC ULTRASOUND-GUIDED GASTRIC BOTULINUM TOXIN INJECTIONS IN THE TREATMENT OF OBESITY

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Introduction: Obesity is an important public health concern. In rats, botulinum toxin A (BTA) injected subepithelially into the antrum resulted in significant decreases in caloric intake and body weight. Subsequent open-label human studies have reported conflicting results, finding little or no body weight loss after gastric BTA injection. We hypothesized that EUS guidance would help to assure injection of gastric muscularis propria and subserosal layers. Aims and Method: To assess the safety, feasibility and efficacy of EUS-guided gastric Botulinum toxin A injections in obese subjects to reduce body weight. This is a pilot study that included 16 subjects with obesity (BMI > 30). Under EUS guidance, BTA injections (100U) were made with 25G needle. A ring of 5 injections were made into the antral muscularis propria; 2–3 cm proximal to the pylorus. During a 16 weeks follow-up period, subjects were weighed and completed the Gastrointestinal Symptom Rating Scale (GSRS) 2 weeks before and weekly after injection. Nutrient drink tests 1 week before and at 4 and 16 weeks after injection. No behavioral or dietary interventions were offered to study subjects.

Results: Out of 16 subjects; 15 subjects (93.7%) were females. Mean age was 34.5 years (21–43) and mean BMI was 41.5 (33–50). In a follow-up period of 16 weeks, weight loss ranged from 7 to 25 kg. Nutrient drink tests decreased from a baseline value 1200 cc (600–1800) to 420 cc (240–600) at 4 weeks. Mild elevation of the GSRS score was found in 2 subjects who reported diarrhea at 1–4 week in 1 subject and at 5–7 week in another 1. No vomitting, abdominal pain or any other complications were detected in any subject.

Conclusion: EUS-guided botulinum toxin injection is an effective method for weight reduction which can be performed safely with minimal adverse events. However, further studies are still warranted.

Disclosure: Nothing to disclose
Results: A total of 45 patients (mean age 64.2±13.3 years; 60% men) were included in the analysis. Mean lesion size was 44.1 mm, range 18-222 mm. The following sites were sampled: pancreas (n = 25; 55.6%), gastric/duodenal subepithelial lesion (n = 12; 26.7%), lymph nodes (n = 6; 13.3%), retroperitoneum (n = 1; 2.2%) and liver (n = 1; 2.2%). Technical success (adequate cellularity for cytogenetic/pathologic analysis) was similar between the two groups (n = 42; 93.3%) and TTNB (n = 39; 86.7%) (p = 0.48). Diagnostic yield with FNA was 83.3% compared to 97.9% with TTNB (p = 0.5). There were no intra-procedural or post-procedural adverse events reported with FNA and TTNB.

Conclusion: Analysis of our prospective study suggests that EUS-TTNB is a safe and feasible technique for tissue acquisition of solid lesions. The diagnostic yield with TTNB was similar to that of FNA. EUS-TTNB represents a novel tissue acquisition method for the evaluation of solid lesions adjacent to the GI tract.

Disclosure: Nothing to disclose.
During study period, 58 patients (23 female; mean age, 68.0±18.2 years) were enrolled. The variable evaluated were mass size, route of puncture, needle type, success rate, age of the stent (mean size of 21.4±7.9 mm). Biopsy results increased sensitivity, and diagnostic accuracy of 93.1%. The sensitivity and specificity of EUS-FNB were 89.7% and 100%, respectively. Additional information regard- ing cytology results increased sensitivity, and diagnostic accuracy of 93.1%, respectively. There was 1 bleeding complication, but well-controlled with endo- scopic hemostasis. The median score of the procedure related pain using visual analog scale was 8.7±2.8. The median number of needle passes was 2.6±0.8 (range, 1-5). The diagnostic accuracy were 89.7%, but both specimen adequacy for histology and diagnostic accuracy were 89.7%, but both specimen adequacy for histology and diagnostic accuracy were 89.7%, but both specimen adequacy for histology and diagnostic accuracy were 89.7%, but both specimen adequacy for histology and diagnostic accuracy were 89.7%, but both specimen adequacy for histology and diagnostic accuracy were 89.7%.

Conclusion: Combining the 3 parameters on the computerized analysis of the performances, to discriminate between adequately and inadequately cleansed still frames. Sensitivity was of 90.01% (95% CI [84.12–95.88]) and specificity 87.73% (95% CI [81.63–94.37]), positive and negative predictive values were respectively of 81.10% (95% CI [73.31–88.69]) and of 93.70% (95% CI [88.94–98.46]). The mean time required to electronically analyze a still image using the 3 criteria test method was 34±2 milliseconds using the MATLAB® software. An extrapolation on 50,000 images suggests a 28 minutes analysis of a full-length CE video.

Conclusion: We propose a novel, efficient, perfectly reproducible, automatic and rapid multi-criterion electronic score to determine the level of cleanliness of SB-CE still frames. This tool will be able to serve in clinical practice (to determine if the quality of preparation of SB-CE is acceptable) and research (testing different modalities of bowel preparation). A European patent is pending.

Disclosure: Xavier Dray has acted as a consultant for Boston Scientific, Fujifilm, Medtronic, and Pentax. Sarra Oumrani, Aymeric Histace, Einas Abou Ali, Olivia Pietri, Aymeric Beccq, Guy Housit, Isabelle Nion-Larmurier, Marine Camus, Christian Florent disclose no conflicts of interest related to this subject.

References
Disclosure: Xavier Dray is a consultant for Boston Scientific, Fujifilm, and Medtronic. Gabriel Rahmi is a consultant for Medtronic. Jean Christophe Saurin is a consultant for Capsvision, Medtronic and Intromedic. Sylvie Sacher Huvelin is a consultant for Medtronic.

References

P0232 CAD-CAP: A 26000 IMAGES DATABASE SERVING THE DEVELOPMENT OF ARTIFICIAL INTELLIGENCE FOR CAPSULE ENDOSCOPY

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nephropathy alone did not significantly influence SBTT. No correlation was found for peak HgA1c and small bowel risk factors. Gastric transit time (GTT) was similar between the DM and non-DM cohorts (0.54 +/-0.67 hours VS 0.6 +/-0.82 hours, p = 0.55), and no correlation was found between GTT and either the presence of end-organ damage, HgA1c levels within 3 months from VCE, peak HgA1c or the duration of the disease. VCE completion rate was significantly lower in DM patients with neuropathy compared to those without end organ damage (87.5% VS 98%, p = 0.03). There was a trend towards lower VCE completion rate in patients treated with insulin or with combined end-organ damage, however it didn’t reach statistical significance. VCE completion rate was similar between non-DM patient and DM patients without end-organ damage (94% VS 98%, p = 0.11).

Conclusion: SBTT is significantly prolonged in DM patients with neuropathy or insulin treatment, and might lead to lower VCE completion rate in those patients. An a priori longer VCE recording time should be considered for patients with these conditions. For DM patients without end-organ damage or insulin treatment, bowel transition times and VCE completion rates are similar to those without DM, thus examination time adjustments are not needed.

Disclosure: One of the authors (Dr. Stein Assal) is also a member of R&D team, Medtronic, Yokneam site, Israel.

P0234 VIDEOCAPSULE ENDOSCOPY IN UNEXPLAINED IRON DEFICIENCY ANEMIA: A RETROSPECTIVE COHORT STUDY

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Introduction: Iron deficiency anemia (IDA) may affect 1-2% of all adults. After conventional endoscopy, the cause of IDA remains unknown in up to 40% of patients. Video-capsule endoscopy (VCE) detects the most distinct images that may contain abnormalities. A complete medical history and laboratory tests were collected. All subjects received VCE (PillCam SB2/SB3) and Lewis score was calculated. Comparison between continuous variables was performed by unpaired t-test and between categorical variables by Fisher’s exact test. Variables with statistical significance at univariate analysis were evaluated by a multivariate binomial or linear regression analysis. The risk was expressed with Odd Ratio (OR) and 95% confidence intervals (CI).

Results: 109 (female/male ratio 53:56, aging 63.4 ±18.9 years) were recruited according to exclusion and inclusion criteria. All patients had hemoglobin levels < 10 g/dl and a strong suspicion of obscure bleeding. Eighty (73.4%) presented 1 or more small bowel lesions at VCE (11 petechiae, 13.7%; 29 erosions, 36.2%; 7 hemorrhagic masses, 8.7%; 3 denuded areas, 3.7%; 3 strictures, 6.25%; 15 neoplasms, 18.75% and 25 angiodyplasia, 31.25%; 14 patients had multiple lesions, 18.75%).

52 patients (65%) showed a mild Lewis score (<135), 52 (31.2%) a moderate score (135 to 790), and only 3 (3.8%) showed a score >790. The mean Lewis score in patients with lesions was 193±198. We did not find a significant correlation between hemoglobin levels and severity of damage: Pearson’s r = 0.10, p = 0.41.

When compared to patients without small bowel injury, subjects with lesions had a longer small bowel transit time (6.2 ± 2.9 vs 5.2 ± 1.1 hours), had used non-steroidal anti-inflammatory drugs for at least 2 weeks (17.5% versus 0%, p = 0.01) and used more frequently oral anticoagulants (20% versus 6.9%, p = 0.10) at univariate analysis. None of the factors statistically significant in univariate analysis was associated with the presence of small bowel injuries at multivariate analysis (table 1).

Age (b = 1.05, 95% CI 0.76-1.38, p = 0.01), small bowel transit time (b = 1.26 95% CI 1.05-1.46, p = 0.009), and PPI use (b = 5.81 95% CI 4.54-7.45, p = 0.09) showed a favorable trend, correlating directly with the severity of the lesion at univariate analysis. In the multivariate analysis, only the use of PPI correlate showed a favorable trend, correlating directly with the severity of the lesion at VCE, peak HgA1c or the duration of the disease.

Conclusion: VCE can reveal a source of obscure bleeding in unexplained IDA in 15-20% of subjects. Only the use of PPI correlates showed a favorable trend, correlating directly with the severity of the lesion at VCE, peak HgA1c or the duration of the disease.

Disclosure: Nothing to disclose.

P0235 A ROPEWAY CAPSULE ENDOSCOPY FOR EXPLORING THE ENTIRE GASTROINTESTINAL TRACT WITH A NON-PER OS PREPARATION AND A SHORTER EXAMINATION TIME

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Introduction: Capsule endoscopy is designed for screening a long tube organ such as the small intestine or colon. Though they are non-invasive, they have various drawbacks compared to conventional endoscopes, such as inadequate observation in the esophagus and stomach, an unacceptable amount of preparation solution for colon screening and a long examination time. Aims and Methods: Our aim was to realize an entire gastrointestinal (GI) tract examination with high accuracy, easy preparation and a short examination time. Our system was composed of a current colon capsule endoscopy (CCE: PillCam colon2, Covidien, USA), a length of carbon thread attached to the CCE and a 7.5 Fr. catheter with a tilting function at the tip (Smart touch: Biosense Webster, USA). At first a 0.04mm carbon thread was inserted into the nose and taken out through the mouth using a magnet. After the AFR function was turned on, a CCE was attached to the thread and swallowed. After confirming the CCE’s position in the stomach, the catheter was inserted into the stomach along the thread. The extractor used the catheter to control the volume of air in the stomach to flush water through it if the stomach needed cleaning. After observing all parts of the stomach, the CCE was navigated into the duodenum. The capsule was detached from the tip of the catheter by pulling on the thread. After the detachment, the catheter was used for injecting a large volume (over 2 liters) of preparation solution into the small bowel quickly to accelerate the CCE’s movement and cleanse the colon easily. To evaluate this method, 15 volunteers were enrolled in a pilot study.

Results: 1) We could observe all the parts of the stomach easily and manipulation of the catheter was the same as current endoscopy. Image quality was not inferior to conventional gastroscopy. 2) The preparation solution was injected into the duodenum through the catheter at a speed of 10cm/sec, which meant that we could inject 3 liters in 300 seconds. 3) The chief adverse reaction was abdominal distention (3/15). 4) The average examination time for the small bowel transit time was 12 minutes and the colo-rectal transit time was 33 minutes. 5) The cleanliness was similar to or better than the current colon capsule endoscopy preparation. 6) The VAS scores for acceptability were better than the scores for current colon capsule endoscopy preparation.

Conclusion: We have developed a simple, inexpensive and practical method for examining the entire GI tract with only one CCE.

Disclosure: Nothing to disclose.

P0236 CAPSULE ENDOSCOPY: IS THE SOFTWARE TOP 100 A RELIABLE TOOL IN MID-GASTROINTESTINAL BLEEDING?

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Introduction: Capsule endoscopy (CE) is the gold standard for diagnosing mid-gastrointestinal bleeding (MGB). In 2017 emerged a new functionality in the RAPID Reader® the TOP100, that performs the automatic selection of the 100 most distinct images that may contain abnormalities.

Aims and Methods: We aimed to compare the Concordance of findings between the classical CE reading (CR) and the use of TOP 100 in suspected MGB. Retrospective study including consecutive patients submitted to CE for suspected MGB. 2 experienced readers performed CR and reported the most important findings. Another experienced reader, blinded to the CR results, reviewed all SBCE videos using TOP100 and reported the most important findings, excluding false positive results. In MGB the relevant findings were defined as the presence of P2 lesions, namely angiectasias, ulcers or tumors.

Results: 69 patients were included, 56.5% females, with mean age 60 ±18 years. 62 patients (89.9%) performed CE for anemia and 7 (10.1%) for obscure-outer gastrointestinal bleeding. The overall diagnostic yield was 42% and the P2 lesions more frequently observed were angiectasias (34.85) followed by ulcers (11.6%). No tumors of the small bowel were observed.

TOP100 detected 53.66 (80.3%) of the P2 lesions, in particular 45.46 (93.75%) of the TOP100 detected 53.66 (80.3%) of the P2 lesions, in particular 45.46 (93.75%) of the angiectasias and 8/18 (44.4%) of the ulcers. The TOP 100 identified all active bleeding.
All images that were false positives selected by the TOP 100 were easily identified by an experienced reader.

**Conclusion:** The TOP100 identified all active bleeding, as well as the vast majority of significant lesions (80%), in particular, detected about 94% of angioectasias. Although CR remains the gold standard in the EC review, these findings demonstrate that TOP100 allows a quick reading with early identification of the most important findings in MGIB, constituting an extraordinary tool in an urgent context.

**Disclosure:** Nothing to disclose

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**P0237 SIGNIFICANCE OF INCIDENTAL FINDINGS IN VIDEO CAPSULE ENDOSCOPY**

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**Introduction:** Video Capsule Endoscopy (VCE) is the procedure of choice for the investigation of small bowel pathologies. VCE examinations also provide limited views of the esophagus, good visualization of the stomach/proximal duodenum, and some visualization of the colon. Incidental gastrointestinal pathologies in the upper gastrointestinal tract and colon are often seen during VCE but there is limited data regarding the significance of incidental findings. These pathologies, may not be directly linked to the patient's presenting complaint, may not be clinically significant and can lead to unnecessary investigations and consumption of health care resources.

**Aims and Methods:** The aim of this study is to evaluate if incidental pathologies found during VCE have any effect on patient outcome. 2 experienced gastroenterologists consulted prospectively reviewed the upper GI segment and colonic segments of VCEs performed over a 5-year period and identified those with UGI and colonic findings. These patients were then reviewed in the electronic databases for follow up visits, investigations, and treatments up to a year following their VCE procedure.

**Results:** We identified 103/733 (14.1%) patients with incidental findings, of which, 51 patients (49.5%) had completed charts that allowed for analysis. Incidental upper GI pathologies were identified in 45/103 (43.7%) patients in the original VCE reports, and 88/103 (85.4%) in the prospective dedicated VCE reading (p = 0.001). Incidental colon pathologies were identified in 7/103 (6.8%) patients in the original reports, and 19/103 (18.4%) in the prospective dedicated VCE reading (p = 0.012). 40 (38.8%) patients had only incidental upper GI and/or colon VCE findings without small bowel findings. 32 out of 51 (62.7%) patients with incidental VCE findings were seen for follow up. 19 of 51 (37.3%) patients had further investigations related to pathologies outside the small intestine; 9 underwent repeat EGD only, 4 underwent repeat colonoscopy only, and 6 underwent both repeat EGD and repeat colonoscopy. 5 out of 15 (30%) documented follow up EGDS attributed to a positive incidental finding on VCE were found to have significant findings that were not documented in their respective pre-VCE EGD reports. 2 out of 10 (20%) documented follow-up colonoscopies attributed to a positive incidental finding on VCE were found to have significant findings which were not documented in their respective pre VCE colonoscopy reports. No patients had recorded repeat hospitalizations, required blood products, or invasive interventions during the follow-up period.

**Disclosure:** Nothing to disclose

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**P0239 ENDOSCOPIC ULTRASOUND-GUIDED TRANSMURAL GALLBLADDER DRAINAGE USING ELECTROCAUTERY-ENHANCED LUMEN-APPOSING METAL STENT VERSUS STANDARD TUBULAR METAL STENT**

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**Introduction:** In high-risk patients, EUS-guided gallbladder drainage (EUS-GBD) is a validated alternative to percutaneous transhepatic gallbladder drainage (PT-GBD) based upon the Tokyo guidelines for endoscopic ultrasound-guided gallbladder drainage. Although EUS-GBD has been used for cholecystostomy, it has a higher technical success rate compared to PT-GBD. EUS-GBD is reported to be a safe and effective procedure for patients undergoing transluminal cholecystostomy, with high clinical success rates and low rates of adverse events. In recent years, endoscopic ultrasound-guided transcystic drainage (EUS-TCD) has become an attractive alternative to PT-GBD. However, the choice of drainage method remains controversial, and more studies are needed to determine the optimal method for each patient.

**Aims and Methods:** We conducted a randomized controlled trial comparing EUS-GBD and EUS-TCD for the management of symptomatic cholecystitis in high-risk patients. The primary endpoint was technical success, defined as placement of the stent without complications. Secondary endpoints included clinical success, defined as resolution of symptoms within 3 days, and adverse events. The study included 34 patients with symptomatic cholecystitis, who were randomized to either EUS-GBD or EUS-TCD. The mean age of the patients was 49 years (range, 23-74), and 21 (62%) were women. The mean body mass index was 27.6 (range, 18.2-36.5). The mean Cholecystitis and Cholelithiasis Grade Scale score was 9 (range, 6-12). The mean procedure time was 22.5 minutes (range, 10-40) in the EUS-GBD group and 7 minutes (range, 3-30) in the EUS-TCD group. The mean length of stay in the hospital was 4 days (range, 2-10) and 5 days (range, 4-10), respectively.

**Conclusion:** EUS-GBD technique is associated with improved technical success rates, shorter procedure times, and lower rates of adverse events compared to EUS-TCD. However, further studies are needed to determine the optimal drainage method for each patient, taking into account factors such as patient characteristics, disease severity, and other clinical factors. In conclusion, our study provides valuable insights into the management of symptomatic cholecystitis, and highlights the importance of individualizing the approach to each patient.
also observe no stent migration and no recurrence of cholecystitis with the ECE-LAMS, so this is contrary to the literature.


References

P0240 STENT PATENCY ACCORDING TO THE CHEMOTHERAPY AND ITS REGIMEN
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Introduction: Jaundice and subsequent biliary infection caused by tumor can be detrimental for the patients with pancreatic cancer. Therefore, stent insertion for biliary decompression is necessary for the patients with biliary obstruction by pancreatic cancer and it is important to keep the stent patent as long as possible. However, few studies have compared stent patency according to chemotherapy itself and chemotherapy regimen. Aims and Methods: Therefore, in this study, we aimed to evaluate the difference of stent patency according to chemotherapy and the factors associated with better stent patency. Between January 2015 and May 2017, 102 patients with pancreatic cancer who underwent biliary stent insertion with metal stent for the first time were retrospectively analyzed. The relationship between chemotherapy and stent patency were assessed. Additionally, factors for better stent patency and stent patency according to the chemotherapy regimen were also assessed. Results: Median stent patency was 163 days for patients with best supportive care, 338 days for patients with chemotherapy, respectively. (p = 0.041) Univariate analysis showed that chemotherapy itself and chemotherapy regimen stent were significantly associated with better stent patency. Compared with patients who received best supportive care only, patients who underwent chemotherapy after stent insertion had better stent patency in multivariate analysis (OR 0.494; CI 0.247–0.988; p = 0.046). FOLFIRINOX also showed better stent patency than gemcitabine-based chemotherapy in multivariate analysis (OR 0.318; CI 0.113–0.900; p = 0.031). Conclusion: Compared with patients who received best supportive care only, patients who underwent chemotherapy after stent insertion had better stent patency. Better stent patency can be expected for the patients with FOLFIRINOX. Disclosure: Nothing to disclose

P0241 DRAINAGE OF THE RIGHT LIVER UNDER EUS: BRIDGE TECHNIQUE WITH HEPATICOGASTROSTOMY ALLOWING DRAINAGE OF THE RIGHT LIVER THROUGH THE LEFT LIVER INTO THE STOMACH
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Introduction: EUS (Endoscopy ultrasonore)-guided biliary drainage is now a comparable technique to percutaneous drainage. This drainage can also be performed in cases of complex drainage of the hilum, mainly described for salvage technique in patients who underwent biliary stent insertion with metal stent for the first time were retrospectively analyzed. The relationship between chemotherapy and stent patency were assessed. Additionally, factors for better stent patency and stent patency according to the chemotherapy regimen were also assessed. Results: Median stent patency was 163 days for patients with best supportive care, 338 days for patients with chemotherapy, respectively. (p = 0.041) Univariate analysis showed that chemotherapy itself and chemotherapy regimen stent were significantly associated with better stent patency. Compared with patients who received best supportive care only, patients who underwent chemotherapy after stent insertion had better stent patency. Better stent patency can be expected for the patients with FOLFIRINOX. Disclosure: Nothing to disclose

P0242 FULLY COVERED SELF-EXPANDABLE METALLIC STENT, AS SUPERIOR TREATMENT OPTION FOR BILIARY ANASTOMOSIS STRICURE AFTER LIVER TRANSPLANTATION COMPARED TO PLASTIC STENTS: A CASE-CONTROL STUDY
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Introduction: Fully covered self-expandable metallic stent (FCSEMS) was reported as endoscopic treatment option for biliary anastomotic stricture (AS) after liver transplantation (LT). However, there were only few studies compared FCSEMS to conventional plastic stent insertion to biliary strictures. The aim of this case-control study was to evaluate resolution rate of biliary AS and 1-year recurrence rate after stent removal between FCSEMS and plastic stents in LT patients. Aims and Methods: 35 cases with biliary AS after LT were enrolled between 2012 and 2016. There were 20 patients in plastic group and 15 in FCSEMS group. ERCP were repeated every 3 months for evaluate stent function and AS resolution. Stent was removed if AS resolution was confirmed with radiologic remission. Patients were followed up until 1yr after stent removal for evaluate AS recurrence. Results: There were no significant differences between groups in age, gender, and other baseline characteristics. The median stent indwelling period was 4.7 vs. 8.9 months in FCSEMS and plastic group (p = 0.039). The numbers of ERCPs were 2.3 in FCSEMS group and 3.1 in plastic group (p = 0.065). The mean number of inserted stents and ballooning during treatment period were lower in FCSEMS group (p = 0.004 and 0.007). The AS resolution rate was superior in FCSEMS group to plastic group (100% vs. 65%, p = 0.012). The 1-year AS recurrence rate were lower in FCSEMS group than plastic group (0 of 15 vs. 4 of 13, p = 0.042). Complication rate associated with stent insertion was 20% in FCSEMS group and 45% in plastic group (p = 0.049). Table 1. Comparison of plastic versus Kaffes stent for anastomosis stricture after liver transplantation

<table>
<thead>
<tr>
<th>Plastic</th>
<th>FCSEMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (20)</td>
<td>N (15)</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
</tr>
<tr>
<td>Male gender, N (%)</td>
<td>16 (80.0%)</td>
</tr>
<tr>
<td>Age, mean ±SD</td>
<td>53.1 ± 13.9</td>
</tr>
<tr>
<td>AS onset from LT, mo., median (range)</td>
<td>12.4 (0.7–74.6)</td>
</tr>
<tr>
<td>AS duration, mo., median (range)</td>
<td>12.4 ± 27.6</td>
</tr>
<tr>
<td>Number of ERCPs, mean ±SD</td>
<td>3.1 ± 1.3</td>
</tr>
<tr>
<td>Number of stents, mean ±SD</td>
<td>2.6 ± 2.0</td>
</tr>
<tr>
<td>- Leth of FCSEMS, cm</td>
<td>4.9 ± 1.0</td>
</tr>
<tr>
<td>- Width of FCSEMS, mm</td>
<td>6.9 ± 1.0</td>
</tr>
<tr>
<td>Number of ballooning, mean ±SD</td>
<td>1.7 ± 1.8</td>
</tr>
<tr>
<td>Stent indwelling period, mo., median (range)</td>
<td>8.9 (65.8–47.5)</td>
</tr>
<tr>
<td>Stricture resolution, N (%)</td>
<td>13 (65.0%)</td>
</tr>
<tr>
<td>1-year Recurrence, N (%)</td>
<td>4 (30.8%)</td>
</tr>
<tr>
<td>Complication during treatment, N (%)</td>
<td>9 (45.0%)</td>
</tr>
</tbody>
</table>

Conclusion: FCSEMS was superior compared to plastic stent in aspect of AS resolution rate of and 1year-recurrence rate without increasing complication rate. In addition, stent indwelling period, number of stents and ballooning procedure were reduced in FCSEMS group than plastic group. The FCSEMS is safe and effective treatment option for biliary AS after LT. Disclosure: Nothing to disclose

P0243 IN VIVO EVALUATION OF A NOVEL ANTIREFLUX BILIARY METAL STENT
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Introduction: The efficacy of antireflux valve (ARV) biliary stent has not been well established and previous studies showed mixed results. ARV metal stents may be ineffective due to morphological change of the ARV. A novel ARV metal stent is a graft of 2 different stents, and each part has a different radial force. Distal part, ARV area, can be freely bent in multiple directions and has an unchanging stent lumen.

Disclosure: No conflict of interest
P2044 INTRA-DUCTAL MIGRATION OF BILARY AND PANCREATIC STENTS, HOW TO MANAGE SUCH COMPLICATION? MONO-CENTERED EVALUATION OF A RETRIEVAL TECHNIQUE USING RAT-TOOTH FORCEPS

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Introduction: Intra-ductal stent migration, biliary or pancreatic, with a removal attempted using rat-tooth forceps were included. For each case, the procedure was consisting of first catheterizing the involved duct with a guide wire pushed along the stent, then advance forceps up to the distal tip of the stent, and finally open it for grasping the stent to pull it outside of the duct. A balloon dilation or an enlargement of sphincterotomy could be applied in association to help for extracting the stent.

Aims and Methods: This was a retrospective observational monocentered study. All the patients with intra-ductal stent migration, biliary or pancreatic, with a removal attempted using rat-tooth forceps were included. For each case, the procedure was consisting of first catheterizing the involved duct with a guide wire pushed along the stent, then advance forceps up to the distal tip of the stent, and finally open it for grasping the stent to pull it outside of the duct. A balloon dilation or an enlargement of sphincterotomy could be applied in association to help for extracting the stent.

The age, sex, pathology of the patients, the indication for ERCP, the location, the type of stent, the presence of a stricture and stones, the associated techniques have been recorded. The main objective was to document the technical success of the stent removal using rat-tooth forceps.

Results: In total, 2152 ERCPs with biliary or pancreatic stenting have been performed between 2009 and 2017. The overall migration rate was 5%, with 2.5% of the biliary stents and 3.5% for biliary stents. Several techniques have been proposed for removing those stents, but to date, none has been objectively assessed in terms of technical success and complication rate. Thus, we propose a study with the aim to evaluate the outcomes of the stent removal using rat-tooth forceps.

Discussion: Nothing to disclose

References


P2045 URGENT ERCP AND PANCREATIC DUCT STENTING FOR THE MANAGEMENT OF POST-ERCP PANCREATITIS

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Introduction: Post-ERCP pancreatitis (PEP) is the most common and dreadful complication of ERCP, with an incidence ranging from 3 to 15% incidence rate among patients (pts.). Traditional methods of treatment of acute PEP like surgical approach or conservative treatment are well known, meanwhile endoscopic treatment, in particular duct stenting, are still controversial.

Aims and Methods: To evaluate the results of endoscopic stenting of the main pancreatic duct (MDP) as a new perspective treatment method of PEP. From 01.01.2009 till 01.01.2016 we performed 3366 endoscopic interventions on major duodenal papilla (MDP), Complications occurred in 57 (1.7%) cases and PEP was diagnosed in 33 (0.98%) of the 3366 procedures (mean age 59.7 ± 11.1). The indication for primary endoscopic interventions was jaundice in all cases, caused by stenosis of the MDP and micro lithiasis (21), cholecystolithiasis (7), duodenal parapapillary diverticulism (2), polyps of the MDP (2), perforations on the sides, pig-tail and straight type with flaps by both ends. The most common complications of risk factors in patients with PEP were conjunction of 2 (21%), 3 (31%), and 4 (21%) risk factors.

Results: Promptly after confirmation of the diagnosis of acute PEP we tried to perform stenting of the MDP in 33 patients (1.0%) with acute PEP (88.0%) of them. Complications of pancreatic stenting have not been revealed; all patients recovered. Inserted stents were short length, 5 and 7 Fr diameter with perforations on the sides, pig-tail and straight type with flaps by both ends. Pancreatic stents were removed in 5–12 days after their placement. The average time of pancreatic stenting was 11.2 ± 3.2 days. The average length of hospitalization was 10.4 ± 3.7 days. Other 11 (33.3%) pts., including 3 pts, with failed attempts of stenting, underwent medical therapy and 2 of them - surgical interventional procedures. There were 2 (18.2%) lethal outcomes in this subgroup. The average time of hospitalization was 22 ± 17.1 days.

Conclusion: Endoscopic stenting of the MDP is technically feasible in 88.0% (22/ 25) of patients with acute PEP and it leads to recovery in all cases. Urgent pancreatic stenting should be done as fast as it is possible, not more than 24 hours after the primary endoscopic retrograde intervention. Successful stenting is effective and safe method of treatment of this dangerous complication of ERCP. Moreover using pancreatic stenting reduces length of hospitalization by 55%, which brings economic benefits. Meanwhile the subgroup of patients where pancreatic stenting was not performed or failed, mortality reached 18.2% and average time of hospitalization was in 2 times longer. Prospective randomized trial is needed to prove these promising results.

Disclosure: Nothing to disclose

References

MRI signal intensity (SI) as a biomarker for water content, where higher values mean drier liver.

Results: After oxycodone treatment, total colonic fecal volume was significantly increased [mean 101 mL, 95% CI 15 to 187 mL] compared to placebo treatment [mean –14 mL, 95% CI –74 to 46 mL] (p = 0.001), with the largest difference (24%) observed in the ascending colon. Stool volume increased after oxycodone treatment [mean 0.09 SL, 95% CI 0.01 to 0.17 SL] compared to placebo [mean –0.02 SL, 95% CI –0.08 to 0.04 SL] (p = 0.001).

Conclusion: The MRI analysis methods showed differences in colonic fecal volume after oxycodone treatment for both control and treated groups. The MRI-based method for non-invasive assessment of colonic content have the potential to characterize gastrointestinal symptoms in general, such as in constipation.

Disclosure: Nothing to disclose

Reference

P0247 THE SAFETY TRIAL OF SONODYNAMIC THERAPY FOR UNRESECTABLE INTRACTABLE CANCER
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Introduction: High-intensity focused ultrasound (HIFU) is expected to be the new and improved advanced therapy for unresectable intractable cancer (UIC) like pancreatic cancer (PC). The combination of HIFU therapy and chemotherapy can be used to effectively control the locally advanced tumor of unresectable intractable cancer by the site-direct manner. HIFU therapy has showed effectiveness of anti-tumor effect for unresectable PC. From that, we have developed the new method, Sonodynamic therapy (SDT) in order to enhance anti-tumor effect and limit the damage done to the normal tissues during treatment. SDT is a novel therapeutic method of cancer treatment deriving from the cytotoxicity reaction, which is based on preferential uptake of sonosensitizer with anticancer drug in tumor tissues and subsequent activation of drug by ultrasound irradiation form an extracorporeal.

Aims and Methods: We have evaluated the safety and clinical tolerability of SDT in UIC. This is the prospective exploratory clinical non-random sampling and a series of registration studies. We have treated UIC patients using SDT, with whom an agreement was obtained in adequate IC, from May 2017 in our hospital. This study had received approval from the members of the ethic society of our hospital, and obtained research support from the Japan Agency for Medical Research and Development (AMED). The participants of the study were 12 UIC patients, i.e. 11 of pancreatic cancer and 1 of cholangiocarcinoma of Stage IV. The average age of the participants was 63.7 years old. The performance status was PS 0.6 and PS 1.6 patients, of whom 11 have had chemotherapy previously and 1 had no therapy. The HIFU device used was MS-2 (joint production equipment by Hitachi, Ltd., Denso, Inc., Tohoku University and Tokyo Women’s Medical University, Japan, which was provided by Tokyo Woman’s Medical University. The drug used for the study was epirubicin-conjugated polymer micelles; NC-6300 (manufactured by NanoCarrier Co., Ltd. And supplied by Kowa Company, Ltd., Japan). NC-6300 was administered in UIC. This is the prospective exploratory clinical non-random sampling and a series of registration studies. We have treated UIC patients using SDT, with whom an agreement was obtained in adequate IC, from May 2017 in our hospital. This study had received approval from the members of the ethic society of our hospital, and obtained research support from the Japan Agency for Medical Research and Development (AMED).

Results: Side effects of NC-6300 after administration were not seen in which step in quantity of four steps of HIFU power and doses of NC-6300 was performed. Which induces a cavitation and heightens the SDT effect. 3 radiation, and performed HIFU irradiation by the triggered HIFU sequence was the high strength pulse irradiation addition to the usual continuous-wave irradiation.

Disclosure: Nothing to disclose

P0248 SAFETY AND EFFECTIVENESS OF EU-GUIDED HEPATICOGASTROSTOMY (EUS-EGHS) COMPARED WITH PTBD IN PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION
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Introduction: EUS-guided hepaticogastrostomy (EUS-EGHS) is recognized as an effective palliative treatment as peritoneal resection for unresectable intractable cancer like pancreatic cancer/biliary tract cancer/Gastric cancer Other 17/10/11/8 vs. 7/6/0.0 (p < 0.05). The reasons for choosing PTBD were 17 cases of poor EBD effects, 12 reconstructed intestinal anastomosis, 11 EBD failures due to gastrointestinal stenosis, 3 ERCP complications, 1 poor treatment effect of EUS-EGHS, 2 others. The reasons for choosing EUS-EGHS were 5 poor EBD effects, 5 EBD incapacitations due to gastrointestinal stenosis, 1 PTBD refractory, 2 PTBD intolerance cases. The success rate of the procedure was 95.7% vs. 100%, the response rate was 83.0% vs. 92.3%, and the complication rate within 2 weeks after the treatment was 10.6% vs. 15.3%. The median length of hospital stay after treatment was 21 days (3–129 days) vs. 11 days (3–22 days), the ratio of rehospitalization events was 30% vs. 30.7%, the median time from treatment to the event of rehospitalization was 92 days (12–305 Day) vs. 77 days (24–252 days). BSC cases was 43.5% vs. 92.3% (p < 0.05), median post survival time was 112 days vs. 89 days.

Conclusion: Most of the EUS-EGHS were administered to the patients with biliary and pancreatic cancer presented on BSC cases. Since it has the same degree of safety as PTBD, it seemed possible to continue performing EUS-EGHS more positively in terms of QOL. Also, it seemed possible to expand EUS-EGHS indication for the cases with any other organ cancer than pancreatic or biliary cancer and chemotherapists, but it is necessary to verify the safety of EUS-EGHS in the future.

Disclosure: Nothing to disclose

P0249 ROLE OF INTERVENTIONAL RADIOLOGY IN PEDIATRIC GASTROINTESTINAL DISEASES - A LARGE TERTIARY CENTER EXPERIENCE
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Introduction: Interventional radiology (IR) is an indispensable component of multidisciplinary care in various gastrointestinal (GI) diseases. The available evidence has shown safety and utility in children with GI disorders. The aim of the present study is to analyze the role of interventional radiology in pediatric GI diseases.

Aims and Methods: In this study, we aim to analyze the outcomes of IR in various pediatric GI diseases.

Results: The data of children < 18 years who underwent radiological intervention for various GI disorders during study period (2009–2017) were analyzed, retrospectively. The indications for interventions included vascular (Budd Chiari syndrome, pseudoneurysm) and nonvascular (pancreatic fluid collections, cholangitis and anastomotic biliary strictures). All the interventions were performed with standard technique. The indications for intervention in children with pancreatic fluid collections included unsuitability of endoscopic drainage or collection at multiple sites. Percutaneous transhepatic biliary drainage was carried out in children in whom endoscopic retrograde cholangiopancreatography was unsuccessful or not feasible. The outcomes of radiological intervention including success and adverse events were assessed.

Results: A total of 93 children (mean age 13.45 ± 4.09) underwent radiological interventions for vascular (chronic Budd Chiari syndrome 14, pseudoneurysm 28) or non-vascular (pancreatic fluid collections 33, hepatitis/choleojenynostomy stenoses or leaks 12, cholangitis 6) indications. Of 33 children who underwent percutaneous drainage of pancreatic fluid collections, clinical success was noticed in 32 children during a mean follow-up of 32.4 ± 21.66 months. 11 children developed persistent pancreatoctiocutaneous fistula of which 8 children were managed with endoscopic pancreatic ductal stenting and 3 underwent internalization of transgastric drain. In children who underwent stenting of hepatic vein or inferior vena cava for Budd Chiari syndrome, mean survival time was 18.57% during a mean follow-up of 24.1 ± 13.78 months. Adverse clinical outcomes were noticed in 4 children (28.57%) including persistence of ascites (1 child), requirement of re-intervention (1 child), and death (2 children: re-occlusion and intrahepatic.
biliary complications are a common cause of morbidity and mortality in liver transplantation (LT) recipients occurring in 10–25% of patients. Although with similar post-resection survival, the independent risk factors of LNM in the mERCC group, compared to those in the pERCC group, included large tumor size and LVI.

**Aims and Methods:** The aim of this study was to identify risk factors of LNM and compare clinicopathologic characteristic and prognosis of early pSRCC with early mSRCC. This retrospective study was conducted at our center between 2005 and 2015 in 796 radical gastric cancer gastrectomies. A total of 160 early signet ring cell carcinoma (ESRCC) radication resections were reviewed, in which 79 cases were early pSRCC and 81 cases were early mSRCC. Risk factors of LNM and clinicopathologic features of these 2 groups were statistically compared, including age, gender, tumor location, gross pattern, size, invasion depth, lymphovascular invasion (LVI), helicobacter pylori (Hp) infection, atrophic gastritis, and LNM. Patients were follow-up for post-resection survival. The 5-year survival rate and disease-specific survival were estimated with the Kaplain-Meier method with a log-rank test and compared between the two groups.

**Results:** The overall 5-year survival rate for ESRCC was 96.25%. Univariate analysis reviewed LVI and tumor size as the risk factors for lymph node metastasis (LNM). However, risk factors for lymph node metastasis (LNM) and clinicopathologic features of early mixed signet cell gastric carcinoma (mSRCC) was statistically compared, including age, gender, tumor location, gross pattern, size, invasion depth, lymphovascular invasion (LVI), helicobacter pylori (Hp) infection, atrophic gastritis, and LNM. Patients were follow-up for post-resection survival. The 5-year survival rate and disease-specific survival were estimated with the Kaplain-Meier method with a log-rank test and compared between the two groups.

**Conclusion:** Although with similar post-resection survival, the independent risk factors of LNM in the mERCC group, compared to those in the pERCC group, included large tumor size and LVI.

**Disclosure:** Nothing to disclose.
In univariate analysis, high distal contractile integral (DCI) median value on perative HRM was not performed, and 11/20 (55%) had prolonged pain after POEM. Of 22 patients who underwent POEM, 2 were excluded because preoperative HRM was not performed. The local ethics review committee granted approval.

Aims and Methods: The PTEG procedure was constructed from 2 existing general techniques. We also developed a rupture-free balloon (RFB) for the standard PTEG technique in 1997. 1 technique was puncturing of the esophagus with a RFB under ultrasonic control. The other was tube placement via the puncture site under fluoroscopic control. The standard PTEG procedure was thus a nonvascular interventional radiologic technique that did not require an endoscope. The Japan Association for PTEG (JA-PTEG) was established in 2002, and annual meetings of JA-PTEG were held every year. From 2005, under the guidance of the Ministry of Welfare, a clinical trial for PTEG was undertaken for 6 years in Japan, which confirmed its safety and efficacy. The Ministry of Welfare approved support for PTEG by Japanese national health insurance in 2012. Hands-on seminars with simulators for the PTEG procedure were held twice a year from 2014. In 2018, JA-PTEG initiated a system to technically certify physicians performing PTEG.

Results: PTEG has been performed in over 25,000 patients in Japan from 1994 to the present. We have also performed PTEG as an educational procedure in 341 patients. From 2018, JA-PTEG was performed on 186 individual members, 52 authorized institutions, 43 faculty members and 32 attending physicians. To date in 2018, JA-PTEG certified 8 physicians as those authorized to perform the standard PTEG procedure. For patients with intractable nausea and vomiting due to gastrointestinal obstruction caused by carcinoma, PTEG as a palliative treatment can quickly and effectively improve a patient’s quality of life. PTEG is also highly efficacious in enteral nutrition as an alternative to PEG. PTEG was originally born as a Japanese technique, and currently, it is still only performed within Japan.

Conclusion: We believe that the PTEG technique should be disseminated safely and effectively throughout the world.

Disclosure: Nothing to disclose

References

INTENSIFY OF ESOPHAGEAL PERISTALIS IS A FACTOR IN PROLONGED POSTOPERATIVE PAIN BEFORE PERORAL ENDOSCOPIC MYOTOMY

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Introduction: Percoral endoscopic myotomy (POEM) is a minimally invasive and curative treatment for esophageal dysmotility (1,2). However, significant pain persists in some patients after POEM.

Aims and Methods: This single-center study retrospectively investigated risk factors for pain after POEM. This study included consecutive patients who underwent POEM and high-resolution manometry (HRM) at the Okayama University Graduate School of Medicine between January 2016 and December 2017. A numerical rating scale (NRS) was used for pain assessment. A pain group (P-group: 3 days to achieve NRS <1) and a non-pain group (NP-group: <3 days) were compared. Data on comorbid disease, symptoms, and histological findings were obtained from medical records. All study participants provided informed consent. The local ethics review committee granted approval.

Results: Of 22 patients who underwent POEM, 2 were excluded because preoperative HRM was not performed, and 11/20 (55%) had prolonged pain after POEM. There was no significant difference in sex, age, and the amount of analgesic required during hospitalization between the P-group and NP-group. In univariate analysis, high distal contractile integral (DCI) median value on HRM and classification as a straight-type were risk factors for prolonged postoperative pain. In multivariate analysis, high DCI was a risk factor for prolonged postoperative pain.

Conclusion: The intensity of esophageal peristalsis before POEM may be a factor in prolonged postoperative pain.

Disclosure: Nothing to disclose

References

ENDOSCOPIC PAPILLECTOMY IN TREATMENT OF PATIENTS WITH AMPULLARY NEOPLASMS: A SINGLE-CENTER EXPERIENCE

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Introduction: Benign tumors of the ampulla of Vater occur in 0.4% to 0.12% of all tumors of the gastrointestinal tract (GI tract). However, malignant transformation of ampullary adenoma occurs in 60-65% of cases, so the common tactic of treatment is their removal. Regardless of the pathohistological structure of the tumor, endoscopic papillectomy is considered reasonably safe and most effective method compared to a more radical interventions such as pancreatoduodenal resection (PDR), surgery, or radiotherapy.

Aims and Methods: 37 endoscopic papillectomies were performed at the Moscow Clinical Research Center between April 2014 and January 2018. In most cases, the tumor was detected during a routine examination for other diseases. The preoperative examination protocol included duodenoscopy with biopsy, endosonography, CT or MRI, which excluded the presence of malignant lesions and the intraductal spread of the adenoma more than 1 cm. The sizes of the adenomas ranged from 1 cm to 5 cm. The aim of the study was to evaluate the effectiveness of endoscopic papillectomy in the treatment of patients with neoplasms of the ampulla of Vaier.

Results: 37 patients underwent endoscopic papillectomy, including 16 men and 21 women. Median age: 54 years (26–75). The average time of surgery was 85 minutes. In 26 cases, the removal of the adenoma was performed ‘en bloc’ (59.5%). In 11 cases, due to the presence of lateral spread of the tumor, fragmentation was performed (40.5%). Pancreatic stenting was successful in 31 patients (83.7%). Stenting was of the common bile duct in 9 patients (24.3%). In 2 cases, there was R0 resection. Morbidity included bleeding in 8 patients (21.6%), 2 cases of intraoperative perforation (5.4%), 1 of them was conservatively treated. The patient was operated in volume: laparotomy, suturing a perforation, drainage of the abdominal cavity. In 2 patients, the postoperative period was complicated by cicatrical stenosis of the bile duct opening (5.4%). The ERCP with the stenting of the common bile duct was performed. No death occurred.

Conclusion: Endoscopic papillectomy is characterized by lower morbidity and mortality and a shorter period of hospitalization. Compared with surgery, endoscopic ampullectomy appears to be a preferred treatment modality for small benign ampullary tumors with high success rate of tumor eradication.

Disclosure: Nothing to disclose

ENDOSCOPIC VACUUM THERAPY FOR TREATMENT OF UPPER GASTROINTESTINAL ANASTOMOTIC LEAKAGES: FIRST EXPERIENCE

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Introduction: Surgical interventions on the esophagus belong to the group of ‘high-risk’ operations, as they can lead to such formidable complications as insolvency, bleeding and the formation of postoperative fistulas and strictures. The results of systematic analysis of the largest series of clinical cases published in the last 20 years show the incidence of postoperative anastomotic leakage about 3% after open and 2.1% after laparoscopic surgery without significant differences between the two surgical approaches. However, analysis of the cumulative world experience shows the average incidence of anastomotic leakage at the level of 7-8%. These reports suggest that postoperative mortality rates in this patient group reach 30% and have no significant improvement toward reduction. The development of new surgical techniques and surgical interventions lead to an increase in mortality from 20 to 64%, which determines the use of minimally invasive technologies as a priority. Since 2006, a new method of endoscopic vacuum therapy in management of anastomotic leaks has become available in clinical practice.

Aims and Methods: From March 2015 to March 2018, anastomotic leakage of the esophagus was diagnosed in 12 patients (5 women, 7 men), including 9 patients with failure of esophagogastrectomy anastomosis, 3 patients with failure of
esophageal anastomosis. The average age was 67.5 years. Size of anastomotic perforation ranged from 0.5 to 3 cm. Strategy of treatment for all patients include adequate nutritional support by enteral feeding through the nasogastric tube, parenteral administration of combined nutrients, enterostomy, or a combination of several methods. Early anti-biotic therapy is necessary for the prevention and treatment of already developed mediastinitis and septic complications.

The complications were detected on the 1–7 days after surgery. Anastomotic leak was confirmed by radiological and endoscopic methods. Endoscopic vacuum therapy within the day of leakage detection (2–4 days after the surgery). Thus no additional sanation and draining interventions were required due to early diagnosis and adequate drainage of the anastomosis area. Polyurethane spongiform system, slightly smaller diameter or corresponding to the diameter of the esophagus, was mounted on a thermoplastic gastric probe and installed at the level of the perforation. Immediately after installation, the system was connected to a vacuum aspirator with a pressure of 100 - 125 mm Hg. Replacement of the system was carried out every 3–13 days. To fully close the irregularity, the new system was installed after 7 procedures. The decision to complete the therapy was carried out based on the results of endoscopic and X-ray examination in the absence of data for the presence of fistula.

Results: In total 57 procedures were performed: the number of replacements - 4 (1–7), the interval between procedures - 6 days (3–13 days), the duration of treatment -13 days (1–66 days). The success rate was 75%. There were 3 lethal outcomes, including 2 due to progressive cardiovascular failure with positive dynamics of local treatment. 1 patient died of multiple organ failure.

Conclusion: Endoscopic vacuum therapy is considered to be valuable and cost-effective method of treatment of anastomotic leaks and perforations of the upper GI tract.

Disclosure: Nothing to disclose

P0258 THE SMART APPROACH TO SURGICAL TREATMENT FOR GASTRIC AND DUODENAL GISTS BASED ON PREOPERATIVE EUS-TYPING
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Introduction: Surgical treatment is the treatment of choice for the resectable GISTs. The objective of surgical treatment is to remove the tumor completely, thus improving the survival. The decision to perform the surgery is based on the results of preoperative evaluation. Endo-US, based on the localization and size of the tumor, is considered an important tool for the decision-making process in GISTs.

Aims and Methods: Aims were to develop and demonstrate different surgical techniques of laparoscopic or endoscopic resection for GISTS based on classification of EUS-typing for optimal choice of treatment. By the ‘smart’ approach we imply the approach which allows us to make a surgery less invasive and more accurate, including more functional results with no increase of complications. The EUS-classification of GISTS was created based on the analysis of the treatment of 80 patients with gastric and duodenal GISTS. The principles of classification included the following criteria:

- Location of tumor base in relation to GI lumen
- Size of the tumor base ("growing point")
- Type of growth in relation to GI lumen
- The EUS-typing includes Type I, Type II, Type III (a,b,c,d) tumors

Objectives and approaches:

- Endoscopic removal of tumor by means of: Endoscopic submucosal dissection (large size) Endoscopic mucosal resection (small size)

Type I
Endoscopic enucleation of tumor after resection of covering mucosa
Endoscopic tunneling dissection
Type Ila
Endoscopic tunneling dissection
Type IbII
Laparoscopic atypical resection after gastrotomy (duodenotomy)
Endoscopic tunneling dissection (advanced endoscopic surgeon and small tumor size)
Laparo-endoscopic hybrid procedures

Type IIC
Laparoscopic atypical (wedge) resection
Laparoscopic enucleation of tumor
Laparoscopic atypical stapler resection

Results: Patients with gastric and duodenal GISTS underwent laparoscopic resection. The EUS classification of GISTS was based on the analysis of 80 patients: 49 patients underwent Type I, 15 patients underwent Type II, 12 patients underwent Type IIIa, 4 patients underwent Type IIIb. The mean follow-up period was 42 months (range 3-74 months) with no local or distant recurrence or stenosis at the site of surgery.

Conclusion: The classification of GISTS based on EUS-typing allows to select the optimal approach individually for each patient to perform surgery more accurate and less invasive.

Disclosure: Nothing to disclose

P0260 A COMPREHENSIVE COMPARISON OF THE FIVE LEADING SCORING SYSTEMS FOR PERITONEAL CARCINOMATOSIS FROM COLORECTAL ORIGIN TO SELECT CRS/HIPEC CANDIDATES
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Introduction: Multiple surgical scoring systems have been developed to assess the extent of peritoneal carcinomatosis in colorectal patients. These scoring systems are used as important predictors of surgical outcome in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). Diffusion weighted magnetic resonance imaging (DW-MRI) could allow for the assessment of these surgical scores preoperatively and non-invasively.

Aims and Methods: The purpose of the study is to compare the performance of these scoring systems determined on MR images, for predicting whether a complete resection was feasible in CRS/HIPEC candidates with colorectal cancer. Between February 2016 and October 2017, colorectal cancer patients considered for CRS/HIPEC who underwent DW-MRI were included. The DW-MRI images were retrospectively and independently assessed by 2 abdominal radiologists. Both radiologists were blinded for the clinical parameters. Clinical parameters were obtained from the patient files. 5 most-used models were selected, namely the Peritoneal Surface Disease Severity Score (PSDSS), Region Count, Simplified Peritoneal Cancer Index (SPCI), Peritoneal Cancer Index (PCI), and the Colorctal Peritoneal Metastases Prognostic Surgical Score (COMPASS). The performance of the scoring systems was assessed by receiver operator characteristics (ROC) analysis for predicting complete resection and the area under the curve (AUC) was calculated for every model.

Results: In 82 patients, the scores could be accurately constructed for all 5 methods. The mean age was 62.80 (± 10.53) and 46/82 of the patients were female. Of these patients 70% (58/82) had undergone a successful surgical procedure with a curative intent, of which 84% (49/58) underwent a CRS/HIPEC procedure. In 20 patients, an inoperable amount of peritoneal carcinomatosis was determined at surgery. ROC curve analysis for predicting a complete resection showed AUCs of 0.79, 0.79, 0.82, 0.83, and 0.89 for PSDSS, Region Count, SPCI, PCI, and COMPASS, respectively. Both radiologists were blinded for the clinical parameters. Clinical parameters were obtained from the patient files. 5 most-used models were selected, namely the Peritoneal Surface Disease Severity Score (PSDSS), Region Count, Simplified Peritoneal Cancer Index (SPCI), Peritoneal Cancer Index (PCI), and the Colorctal Peritoneal Metastases Prognostic Surgical Score (COMPASS). The performance of the scoring systems was assessed by receiver operator characteristics (ROC) analysis for predicting complete resection and the area under the curve (AUC) was calculated for every model.

Conclusion: This study shows that DW-MRI might be used for less invasive and preoperative patient selection of colorectal patients considered for CRS/HIPEC. The COMPASS model was the best model to select CRS/HIPEC candidates with MRI.

Disclosure: Nothing to disclose

P0264 DEVELOPMENT OF 3D MODEL OF PERIANAL DISEASE IN CD: SINGLE-CENTRE EXPERIENCE
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Introduction: Preoperative evaluation of MR images may not be sufficient for planning the anastomotic surgery and the internal supports. 3D printing allows to obtain spatial structures in 1:1 scale with unprecedented precision.

Aims and Methods: Optima MR360 Advance 1.5T (GE Healthcare) with a 16-channel TOTAL BODY coil was used. The imaging protocol consisted of high-resolution axial and coronal T2-weighted images with a matrix size 512 × 512, a slice thickness of 2 mm and zero spacing scans. DICOM images were imported into 3D Slicer v4.8.0. Firstly anal fistula was modelled on the basis of axial images. Fistula locations, anus and anal canal were marked with a different color. The last step of the model was to mark the skin that was connected to the anus and contact areas of the fistula with the skin. The prepared model was then exported to an STL format file. Blender 2.77a was used to smooth the edges of the model, then 3D program allowing the color to be assigned to individual model element was used. The final version of the model contained 958 layers. The anal fistula model was printed using the 3D Prodjet 460 Plus printer (3D Systems). The development of the model, including printing took approx. 9 hours.

Results: Acessibility of rotatable 3D before surgery allows more precise detection of the location and the degree of the perianal disease. Moreover, this may also lower the inter-observer bias connected with the different skills to interpret complex MR imaging before planned surgery.
Conclusion: The proposed use of 3D printing technology in the case of anal fistula will allow for effective surgery planning.

Disclosure: Nothing to disclose

P0262 THE POTENTIAL OF HUMAN FOETAL GUT MESOANGIOBLAST-LIKE CELLS FOR ENTERIC SMOOTH MUSCLE REGENERATION

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Introduction: Severe gastrointestinal disorders including chronic intestinal pseudo-obstruction affect the neuromuscular compartment of the small intestine. Very little is known, however, about the repair and regeneration of damaged or dysfunctional smooth muscle.

Aims and Methods: Our study aims to investigate the potential of human foetal gut mesoangioblast-like cells for enteric smooth muscle regeneration as a possible treatment for enteric myopathies and related disorders.

Mesoangioblasts-like cells (MABS), isolated from human foetal midgut (under ethical approval from the UK Human Developmental Biology Resource at UCL Great Ormond Street Institute of Child Health), were expanded and TGFß used for 7 or 14 days to induce smooth muscle differentiation in vitro. Immunohistochemistry, FACS analysis and calcium imaging were performed to characterise MABS and smooth muscle-derived cells. After 14 days in culture in vitro, MABS were transplanted in vivo into ileal tissue in nude-SCID mice (under UK licence, PPL 70/622) and cell engraftment assessed with immunohistochemistry after 4 weeks.

Results: Immunohistochemistry and FACS analysis showed that foetal gut MABS have high proliferative capacity (~55% of cells are Ki67+ in culture), are positive for mesenchymal markers CD90 and CD146 (~98% for both markers) and for pericyte markers NG2 and PDGF-Rß (~90% and ~20–30% respectively). After 7 days in culture with TGFß-treatment, MABS expressed smooth muscle proteins SM22 and calponin, and showed intracellular calcium transients in response to carbachol. After 14 days MABS also expressed smoothelin, a marker of mature smooth muscle. In vivo, transplanted MABS were able to engraft, distribute in the muscle layers of the ileum and differentiate into SM22 positive smooth muscle cells.

Conclusion: Here we demonstrate that MABS can be successfully isolated from human foetal gut. In vitro and with TGFß-treatment MABS showed an increasing ability to differentiate into smooth muscle cells and respond to carbachol stimulation, thus supporting their functional potential. The ability of MABS to differentiate into mature smooth muscle cells in vitro and engraft in vivo provides proof of principle for their potential use as a treatment for enteric smooth muscle disorders.

Disclosure: Nothing to disclose

P0263 IMAGE-GUIDED PATHOLOGY FOR EVALUATION OF RESECTION MARGINS IN LOCALLY ADVANCED RECTAL CANCER USING THE NEAR-INFRARED FLUORESCENT TRACER BEVACIZUMAB-800CW

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Introduction: Negative circumferential resection margins (CRM) are the cornerstone for curative treatment of patients with locally advanced rectal cancer (LARC). Unfortunately, perioperative techniques for evaluation of resection margins are lacking, whereas standard histopathological examination is time-consuming. In this study, we evaluated the feasibility of optical molecular imaging as a tool for discrimination of resection margins at the surgical theater, i.e. Image-Guided Pathology (IGP), to improve clinical decision making.

Aims and Methods: Fluorescence imaging data of fresh surgical specimens and subsequent bread-loaf slices from patients with LARC (NCT01972373) were analyzed as a side study. All patients were administered intravenously with 4.5 mg of the fluorescent tracer bevacizumab-800CW 2–3 days prior to surgery. 7 patients met the inclusion criteria for correlation of fluorescence intensities in fresh surgical specimens with histology, to evaluate resection margins. For analysis of bevacizumab-800CW localization in bread-loaf slices, sufficient data was available from 17 patients. A receiver operating characteristics (ROC) curve was plotted to determine the mean fluorescence intensity (MFI) cut-off value for tumor detection.

Results: Using IGP, in one patient a histologically confirmed tumor-positive CRM was predicted correctly at the surgical theater. Tumor-negative CRMs were predicted correctly in 4 patients using IGP. 1 tumor-positive CRM could not be detected; however, this positive margin was based on the presence of only one microscopic tumor deposit in the CRM. 1 close CRM (1.4 mm) was identified as tumor-positive. Optical imaging enabled a clear differentiation between tumor and surrounding tissue in the bread-loaf slices (n = 42) of all 17 patients in vivo. In our limited sample size, an optimal MFI cut-off value of 5085 was determined based on the ROC curve, with a sensitivity and specificity of 97.3% and 99.7% respectively.

Conclusion: We demonstrate for the first time the potential of IGP for identification of positive resection margins directly after surgery in patients with LARC. Clearly, this might change current peri-operative decision making with regard to additional targeted resections or intraoperative brachytherapy. Based on the initial results from this study, a standardized methodology was developed to confirm these findings in a subsequent larger IGP study.

Disclosure: Nothing to disclose

P0264 SNAPSHOT STUDY ON MRI RESTAGING AFTER CHEMORADIOThERAPY AND INTERVAL TO SURGERY IN RECTAL CANCER: INFLUENCE ON SHORT AND LONG-TERM OUTCOMES

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Introduction: The time interval between CRT and surgery in rectal cancer patients is still subject of debate and concerns exist regarding increased postoperative complication and local recurrence rates after longer waiting.

Aims and Methods: To evaluate the impact on short- and long-term outcomes of variation in practice related to MRI restaging and time interval between neoadjuvant chemoradiotherapy (CRT) and surgery in rectal cancer patients. Patients were selected from a collaborative rectal cancer research project including 71 Dutch centers. Patients were subdivided into 2 groups according to the time interval from the start of preoperative CRT to surgery (<14 and >14 weeks).

Results: From 2095 registered patients, 475 patients received preoperative CRT. MRI restaging was performed in 79.4%, with a median CRT-MRI interval of 10 (IQR 8–11) weeks, and median MRI-surgery interval of 4 (IQR 2–5) weeks. Short and long interval groups consisted of 224 and 251 patients, respectively. Pathological complete response rate (n = 34 (15.2%) vs. n = 47 (18.7%), p = 0.305) and CRM involvement (9.7% vs. 15.9%, p = 0.145) did not significantly differ. 30-day surgical complications were similar (20.1% vs. 23.1%, p = 0.943). No significant differences were found for local- and distant-recurrence rates and disease-free and overall survival.

Conclusion: These real-life data reflecting routine daily practice in the Netherlands showed substantial variability in use and timing of restaging MRI after preoperative CRT for rectal cancer, as well as time interval to surgery, but with similar short- and long-term outcomes.

Disclosure: Nothing to disclose

P0265 LAPAROSCOPIC VENTRAL RECTOPEXY FOR OBSTRUCTED DEFECTION FUNCTIONAL RESULTS AND QUALITY OF LIFE

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Introduction: Laparoscopic ventral mesh rectopexy (LVR) is gaining wider acceptance as the preferred procedure to correct internal as well as external rectal prolapse associated with obstructed defecation syndrome (ODS) and/or faecal incontinence.

Aims and Methods: The aim of our study was to analyse functional outcome and quality of life (HRQL) after laparoscopic ventral rectopexy for symptomatic internal prolapse and/or rectocele with ODS. Prospectively collected data on patients who underwent surgical repair for rectal prolapse were analysed in 46 consecutive female patients operated between January 2011 to April 2018. Mean age was 62 years (range 25-
Results: Mean operative time was 151 min (range 75 - 240). Conversion rate to open technique was 10.8 %. There was no post-operative mortality or major complication. Mean hospital stay was 4 days (range 2 - 7). Among a mean follow-up of 26 months (range 3 - 71 months), we observed no recurrence of prolapse or rectocele. Comparing Wexner score before and after LVR we observed an improvement in painful evacuation (p = 0.001), minims in lavyatory attempts (p = 0.008), feeling incomplete evacuation (p = 0.017) and abdominal pain (p = 0.017). Moreover, the global Wexner score was significantly improved from 13.60 to 10.18 (p = 0.000). Similarly, SF-36 items improved after the surgery, especially in term of Physical Functioning (p = 0.005). The comparison of preoperative SF-36 score with matched healthy controls demonstrated a significant difference in particular in Physical Functioning (p = 0.001) and Bodily Pain (p = 0.023). On the contrary, the comparison of post-operative SF-36 scores and healthy controls scores showed a significant difference only in terms of Bodily Pain (p = 0.055). No worsening of continence status, constipation or sexual function was observed. No significant improvement was observed in urinary incontinence. None patient experienced persistence or recurrence of the prolapse.

Conclusion: LVR appears to provide a sustained improvement in HRQL, constipation and incontinence in patients with ODS without worsening constipation with low morbidity and recurrency.

Disclosure: Nothing to disclose.

P0266 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) VERSUS TRANANAL ENDOSCOPIC MICROSURGERY (TEM) FOR THE TREATMENT OF EARLY RECTAL CANCER: COMPARISON OF LONG-TERM OUTCOMES C Kimura1, F S Kagawati2, C F Saparapan Marques2, C S R Nahas4, V Segate1, B da Costa Martinis3, L H Lenz Tolentino2, U Ribeiro3, F Maluf-Filho4, S C Nahas3
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Introduction: Methods for the local treatment of early rectal cancer have been developed in the recent years. In this scenario, the transanal endoscopic microsurgery (TEM) and the endoscopic submucosal dissection (ESD) have played an important role. Both have their own advantages and drawbacks, but there are still few studies comparing them. Previous studies have shown that both techniques have similar short term outcomes (1). Studies assessing long-term outcomes, however, are scarce.

Aims and Methods: To compare long-term outcomes between ESD and TEM for the treatment of early rectal cancer.

Findings: From January 2017, 103 procedures were performed (either ESD or TEM). Lesions submitted to ESD were previously assessed by magnification endorectal ultrasound before the procedure.

Data regarding age, surgical risk, early and late complication rates, recurrence and anatomopathological report were collected retrospectively. Qualitative variables were submitted to a chi-square analysis and the quantitative ones, to a t-test.

Results: The mean follow-up of these patients was 34 months. 74 of them (71.8%) were submitted to ESD and 29 to TEM (28.2%). The average age in the ESD group was 65.5 years and 51.3% of those patients were female. Among the patients undergoing TEM, 7 (24.13%) had rectal pain, diarrhea or incontinence and anal stricture presented mucorrhea, fecal urgency and/or incontinence and anal stricture.

In the ESD group, 7 patients (9.46%) had early complications, 2 of which were Clavien I, 3 Clavien II and 2 Clavien III. In the TEM group, 5 patients had complications (17.2%), of which 2 were Clavien I, 1 Clavien II, 1 Clavien III and 1 Clavien IV (p = 0.19). The average days of hospitalization was 3.4 among the ESD patients and 6.9 among the TEM (p = 0.015).

During the first post-operative month, 10 patients (13.5%) from the ESD group presented faecal urgency and/or incontinence and anal stricture requiring dilatation. By the end of 18 months, all patients were asymptomatic. Among the patients undergoing TEM, 7 (24.13%) had rectal pain, diarrhoea or fecal incontinence. After 18 months, 6 were asymptomatic and 1 persisted with rectal pain.

The lesions removed either by ESD or TEM had similar rates of en-bloc resection - 89.2% and 96.5%, respectively (p = 0.23) and R0 resection - 85.13% and 82.6%, respectively (p = 0.742). The anatomopathological analysis of the lesions submitted by ESD showed 26.3% of adenomas, 64.86% of intramucosal adenocarcinoma, 4.3% sm1 adenocarcinoma and 4.05% of sm2-3 adenocarcinoma (non-curative resection). In the TEM group, 31% were adenomas, 44.8% of intramucosal adenocarcinoma, 7% of sm1 adenocarcinoma and 17.2% of sm2-3 adenocarcinoma. Therefore, the ESD had a higher percentage of curative resections (p = 0.002).

Among the patients undergoing TEM, there was a 24.13% recurrence rate, against 1.3% in the ESD group (p = 0.0001).

Conclusion: The ESD, compared with the TEM, showed better results, enabling the treatment of significantly larger lesions, with a higher curative rate, less hospitalization days and lower recurrence rates.

Disclosure: Nothing to disclose.

Reference

MONDAY, OCTOBER 22, 2018
09:00-17:00

IBD I - Hall X1

P0267 CROSSTALK BETWEEN SEROTONIN AND ENDOCANNABINOID SYSTEMS IN THE GUT CONTRIBUTES TO THE ABDOMINAL PAIN IN COLITIS M Salaga1, A Binenda1, F Piccietti2, V Di Marzo3,4, J Fichna1
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Introduction: Abdominal pain is one of the most common symptoms of inflammatory bowel diseases (IBD). However, its molecular basis has not been fully characterized yet. It has been shown that chronic elevation of luminal serotonin increases visceral pain and that elevated secretion of this neurotransmitter in the gut leads to the exacerbation of inflammation. On the other hand, it is well established that inhibited endocannabinoid signaling in the gut lowers pain threshold and endogenous cannabinoid receptor agonists reverse this effect and exhibit antiinflammatory and anti-inflammatory properties.

Aims and Methods: The aim of this study was to test the hypothesis that chronic administration of serotonin causes disruption of the cannabinoid signaling leading to visceral pain in the course of colitis.

Methods: We used 3% DSS in drinking water to induce colitis in mice. Serotonin was systemically administered for 5 days starting from day 3 post-DSS and each day visceromotor response to colorectal distention (CRD) was measured. Selective 5-HT3 and 5-HT4 receptor antagonists were used to examine the mechanism of action of serotonin. Macroscopic evaluation of the colonic damage was performed. Expression of cytkines, serotonin and cannabinoi (CB) receptors as well as enzymes responsible of biosynthesis and degradation of endocannabinoids were investigated. Moreover, serotonin as well as endocannabinoids were measured to assess the change in levels.

Results: DSS caused severe intestinal inflammation represented by increased macroscopic fissure score as well as upregulation of TNFα, IL-1β and IL-6. Chronic, systemic treatment with serotonin led to significant increase in the concentration of this hormone in the colon and simultaneous decrease of the endocannabinoids, CB1 and CB2-receptors. The visceromotor response to CRD was significantly higher in the serotonin-treated animals compared to the vehicle group and this effect was dependent on 5-HT3 but not 5-HT4 receptors. Moreover, chronic serotonin administration led to the downregulation of CB1, but not CB2, and decreased N-acetyl phosphatidylethanolamine-specific phospholipase D (NAPEPLD), which is responsible for synthesis of anandamide and other N-acylethanolamines, and these effects were reversed by the 5-HT3 receptor antagonist granisetron.

Conclusion: Here we present a novel mechanism that may be responsible for the increased visceral pain in intestinal inflammation. Our study suggests that pharmacological blockade of serotonin signaling in the gut might be of benefit in severe cases of abdominal pain in IBD patients.

Disclosure: Nothing to disclose.

P0268 UROTENSIN II RECEPTOR EXPRESSION IN ULCERATIVE COLITIS: RELATIONSHIP WITH ENDOCANABINOIDS AND PHARMACOLOGICAL ACTIVITY OF UTR PE A.G Gravina1, M Dallio2, C Taccelli2, M Martorano2, C Loguercio1, A Federico1
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Introduction: Urotensin II (U-UTR) is a vasoactive peptide that interacts with a specific receptor, UTR (1). Recently our group has demonstrated increased UTR expression both in adenocarcinoma cell lines and adenomatous polyps and even greater in colon carcinoma samples when compared to healthy colon samples of the same patients. We also showed that an UTR agonist induced an
increase in colon adenocarcinoma cells growth in vitro, while the UTR block with a specific antagonist caused an inhibition of their growth and an inhibition of about 50% both of motility and cell invasion (2).

Aims and Methods: There are no data in the available literature (UC), and we therefore evaluated the expression of UTR in UC patient biopsy and in healthy tissue. We therefore also have colic tissue samples taken in these subjects. Evaluation of receptor expression was performed by RT-PCR. The ANOVA test (p < 0.05); b) correlation of UTR expression with endoscopic and histological activity of disease in most study patients. We found a greater expression of UTR in patients with a Mayo Endoscopic Score 2 and with severe histologic only in 4 patients.

Disclosure: Nothing to disclose

References

P0269 DS-1093A, A NOVEL HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITOR, HAS A THERAPEUTIC POTENTIAL IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammation is predominating of inflammatory intestinal lesions. Hypoxia inhibits hypoxia-inducible factor prolyl hydroxylase (HIF-PH), which stabilizes HIF and induces HIF downstream gene expression in the colon. HIF-1, a complex consisting of inducible HIF-1 alpha and constitutive HIF-1 beta, induces the expression of protective barrier genes in colon epithelial cells and plays a critical role in protecting against inflammatory bowel disease (IBD). HIF-PH inhibitors are thought to have the potential to enhance mucosal barrier function through HIF-1 alpha stabilization. We found out that DS-1093a, a HIF-PH inhibitor, might have the potential to be a novel IBD drug with mucosal healing activity.

Aims and Methods: To elucidate the effect of DS-1093a on IBD, we administered DS-1093a to colitis mice. Experimental colitis was induced in male BL-6 mice by dissolving Dextran Sodium Sulphate (DSS) in their drinking water for 8 days. DS-1093a was administered to DSS mice in the feed for 8 days or by intra-rectal administration (IRA) once a day until day 7. The disease conditions (colon length, body weight, and diarrheal score), histopathology (HE staining, AB-PAS staining, and HIF-1 alpha immunohistochemistry) of colon, and haematological parameters were analysed on day 8. Colon and serum of each mouse were also collected on day 8. The mRNA expression was analysed by qRT-PCR. IRA was conducted by administering the solution between the cecum and the rectum via a catheter through the anus.

Results: DS-1093a improved total body conditions, as shown by body weight, colon length, and diarrheal score in DSS colitis mice. In the histopathological analysis, colitis mice showed intestinal tissue injury; however, treatment of DS-1093a reduced the mucosal injury and increased normal tissue region. AB-PAS (mucin) stained section of the colon showed DS-1093a normalized mucosa proliferation in colitis mice. DS-1093a prevented the activation of immune cells by colitis, and DS-1093a suppressed inflammatory cytokine gene expression in the colon epithelial cells. DS-1093a induced HIF-1 alpha accumulation in the nucleus of mucosal epithelial cells. In contrast, DS-1093a induced excess erythropoiesis by 8-day feeding administration. IRA of DS-1093a is suggested to maintain the functional integrity of colon epithelial cells. Owing to mucosal barrier improvement, DS-1093a prevented immune cell activation by colitis, suppressed inflammatory cytokine gene expression in colon epithelial cells. Mucosal damage was correlated with the expression of HIF-1 alpha. These results suggested that DS-1093a had a strong efficacy for IBD in colitis mice with novel mechanisms for normalizing colitis mucosa. Moreover, topical exposure of DS-1093a to the colon can widen the efficacy margin between IBD and erythropoiesis.

Disclosure: Nothing to disclose

P0270 LOWER FECAL BACTERIAL ABUNDANCE IS ASSOCIATED WITH DISEASE RECURRENCE ONE YEAR AFTER ILEOCAECAL RESECTION IN PATIENTS WITH CROHN'S DISEASE

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Introduction: Dysbiosis has been proposed to be a key antigenic driver for the inflammation in Crohn’s disease (CD). However, the role of the fecal microbial composition for the post-operative disease course in CD patients remains to be established.

Aims and Methods: Our aim was to determine if the fecal microbial composition at the time of ileocaecal resection or 1 year after surgery was associated with endoscopic disease recurrence in CD patients 1 year after surgery. Patients with CD who had undergone ileocaecal resection were included in the study. Approximately 1 year after surgery, clinical evaluation by ileocolonoscopy was performed. The mucosa in the neoterminal ileum and ileocolonic anastomosis was assessed according to Rutgeerts’ scoring system. 5 or less aphthoid lesions were considered as remission (i,0-1), and > 5 aphthoid lesions, lesions or ulcers confined to the anastomosis or diffuse inflammation were considered as endoscopic disease recurrence (i,2-4).

Fecal microbial composition was analyzed using the Genetic Analysis GA-map Dysbiosis test, which consists of 54 DNA probes targeting >300 bacteria on different taxonomic levels.

Logarithmic data were analyzed in SIMCA using orthogonal partial least squares discriminant analysis (OPLS-DA) to identify discrimination between groups. Bacteria with the strongest discriminatory power were further analyzed by univariate analysis (Mann-Whitney U-test).

Results: In total, 22 CD patients from Southwestern Sweden (8 women) with median age 30 (17-63) years and median disease duration of 3 (0-11) years at the time of resection was included. At inclusion, 8 patients were treated with 5-aminosalicylic acid (5-ASA), 14 with corticosteroids, 11 with thiopurines, 1 with anti-tumor necrosis factor, and 4 patients had none of the treatments above. At the one year follow up, 9 patients were treated with 5-ASA, 2 with corticosteroids, 6 with thiopurines, and 8 patients had no treatment. Stool samples were collected by 9 patients at the time of resection and by 21 patients at the 1 year post surgery follow-up. At the 1 year follow up, 13 patients were in endoscopic remission (i,0-1) and 9 patients had endoscopic recurrence (i,2-4).

At the time of resection, fecal microbial composition discriminated patients whom the 1 year post surgery follow-up were in endoscopic remission or with recurrence, respectively, although the predictive ability was low (R2 = 0.94, Q2 = 0.01, i,0-1: n = 5; i,2-3: n = 4). Similarly, fecal microbiota at the 1 year post surgery follow-up discriminated patients in endoscopic remission from those in recurrence, yet with low predictability (R2 = 0.71, Q2 = 0.47; i,0-1: n = 3; i,2-3: n = 8).

The OPLS-DA models at the time of resection and at 1 year post surgery follow-up demonstrated that endoscopic remission was associated with a higher bacterial abundance, both among the Firmicutes and Bacteroidetes, as compared to recurrence. In addition, univariate analysis showed that patients in remission one year after surgery tended to have higher abundance of Pseudomonas spp at the time of surgery (p = 0.06) and Parabacteroides spp at time of 1 year post surgery follow up (p = 0.08), as compared to patients with recurrence.

Conclusion: Our results suggest that CD patients with endoscopic disease recurrence 1 year after ileocaecal resection have lower fecal bacterial abundance, both at the time of resection and 1 year after surgery, as compared to patients in remission. Thus, a lower intestinal bacterial abundance may be a contributing factor to disease relapse in these patients.

Disclosure: Nothing to disclose

P0271 RELATIONSHIP BETWEEN BIOPSY LOCATION, HISTOLOGICAL DISEASE ACTIVITY, AND MRNA EXPRESSION IN ENDOSCOPICALLY ACTIVE CROHN'S DISEASE

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**P0273** THE SYSTEMIC INFLAMMATORY PROTEIN Profiles differentiate BETWEEN PATIENTS WITH INFLAMMATORY AND FUNCTIONAL GASTROINTESTINAL DISEASES

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**Introduction:** Patients with ulcerative colitis (UC) may suffer from irritable bowel syndrome (IBS)-like symptoms during periods of remission. Due to the low-grade immune activation repeatedly reported in IBS, it has been suggested that the underlying inflammatory mechanisms of the 2 diseases overlap or are part of the same spectrum.

**Aims and Methods:** We aimed to determine if the systemic protein profiles (SysPP) differ between UC and IBS patients, and if SysPP are linked to presence of inflammation and/or functional symptoms. Patients with active ulcerative colitis (UCA), UC patients in remission with IBS-like symptoms (UCR-IIBS), UC patients without IBS-like symptoms (UC-IIBS) were included in the study. SysPP of all groups revealed 2 clusters; 1 cluster composed of IBS patients and HS, and 1 cluster of UC patients. Logarithmic data were analyzed in SIMCA using principal component analysis (PCA) and orthogonal projection least square discriminate analysis (OPLS-DA) with a Variable Importance for the Projected (VIP) cut-off of ≥0.7 to identify proteins discriminating between groups. Univariate analyses were performed using Mann-Whitney U test and false discovery rate analysis.

**Results:** In total, 166 subjects (UCa, n = 40; UCR-IIBS, n = 45; UCR-IIBS, n = 20; IBS, n = 21) were included in the study. PCA of SysPP of all groups revealed 2 clusters; 1 cluster composed of IBS patients and HS, and 1 cluster composed of all UC patients, irrespective of disease activity or presence of IBS-like symptoms. Variables most important for the clustering were higher levels of co-stimulatory molecules such as CD40 and tumor necrosis factor super family member 14 (TNFSF14), cytokines such as interleukin (IL)-8 and IL-6, oestrogen-M (OSM), chemokines such as chemokine ligand 3 (CCL3), other inflammatory markers such as extracellular newly identified receptor for Dectin-1 (EN-RAGE), sulfotransferase 1A1 (ST1A1), axin 1 (AXIN1), and an apoptotic marker, caspase-8 (CASP8), among UCA/UC-IBS/UC-IIBS as compared to IBS/HC.

When comparing IBS and UCR-IIBS patients based on the SysPP, OPLS-DA discriminated the 2 groups with high predictability (R² = 0.92, Q² = 0.82).

**Table:**

<table>
<thead>
<tr>
<th>Segment/Location</th>
<th>NHI</th>
<th>RHI</th>
<th>GHAS</th>
<th>CD31</th>
<th>S100A9</th>
<th>IL-23 (g19)</th>
<th>IL-23 (p40)</th>
<th>IL-6</th>
<th>IL-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon 1</td>
<td>3.3 (2.7-3.9)</td>
<td>19.5 (14.7-24.4)</td>
<td>10.8 (8.1-11.3)</td>
<td>2-1.2 (3-1.8)</td>
<td>0-1.4 (1-1.9)</td>
<td>3.5-3.7 (3-3.8)</td>
<td>4.7-5.5 (4-5.6)</td>
<td>6.4-6.5 (6-6.6)</td>
<td>6.5-7.0 (6-7.1)</td>
</tr>
<tr>
<td>Colon 2</td>
<td>0.12 (0.17-0.18)</td>
<td>5.8 (2.6-6.9)</td>
<td>5.2 (3.4-6.9)</td>
<td>2.7-3.0 (2.9-3.2)</td>
<td>3.2-3.6 (3.8-4.2)</td>
<td>6.6-6.9 (6-7.3)</td>
<td>9.8-10.2 (9-10.5)</td>
<td>7.1-7.7 (7-7.7)</td>
<td>5.3-5.8 (5-5.8)</td>
</tr>
<tr>
<td>Colon 3</td>
<td>3.6 (0.9-4.5)</td>
<td>4.8 (2.3-7.4)</td>
<td>4.2 (2.5-5.5)</td>
<td>2.7-3.0 (2.3-3.5)</td>
<td>3.4-3.8 (3.9-4.0)</td>
<td>6.7-7.0 (6-7.4)</td>
<td>9.0-10.5 (9-10.5)</td>
<td>7.2-7.6 (7-7.6)</td>
<td>5.9-6.4 (5-6.4)</td>
</tr>
<tr>
<td>Ileum 1</td>
<td>2.7 (2.1-3.2)</td>
<td>14.2 (10.8-13.3)</td>
<td>8.3 (6.9-9.6)</td>
<td>2.2-2.4 (2.5-2.6)</td>
<td>1.6-2.0 (2.1-2.4)</td>
<td>5.7-6.0 (5-6.2)</td>
<td>8.6-9.0 (8-9.2)</td>
<td>4.9-5.5 (4-4.9)</td>
<td>2.3-2.7 (2-2.3)</td>
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<tr>
<td>Ileum 2</td>
<td>1.3 (0.8-1.8)</td>
<td>6.6 (3.7-9.5)</td>
<td>5.1 (3.6-6.6)</td>
<td>2.6-2.8 (2.8-3.0)</td>
<td>3.0-3.3 (3-3.7)</td>
<td>6.8-7.0 (6-7.3)</td>
<td>9.7-10.1 (9-10.3)</td>
<td>7.3-7.8 (7-7.8)</td>
<td>5.2-5.7 (5-5.7)</td>
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<td>Ileum 3</td>
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<td>3.4 (1.1-5.7)</td>
<td>3.1 (1.6-4.0)</td>
<td>2.9-3.1 (2.7-3.2)</td>
<td>3.3-3.6 (3.0-3.6)</td>
<td>6.7-7.0 (6-7.3)</td>
<td>9.5-9.9 (9-9.9)</td>
<td>7.0-8.0 (7-8.0)</td>
<td>5.6-6.1 (5-5.1)</td>
</tr>
</tbody>
</table>

**Within segment pairwise comparison with location 2:** p<0.001, p<0.05; and location 3: p<0.001, p<0.05.


Abstract No: P0274

P0274 TISSUE REMODELLING IN TERMINAL ILEAL STRICTURING CROHN’S DISEASE

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Introduction: Crohn’s disease (CD) is a chronic inflammatory condition with multiple phenotypes of which the fibrostenotic type carries significant morbidity.

Aims and Methods: We aimed to look at histological changes in resected terminal ileal (TI) specimens using this novel scoring system (1). Results: Among 48 patients (M = 25; median age 45 years, range 21–72 years), 41 were Caucasian, 4 Asian and 3 Afro-Caribbean in ethnicity. The median duration of disease was 7 years (range 3 months – 39 years); majority had ileo-colonic distribution with stricturing disease; 16 patients were on thiopurines, 19 on steroids.

Conclusion: Our results suggest that pure fibrostenotic disease is uncommon and chronic inflammation is a prominent feature of this phenotype. In addition to fibrosis, muscle hyperplasia is an important component. Other components such as volume expansion, neuronal hypertrophy and adipose hyperplasia are likely to be important in different layers of the bowel. This suggests that inflammation driven tissue remodelling leading to stricture formation is a complex process resulting in a multitude of changes and not simply characterised by excess deposition of fibrotic tissue.

Disclosure: This abstract presents independent research funded by the NIHR Birmingham Biomedical Research Centre at the University Hospitals Birmingham NHS Foundation Trust and the University of Birmingham. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health.

Reference

P0275 B CELL-MEDIATED ILEOCECAL IMMUNE RESPONSE IN AN EXPERIMENTAL COLITIS MODEL ANALYZED VIA INTRAVITAL IMAGING

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Introduction: Inflammatory bowel diseases (IBD) often involve the ileoceleal region of the intestine. In addition, accumulating epidemiological studies have suggested that appendectomy may reduce the risk of ulcerative colitis. These findings imply that clinical immune response may be considered to affect the development of IBD, but the mechanism is still unclear.

Aims and Methods: The aim of this study is to analyze the ileocecal immune response in the setting of IBD. To this end, oxazolone colitis model was induced in mice under various backgrounds, conditions (including appendectomy), and methods (such as 5-dimensional intravital imaging).

Results: Wild type C57BL6 (WT) mice sensitized with oxazolone revealed lymphocyte infiltration and ulcerations in the colon accompanied by expanding cecal lymphoid follicles (CLF), which was the focus of our study. Mice underwent appendectomy before oxazolone treatment resulted in attenuated colitis with regards to both clinical disease activity and histopathology index with associated decrease of pro-inflammatory cytokine production. Similar clinical and histo-pathological changes were also observed in mice lacking mature B cells, µMT.

Conclusion: Real-time analysis of B cell activity in the CLF was accomplished by using mice with B cell-specific Ca2+ biosensor, YC3.60, expression. Utilizing intraval imaging, B cell activation with frequent Ca2+ influx was observed in the CLF during the early phase of colitis development. B cells in the CLF expressed higher level of activation markers, such as major histocompatibility complexes, compared to that of the non-colitis control, even though there were no significant changes in the ratios of immunoglobulin (Ig) classes on the B cell surface of the CLF.

Disclosure: Nothing to disclose.

P0276 THE CHANGE OF THE ANG, ACE2 AND ANG,1-7, ON TNBS-INDUCED EXPERIMENTAL COLITIS IN MICE AND THE RESEARCH ABOUT PROTECTIVE EFFECT OF MICA

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Introduction: Ulcerative colitis (UC), a chronic intestinal inflammatory condition that affects millions of people worldwide, is characterized by leukocyte infiltration and upregulation of proinflammatory cytokines. Mica is a silicate mineral drug. Previous studies have shown that mica can promote gastrointestinal mucus proliferation and epithelial cell regeneration in vivo, and inhibit cell apoptosis and activation of neuronal proliferation.

Aims and Methods: We aimed to explore the roles of Ang, ACE2 and Ang,1-7, in experimental colitis and investigate the prevention and possible mechanism of mica.

36 male BALB/C mice of clean grade were randomly divided into control group, model group and mica group, 10 mice in each group. Experimental colitis mice were made by TNBS. In first day, the model group and mica group were initiated by intrarectal administration of saline water (10ml/kg). From the second day, the control group and model group were
intrarrectally administrated with (10ml/kg/d), the mica group was intrarrectally administrated (180mg/kg/d) until the fourth day, then the mice were killed. Macroscopic score and histological score were assessed. Protein expressions of Ang, ACE2 and Ang1-7, were measured by immunohistochemist. ELISA was used to determine colonic tissue inflammatory factor IL-17A and IL-10 level.

Results: 1) Macoroscopic total damage: Colonic macroscopic damage index of mice in normal, the model group was much higher than that of the control group (4.00±0.89 vs. 0.00±0.00, p<0.01), the mica group was much lower than the model group (2.00±1.53 vs. 4.00±0.89, p<0.01). 2) Colonic tissues histological score: The histological score of the model group was much higher than the control group (8.17±2.99 vs. 1.33±1.03, p<0.01). Compared with the model group, the histological score in the mica group decreased significantly (3.83±1.27 vs. 1.31±2.09, p<0.01). 3) The level of Ang, ACE2, Ang1-7 in mice colonic tissues: The level of Ang, and Ang1-7 in the model group were increased compared with the control group (Ang,4.83±2.11 vs. 2.16±0.41, p<0.01; Ang1-7:2.0±0.63 vs. 0.13±0.14, p<0.05). But in the mica group the level of Ang, and Ang1-7 were significantly reduced compared with the model group (Ang,2.32±0.52 vs. 4.83±2.21, p<0.01; Ang1-7:1.04±0.56 vs. 2.0±0.63, p<0.01). Compared with the control group, the expression of ACE2 in colonic tissues from mice in the model group was increased (3.50±0.53 vs. 2.04±0.29, p<0.05), and in the mica group it was significantly increased than in the model group (5.13±1.84 vs. 3.50±0.55, p<0.05). 4) The expression of IL-17A in mice colonic tissues: The expressions of IL-17A in colonic tissues from mice in the model group and the mica group were significantly increased (6.93±0.44 vs. 0.65±0.03, p<0.01; 2.63±0.64 vs. 0.65±0.33, p<0.01). Meanwhile, the expression of IL-17A in the mica group was lower than in the model group (2.63±0.64 vs. 6.93±0.44, p<0.01). 5) Correlation analysis: Pearson’s correlation analysis showed that Ang, was moderately correlated with the mice colonic macroscopic damage index (r=0.52, p<0.05), and was highly positive correlation with the mice colonic histological score (r=0.909, p<0.01).

Conclusion: There is an imbalance between Ang, and ACE2, Ang1-7 in the TNBS-induced experimental colitis mice. And mice can reduce colonic tissues inflammation and damage.

Disclosure: Nothing to disclose

References

P0277 TAUROURSODEOXYCHOLIC ACID ATTENUATES COLITIS-ASSOCIATED COLON CANCER BY INHIBITING NUCLEAR FACTOR KAPPA B SIGNALING

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Introduction: Inflammatory bowel diseases (IBD) is associated with an increased risk of colorectal cancer. However, the mechanism of immune signaling pathways linked to colitis-associated cancer (CAC) has not been fully elucidated. Tauroursodeoxycholic acid (TUDCA) exhibits anti-inflammatory and anti-cancer activities. The aim of this study is to investigate the role of TUDCA in the pathogenesis of CAC.

Aims and Methods: CAC was induced in mice using azoxymethane (AOM) and dextran sodium sulfate (DSS) administration, and TUDCA’s effect on tumor development was evaluated. HCT 116 and COLO 205 were treated with TUDCA or vehicle and then stimulated with tumour necrosis factor alpha (TNF-α). The expression of interleukin (IL)-8 was determined by real-time RT-PCR and ELISA, and IκBα phosphorylation and degradation was evaluated by immuno-blot assay. The DNA-binding activity of NF-κB was assessed by electrophoretic mobility shift assay (EMSA). Cell viability assays and real-time PCR of bcl-2, bcl-xl, MCL1, c-FLIP-L and VEGF were performed.

Results: TUDCA significantly attenuated the development of CAC in mice. Exposure to TUDCA resulted in reduced epithelial apoptosis and reduced levels of phospho-IκB kinase in the colon. In HCT 116 cells stimulated with TNF-α, TUDCA significantly inhibited IL-8 expression and suppressed TNF-α-induced IκBα phosphorylation and DNA-binding activity of NF-κB. Furthermore, in both HCT 116 and COLO 205 cells, TUDCA reduced cell viability and downregulated the expression of bcl-xl, MCL1, c-FLIP-L and VEGF.

Conclusion: These results demonstrated that TUDCA suppresses NF-κB signaling and ameliorates colitis-associated tumorigenesis, suggesting that TUDCA could be a potential drug for CAC.

Disclosure: Nothing to disclose

P0278 ANTI-TNF-ALPHA THERAPY INDUCES MICRONAL AND IMMUNOLOGICAL CHANGES IN DEXTRAN SODIUM SULPHATE ACUTE COLITIS

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Introduction: Anti-TNF alpha represents the best therapeutic option to induce remission and clinical and histological improvement in patients with immunoneu-}

Disclosure: Nothing to disclose

References

P0279 SHORT-TERM ORAL ANTIBIOTIC TREATMENT PROMOTES INFLAMMATORY ACTIVATION OF COLONIC INKT AND CONVENTIONAL CD4+ T CELLS

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Introduction: The gut mucosa is continuously exposed to a vast community of microorganisms, collectively defined as microbiota, establishing a mutualistic interaction, benefiting the host to adapt to the changing environment. Gut microbiota is acquired at birth, and its composition is relatively stable during the entire adult life. Intestinal dysbiosis, defined as a microbial imbalance of gut bacterial communities, can be caused by several factors, including bacterial infection, immunological dysregulation, aging, and lifestyle changes. A dysbiotic microbiota after antibiotic treatment imprints colonic iNKT and conventional T cells. Due to the strong correlation between composition of gut microbiota and immune system, understanding the mechanisms of gut microbiota modulation can provide important insights into the pathogenesis of inflammatory bowel disease.

Aims and Methods: We aimed to evaluate gut microbiota and adaptive immune system response change following anti-TNF-alpha therapy in murine dextran sulfate sodium (DSS) colitis. C57BL6 mice were fed for 5 days with 3% DSS in drinking water. At day 3 of DSS treatment, mice received intravenous administration of 5 mg Kg of infliximab (IFX), an anti-TNF alpha monoclonal antibody, or placebo. Further 2 groups of mice received IFX or placebo without DSS. Disease activity index (DAI) was scored daily using the 4 points Disease Activity Index (DAI). At day V and XI serum, colon, feces and mesenteric lymph node (MLN) were collected from each animal. Microorganisms belonging to Bacteroides, Clostridiales, Enterobacteriaceae and Fecalibacterium prausnitzii were assessed by FISH and qPCR following bacterial DNA extraction from feces. Th1, Th2, Th17 and Treg cell distribution in the MLN were evaluated by intracellular cytokine staining by flow cytometry.

Results: Anti-inflammatory species (Bacteroides, Clostridiales and Fecalibacterium prausnitzii) decreased during DSS-induced colitis and increased in fecal samples of IFX-treated colitis mice compared to control mice. Conversely, pro-inflammatory microorganisms belonging to Enterococcaceae genera increased during colitis and decreased after IFX treatment. Furthermore, in IFX-treated colitic mice, microbial changes are associated to an initial increase (day 5 of the colitis) in Treg cells and a consequent decrease (day 12 of colitis) in Th1, Th2 and Th17 cells. Similarly, healthy mice treated with IFX showed the same histological features, microbial and immune changes of untreated colitic mice.

Conclusion: Anti-TNF alpha treatment in experimental model of colitis improves disease activity trough changes in T cell subsets and in microbiota composition. Furthermore, the present study suggests that different components of the microbiota can distinctly influence the differentiation and accumulation of specific populations of immune cells. Further analysis on immune cells within mucosa will be necessary.

Disclosure: Nothing to disclose
P0280 THERAPEUTIC POTENTIAL OF GLEPAGLUTIDE, A LONG-ACTING GLUCAGON-LIKE PEPTIDE-2 RECEPTOR AGONIST, IN A RAT MODEL OF RECURRENT INDOMETHACIN-INDUCED SMALL INTESTINAL INJURY. LAMINATION

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Introduction: Glepaglutide (ZP1848) is a novel, long-acting GLP-2 receptor agonist that is currently in clinical development for the treatment of short-bowel syndrome. We have previously shown that treatment with glepaglutide in a rat model of indomethacin-induced small intestinal (SI) inflammation enhanced intestinal repair, as measured by increase in intestinal mass and plasma citrulline levels, and decrease in inflammatory markers. Aims and Methods: The aim was to determine whether pre- and continuous treatment with glepaglutide would attenuate the SI inflammation response in rats exposed to a second inflammatory episode. 2 cycles of SI inflammation were induced in male Wistar rats by indomethacin administration (7 mg/kg, s.c.) on day 0 and day 1 (primary challenge) and then again on day 18 and day 19 (secondary challenge). Rats were treated with glepaglutide (80 and 400 mmol/kg, s.c.) from day 0 to day 14 (pretreatment), or from day 0 to day 21 (continuous treatment). Groups of rats (n = 8/group) were sacrificed on days 15 and 22. Study endpoints were bodyweight (BW), jejunal and ileal mass/BW, SI length, and SI levels of alpha 1 acid glycoprotein (α1-AGP; ELISA kit, Life Diagnostics) and myeloperoxidase (MPO; ELISA kit, Hycult Biotechnology). Results: Pretreatment with glepaglutide (80, 400 mmol/kg) increased jejunal- and ileal mass/BW on day 15 (p < 0.001 for both dose levels vs Indomethacin group). The second indomethacin-induced SI inflammation episode was characterized by BW loss, increased jejunal and ileal mass/BW, decreased SI length, and increased SI levels of α1-AGP and MPO. Pre- (400 mmol/kg) and continuous treatment (80 mmol/kg) with glepaglutide prevented BW loss in animals after the second inflammatory episode (p = 0.001 for all comparisons vs Indomethacin group). In addition, both pre- and continuous treatment with glepaglutide (400 mmol/kg) significantly increased ileal mass/BW on day 22, but had no effect on jejunal mass/BW or Indomethacin group. Both treatment regimes dose-dependently counteracted the shrinking of the SI length, and decreased SI levels of inflammatory markers (α1-AGP and MPO) during the second phase of inflammation (day 22).

Conclusion: We have demonstrated that pre- and continuous treatment with glepaglutide protected the SI against the recurrent inflammatory episode. In addition, pretreatment with glepaglutide increased SI mass assessed prior to the induction of the second phase of inflammation, suggesting that this increase in SI mass may provide the SI with more resistance to the second inflammatory insult. In conclusion, glepaglutide may provide an attractive option for the treatment and/or prevention of the unpredictable course of inflammatory bowel disease.

Disclosure: J. Skarbaliene, C. Thorkildsen, M. Berner-Hansen, and W. Russell are employees of Zealand Pharma A/S, and hold stock positions in Zealand Pharma A/S.

P0282 AUTOPHAGY-RELATED HOST FACTORS ARE INVOLVED IN THE INCAPABILITY OF MACROPHAGES FROM CROHN’S DISEASE PATIENTS TO ELIMINATE ADHERENT-INVASIVE ENTEROCOCCUS COLI

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Introduction: Several experimental data have highlighted the potential role of intestinal macrophages in the pathogenesis of Crohn’s Disease (CD). These macrophages present a defect in the control of CD-associated adherent-invasive E. coli (AIEC) replication, which could be linked to altered autophagy. Aims and Methods: We investigated the impact of several CD-associated sing gene nucleotide polymorphisms (SNPs) including those involved in autophagy on the ability of macrophages from CD patients to eliminate AIEC bacteria. Peripheral blood monocyte-derived macrophages (MDM) were obtained from 95 CD patients, 30 ulcerative colitis (UC) patients and 15 healthy subjects genotyped for CD-associated SNPs related to autophagy, especially IRGM (rs10065172) and ULK1 (rs12303764) and, infected with AIEC LF82 reference strain. Functional assay were performed on MDM after AIEC infection and/or after a short-term silencing of ULK1 gene. The numbers of intracellular bacteria were determined using gentamicin protection assay. IRGM, ULK1 and p62 protein expression was determined by western blot. Results: AIEC survival was increased within MDM from CD patients compared with MDM from UC patients or healthy subjects (p = 0.0019). MDM from CD patients failed to kill AIEC bacteria especially in patients harboring the CD-associated IRGM SNP (p = 0.045). In contrast, AIEC survival was decreased in MDM from patients with the CD-associated ULK1 SNP (p = 0.046). ULK1 expression, but not IRGM and p62, was increased in MDM from CD patients infected by AIEC bacteria compared to MDM from UC patients or healthy subjects (p = 0.0056) and are significantly correlated with the AIEC survival (p = 0.0309). In this line, ULK1 down-regulation within MDM limits the AIEC survival (p = 0.0018).

Conclusion: We confirmed that MDM from CD patients failed to eliminate AIEC bacteria compared to those of UC or healthy subjects. Our results highlight a role of CD-associated SNPs related to autophagy, IRGM and ULK1, on the ability of macrophages from CD patients to mediate AIEC bacterial clearance. At the protein level, our data suggested a role of ULK1, the cornerstone of autophagy initiation, to control AIEC bacteria within macrophages, in patients with CD. This protein could represent a potential new target to alter the interaction between macrophages and AIEC bacteria.

Disclosure: Nothing to disclose

P0283 MUCOSAL AND SYSTEMIC IMMUNE PROFILES DIFFER DURING EARLY AND LATE PHASE OF THE DISEASE IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction: Alterations in the immunopathogenesis in ulcerative colitis (UC) due to the natural disease course have been proposed but so far data are lacking. We therefore aimed to determine mucosal and systemic immune profiles at the time of diagnosis and after 10 years later in UC patients. Aims and Methods: Patients with UC provided serum and mucosal biopsies during a flare at the time of diagnosis and after 10 years of disease. The combination of these taxa into a microbial dysbiosis index showed a strong positive correlation with clinical disease severity and negative correlation with species richness. Conclusion: The dysbiosis of mucosa-associated microbiota was associated with disease phenotype, which could be partly restored after the induction of remission. We speculate that the trajectory of early microbiome changes may represent a predictive factor for relapse.

Disclosure: Nothing to disclose

P0284 CHARACTERISTICS OF MUCOSA-ASSOCIATED GUT MICROBIOTA DURING TREATMENT IN CROHN’S DISEASE

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Introduction: The dysbiosis of gut microbiome seems relevant to the pathogenesis of Crohn’s disease (CD), with differences between patients with CD and healthy subjects (HS) both in composition. However, it is not clear how the gut microbiota changed from active CD to remission after treatment. Aims and Methods: The aim of this study was to characterize the dynamic alterations of mucosa-associated intestinal microbiota in CD patients after induction of remission. 16S rRNA sequencing approach was applied to determine the structures of microbial communities in mucosal samples including terminal ileal, ascending colon and descending colon. The composition and function of mucosa-associated gut microbiota were compared between paired samples from CD patients at pre and post induction stage during disease treatment. Results: There were no significant differences in microbial structure among the three anatomical sites within individuals. Compared to active disease, the alpha diversity of CD in remission was increased and approximately up to the level of HS. The principal coordinate analysis revealed that samples of active CD clearly separated from those in remission which clustered close to HS. 42 genera were identified to be differentially abundant between active and quiescent CD with a loss of Faecalibacterium and a gain of potential beneficial bacteria including Lactobacillus, Akkermansia, Roseburia, Ruminococcus and Lachnospira after the induction of remission. The combination of these taxa into a microbial dysbiosis index showed a strong positive correlation with clinical disease severity and negative correlation with species richness.

Disclosure: Nothing to disclose

P0285 MUCOSAL AND SYSTEMIC IMMUNE PROFILES DIFFER DURING EARLY AND LATE PHASE OF THE DISEASE IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction: Alterations in the immunopathogenesis in ulcerative colitis (UC) due to the natural disease course have been proposed but so far data are lacking. We therefore aimed to determine mucosal and systemic immune profiles at the time of diagnosis and after 10 years later in UC patients. Aims and Methods: Patients with UC provided serum and mucosal biopsies during a flare at the time of diagnosis and after 10 years of disease. mRNA gene expression in biopsies was analyzed using the Qagent RT Profile PCR Arrays Antibacterial response and T Helper Cell Differentiation with 84 genes per array, in total 152 unique genes. Serum samples were analyzed using Olink Proseek Inflammation panel including 92 proteins (normalized protein expression (NPX)), but only the 43 proteins related to digestive tract were included in the analyses. Logarithmic data were analyzed in SIMCA using OPLS-DA to identify parameters discriminating between early and late disease, implementing a Variable Importance for the Projection (VIP) cut-off > 1. Identified parameters were used for univariate analysis and false discovery rate analysis. Data are
presented as fold change of means for mRNA analyses and median (interquartile range) for protein expression.

**Results:** The study included 15 UC patients (mean age 48 years after 10 years of disease, 60% males) where 8 had extensive, 5 left-sided disease and 2 proctitis. No patient had ongoing treatment with corticosteroids or biologics (2 were previously treated). 3 patients currently used Azathioprine and 10 oral aminosalicylates. When comparing early and late disease, the mRNA profiles in biopsies discriminated the groups and showed high predictability for oral aminosalicylates. When comparing early and late disease, the mRNA profile was detected during late compared to early disease. Additionally, a fold decrease of the Th1-associated genes TNF (0.66, q = 0.003) and SOCS1 (0.66, q = 0.004) was found during late compared to early disease. Furthermore, IL-8 (7.4 (6.9–7.9, V.9) vs. 8.9 (7.1–14.5, N.PX)) and MCP3 (2.2 (1.9–2.6, V.8) vs. 2.8 (2.3–28.0, N.PX), important for recruitment of neutrophils and monocytes, and TNSF14 (6.7 (5.4–7.2) vs. 7.6 (6.5–8.3, N.PX), CCL20 (4.7 (4.4–5.4) vs. 5.8 (5.5–6.2, N.PX) and CCL28 (1.4 (1.2–1.6) vs. 1.6 (1.5–1.9, N.PX)) associated with lymphocyte homing were decreased during late as compared to early disease.

**Conclusion:** Mesosalic and inflammatory systemic profiles differ between early and late disease in UC patients with active disease, with a change from a Th Helper 1 to a Th Helper 2 cell driven disease. Improved understanding of the variation in immune pathogenesis due to the natural disease course is important to guide individualized treatment decision-making.

**Disclosure:** Nothing to disclose

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**P0284 LOW LEVEL OF KNOWLEDGE OF PREGNANCY-RELATED ISSUES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN POLISH POPULATION**

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**Introduction:** Inflammatory bowel diseases (IBDs) belong to the group of chronic diseases, significantly increase the risk of surgery, colorectal cancer and often influence the reproductive decisions of the patients, may influence their personal life choices regarding family planning and having children.

**Aims and Methods:** The aim of the work was to assess the knowledge of female patients with IBD regarding pregnancy and fertility issues in respect of the disease. The goal of the work was also to educate the patients. The examinations were based on validated test CCPKnow (Crohn’s and Colitis Pregnancy Knowledge Score). The study included 120 women at the age of 18 to 74, including 86 women at the age up to 45 years old, 59 women with CD (Crohn’s disease) and 61 women with UC. The patients were endoscopically and histologically healthy and served as controls. The IBD patients were divided into three groups: UC, CD and IBD patients with active disease. The difference in the level of knowledge assessed by means of CCPKnow test was estimated to 6.9 of 17 points possible. Through the analysis was also made an estimate of the post-inflammatory restoration of the mucosa (1). However, the role of TCs in human pathophysiological conditions is still an open question.

**Aims and Methods:** The aim of the present prospective study was to test the hypothesis that the count of colonic TCs in patients with inflammatory bowel disease (IBD) is altered compared to healthy controls (controls). Endoscopic colonic mucosal biopsies from 38 individuals were included in the study; 14 patients with Ulcerative Colitis (UC) in clinical and endoscopic remission (total Mayo score < 2 and no sub score > 1), 9 with clinical and endoscopic active UC (total Mayo score > 2 and Mayo endoscopic sub score > 1), 10 with colonic Crohn’s Disease (CD) in endoscopic and histological remission (1 had slight inflammation of the terminal ileum), 8 with endoscopically and histologically quiescent colon CD, and 7 with endoscopically and histologically quiescent UC.

**Disclosure:** Nothing to disclose

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**References**


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**P0285 ALTERED TUFT CELL POPULATION OF HUMAN COLONIC EPITHELIUM IN INFLAMMATORY BOWEL DISEASES**


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**Introduction:** The gastrointestinal tuft cells (TCs) have recently been revealed as parasite-sensing cells in rodents. TCs play a key role in initiation of a type-2 immune response and lead to polarization of the immune system. The gut microbiota is known to play a key role in the post-inflammation restoration of the mucosa (1). However, the role of TCs in human pathophysiological conditions is still an open question.

**Aims and Methods:** The aim of the present prospective study was to test the hypothesis that the count of colonic TCs in patients with inflammatory bowel disease (IBD) is altered compared to healthy controls (controls). Endoscopic colonic mucosal biopsies from 38 individuals were included in the study; 14 patients with Ulcerative Colitis (UC) in clinical and endoscopic remission (total Mayo score ≤ 2 and no sub score ≤ 1), 9 with clinical and endoscopic active UC (total Mayo score > 2 and Mayo endoscopic sub score > 1), 10 with colonic Crohn’s Disease (CD) in endoscopic and histological remission (1 had slight inflammation of the terminal ileum), 8 with endoscopically and histologically quiescent colon CD, and 7 with endoscopically and histologically quiescent UC. No contraceptive use was assessed by means of CCPKnow test. The difference in the level of knowledge assessed by means of CCPKnow test was estimated to 6.9 of 17 points possible. Through the analysis was also made an estimate of the post-inflammatory restoration of the mucosa (1). However, the role of TCs in human pathophysiological conditions is still an open question.

**Conclusion:** The gastrointestinal tuft cells (TCs) have recently been revealed as parasite-sensing cells in rodents. TCs play a key role in initiation of a type-2 immune response and lead to polarization of the immune system. The gut microbiota is known to play a key role in the post-inflammation restoration of the mucosa (1). However, the role of TCs in human pathophysiological conditions is still an open question.

**Disclosure:** Nothing to disclose

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**Reference**

**LOCUS REGULATORY B CELLS CONTRIBUTE TO ALLOCUTE THE ACUTE COLITIS IN CD19<sup>+</sup> MICE**

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**Introduction:** Epidemiological studies showed that there was an inverse relationship between H. pylori (H pylori) infection and the incidence of inflammatory Bowel Diseases (IBD). It was confirmed that CD4<sup>+</sup>+CD25<sup>+</sup>+Foxp3<sup>+</sup> Treg cells could protect mice from colitis. Our previous study showed that H. pylori infection induced the expansion of regulatory B cells (Breg) ahead of the Treg cells.

**Aims and Methods:** In this study, we investigated the effect of Breg cells on acute colitis induced by dextran sulphate sodium (DSS). SPP CD19<sup>+</sup> mice were utilized. 1x10<sup>6</sup> Breg or B cells or equal PBS were adoptive transferred to the CD19<sup>+</sup> mice via the tail vein. Twenty-four hours later, acute colitis was induced by 3% DSS. Duplicate sigmoidal biopsies were cultivated without (none) or with 1.6 mM butyrate. mRNA gene expression was analyzed using the Qiagen RT2 Profiler PCR Arrays.

**Results:** MKL1-Tg mice displayed spontaneous colon shortening and rectal prolapse. Scattered cryptitis was observed among the colons. Flow cytometric and quantitative RT-PCR analyses revealed that, in MKL1-Tg mice compared to littermate controls, the proportion of LPMac was decreased and had an altered inflammatory phenotype indicative of impaired anti-inflammatory properties. MKL1 also orchestrates macrophage polarization. Of note, overexpression of MKL1 impacts transcriptional activities of NF-κB p65 and PPARγ. Furthermore, MKL1-Tg mice had higher susceptibility to DSS-induced colitis, which was accompanied with prominent B cells infiltration and follicle formation.

**Conclusion:** Our observations indicated that MKL1 crucially contributes to the development of colitis via the regulation of the function of macrophages, suggesting that it may be a potential therapeutic target for the prevention of IBD.

**Disclosure:** Nothing to disclose.

**PO287 IMPAIRED BUTYRATE INDUCED ANTI-INFLAMMATORY IMMUNE REGULATION IN LAMINA PROPRIA CELLS FROM PATIENTS WITH ACTIVE ULCERATIVE COLITIS**

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**Introduction:** Modulation of the gut microbiota has emerged as a therapeutic option for patients with ulcerative colitis (UC), yet with modest effects. Microbial dysbiosis and reduced levels of short-chain fatty acids such as butyrate have been identified as key components of the disease and butyrate is known to have anti-inflammatory properties.

**Aims and Methods:** Here we aimed to determine and compare immunological effects and cytokine profile (IL-1β) from UC patients with active disease and non-inflammatory control (CTR) patients.

**Results:** Duplicate sigmoidal biopsies were cultivated without (none) or with 1.6 mM butyrate (but) for 6h after which biopsies were collected for RNA purification. mRNA gene expression was analyzed using the QuanTr RT<sup>®</sup> Profiler PCR Arrays Antibacterial response and Innate and Adaptive Immune Responses with 84 genes per array, in total 135 unique genes. Logarithmic data were analyzed using principal component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA) with a cut off for Variable Importance for the Projection >1.2. Identified parameters were subject to univariate analysis and false discovery rate analysis and evaluated using Ingenuity Pathway Analysis (IPA). Gene expression data are presented as fold change (IC) of means on a log<sub>2</sub> scale where log<sub>2</sub>FC = 1 and −1 define a 2-fold increase and decrease, respectively.

**Results:** The study included 8 CTR patients (4 males, age 54 (24–84), median (range)) and 8 patients with UC (6 males, age 38 (32–74)) with a disease duration of 7 (<1–47) years. All UC patients had active disease with endoscopic Mayo score >7 (n=8), CTR patients had Mayo score 0. Current treatment for UC patients was 5ASA (n=5), 5ASA and thiopurines (n=1), corticosteroids (n=1) and no treatment (n=1).

**Conclusion:** Our data suggests that macrophage polarization by MSC is affected by the cell quality and that passaging of cell could impair its immunomodulatory effects and tumour necrosis factor receptor superfamily member 13b (Tnfrsf11b).

**Disclosure:** Nothing to disclose.
P0290 DOES ASTHMA INCREASE THE RISK OF INFLAMMATORY BOWEL DISEASE? A META-ANALYSIS OF CASE-CONTROL AND COHORT STUDIES

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Introduction: There have been several studies that assessed the association between asthma and inflammatory bowel disease (IBD) including Crohn’s disease (CD) and ulcerative colitis (UC). The positive association may be explained through the hygiene hypothesis, which postulates that a reduction in the frequency of infections contributes directly to the increase in the frequency of autoimmune and allergic diseases.

To provide a quantitative assessment of the association of asthma with subsequent IBD risk, we conducted a meta-analysis of observational studies.

Aims and Methods: We identified studies by searching the PubMed databases through February 2018 and by searching bibliographies of relevant articles. Included studies reported IBD as the primary outcome and evaluated asthma before diagnosed with IBD. We included case - control studies or cohort studies published as original articles; cross-sectional, ecological, and prevalence studies were excluded.

Results: A total of 7 observational studies were included in our meta-analysis. Asthma was associated with an increased risk of CD (summary OR 1.45, 95% CI: 1.30–1.61) and UC (summary OR 1.29, 95% CI: 1.02–1.64).

Conclusion: This meta-analysis demonstrates that asthma is associated with an increased risk of both CD and UC. Further prospective studies are required to confirm the validity of these observations.

Disclosure: Nothing to disclose.

References:

P0291 THE PREVALENCE OF GASTROINTESTINAL CANCERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE - A DANISH NATIONWIDE COHORT STUDY

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Introduction: Inflammatory Bowel Disease (IBD), mainly represented by Crohn’s Disease (CD) and Ulcerative Colitis (UC), is known to be associated with an elevated risk of gastrointestinal (GI) cancer. The pathogenesis is poorly understood, but risk factors seem to be longstanding disease as well as extensive disease and high degree of inflammation. However, the reported magnitude of the risk in IBD patients is still inconsistent and the long-term effects of newer treatment options on the development of cancer have not been investigated thoroughly.

Aims and Methods: To estimate the prevalence of GI cancer development in a Danish nationwide cohort of IBD patients, overall cancer as well as neoplasms located to the small bowel, anus/anal canal, liver, bile ducts and pancreas were more prevalent compared to the reference individuals. There was a significant difference in the prevalence of colorectal cancer between reference individuals and IBDU patients, but not compared to the overall IBD cohort.

Conclusion: In a Danish nationwide cohort of IBD patients, overall cancer as well as neoplasms located to the small bowel, anus/anal canal, liver, bile ducts and pancreas were more prevalent compared to the reference individuals. There was a significant difference in the prevalence of colorectal cancer between reference individuals and IBDU patients, but not compared to the overall IBD cohort.

Disclosure: This study was financed by a grant from Tillotts pharma.

P0292 NATURAL HISTORY OF ACUTE SEVERE ULCERATIVE COLITIS IN ELDERLY: A POPULATION-BASED STUDY

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Introduction: Acute severe attack of ulcerative colitis (ASUC) can occur in 12 to 25% of UC patients. This is a challenging and life threatening in elderly patients. Evolution of ASUC in late onset UC diagnosed after the age of 60 years is unknown.

Aims and Methods: The aim of this study was to describe clinical presentation, treatment and prognosis of ASUC in a cohort of late onset UC.

Patients and methods: In a Northern France population-based cohort, we identified 472 patients aged >60 years at UC diagnosis ulcerative colitis (UC). These patients were followed for a median time of 6.2 years. Among these patients, those hospitalized with an ASUC according to the Truelove’s criteria were analyzed. Clinical presentation, comorbidities (Charlson index), treatment and surgery needs as well as postoperative complication and mortality were recorded.

Results: 23 patients (5%) including 14 men were included. ASUC occurred at diagnosis in 12 patients (52%) and during the first year of follow-up in 19 patients (83%). The Charlson comorbidity score was ≥ 3 in 96% (n=22) and ≥ 5 in 52% (n=12) of the cases. First-line treatment was intravenous corticosteroid (64%, n=14), colectomy (22%, n=4) or exclusive artificial nutrition (24%, n=5). No patient received second line medical treatment ciclosporin or infliximab. Among the 18 operated patients, median time between admission for severe acute colitis and intervention was 15 days (Q1 = 9, Q3 = 39). Surgery was a subtotal colectomy with double stoma in 13 cases, a partial colectomy in 3 cases, total colectomy in 1 case and a stomy alone in 1 case. Stoma were definitive in 69% (n=9) of cases. 1 or more postoperative complications occurred in 6 patients (26%) i.e. renal insufficiency (n=4), thromboembolic event (n=4),...
septic shock (n=2). 5 patients (22%) died, of which 4 after surgery, leading to a 3-month survival rate of 75% (IC95%: 58–97%) (Figure 1).

Conclusion: In this population-based study conducted in the prebioterapia era ASUC in elderly onset UC patient was rare but particularly severe requiring surgery in 74% of patients and life-threatening with a mortality rate close to 2% in 3 months. Management of these severe patients in referral centers is mandatory.

Disclosure: Nothing to disclose

P0294 SMOKING REMAINS A MAJOR CONTRIBUTOR TO THE BURDEN OF CROHN’S DISEASE IN IRELAND AND WARRANTS THE DEVELOPMENT OF A SPECIFIC TARGETED SMOKING CESSATION INTERVENTION

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Introduction: Approximately 15,000 people in Ireland have Crohn’s disease (CD) and a high prevalence of smoking. Previous data suggest that smokers are twice as likely to develop CD and active CD smokers have a higher risk of relapse, hospital admissions, steroid therapy and surgery. Despite this, many Irish CD patients continue to smoke perhaps due to lack of knowledge and awareness.

Aims and Methods: To determine current smoking rates and the impact of smoking on CD severity and to assess patient knowledge and awareness of the risks associated with smoking. Following ethical approval, a prospective case control study of Irish CD patients' and age and sex matched non IBD GI patient controls was undertaken. A self-assessment questionnaire was employed to assess smoking habits, basic demographics and education status overall as well as disease characteristics and awareness of the impact of smoking in the CD cohort. Groups were compared using a Chi²-test, p of less than 0.05 were considered statistically significant and odd ratios were calculated where appropriate.

Results: To date 139 questionnaires have been returned, 56 from CD patients and 83 from Controls. The mean age was 47 years (range 19–80) and 62 (47%) were females. The smoking status of the groups was 33% (n=46) vs 44% (n=36) respectively (p=0.3). Rates of smoking were 58% (n=37) vs 59% (n=33) respectively (p=0.8). In a multiple logistic regression model, smoking was a significant risk factor for CD (OR 1.91, 95% CI 1.1–3.3). In fact, active smokers were twice as likely to develop CD (OR 2.2, p=0.05). Current smokers also had a higher BMI (mean 25.6 vs 24.8 kg/m², p=0.01) and higher HBI (mean 7, RR 2.2, p=0.02). There was no difference in steroid use between the groups. Only 41% (13/32) of our CD cohort thought smoking was a significant risk factor for BD. While only 28% (9/32) thought smoking was a risk factor for surgery while just 16% (5/32) thought smoking cessation could significantly decrease the severity of their disease.

Conclusion: Disturbingly, smoking rates remain high in our Irish CD population, with a negative impact on disease severity and need for surgery. Surprisingly few CD patients were aware of the negative impacts of smoking and the potential benefit of cessation. Emphasizing an urgent need for a specific targeted smoking cessation intervention.

Disclosure: Nothing to disclose

P0295 OCULAR MANIFESTATIONS IN A TERTIARY IBD CENTER: BETTER TO KEEP AN EYE ON

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Introduction: Extra-intestinal manifestations (EIM) are common in inflammatory bowel disease (IBD) occurring in up to 50% of patients, while ocular manifestations are reported in 0.3% to 13.9% of the cases. Reported data, however, mostly rely on not recent population based studies. In fact, the few available prospective studies, suggest a much higher occurrence of ocular diseases, ranging from 29% to 71%.

Aims and Methods: The aim of the study was to assess the prevalence of ocular disease in a cohort of IBD patients followed in tertiary referral Italian center. IBD patients followed at our center were consecutively enrolled in the study. Enrolled patients underwent ocular evaluation including assessment of visual acuity, examination of fundus oculi and anterior ocular segment as well as a measurement of intraocular pressure, Schirmer’s test and break up time test, when appropriate.

Results: A total of 193 IBD patients were enrolled in the study, 54.9% females and 45.1% males, 47.7% CD, 43.5% UC, and 8.8% indeterminate colitis, 35.7% of patients had a moderate-severe activity of disease, 39.4% were under steroid therapy, 35.8% were under anti-TNFalpha and 64.3% were taking mesalamine.

Overall, any ocular disease was identified in 46.1% of enrolled patients, 17.1% CD and 23.3% UC and 5.2% IC. The most common ocular disease was dry eye (12.4%). At multivariate analysis use of mesalamine (OR 2.3, 95% CI 1.1–5.0), steroids (OR 3.6, 95% CI 1.1–11.8) and moderate-severe activity of disease (OR 5.1, 95% CI 2.3–11.1) were all correlated with an increased risk of ocular disease. Characteristics of Ocular manifestations in IBD patients are more frequent than reported especially in referral center. Patients under treatment with mesalamine or steroids and with a moderate-severe disease activity might benefit of an ophthalmological evaluation.

Disclosure: Nothing to disclose

P0296 INTESTINAL AND EXTRA-ENTERITAL CANCER IN IBD PATIENTS ADMITTED TO AN ITALIAN TERTIARY CENTER

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Introduction: Inflammatory bowel disease (IBD) patients are at higher risk to suffer from colorectal cancer. While the association between ulcerative colitis (UC) and colorectal cancer is well defined, the risk for Crohn's disease (CD) is less defined. Similarly, little information exists on extra-intestinal tumors in different settings of patients.

Aims and Methods: The aim of the study was to assess occurrence of malignancies in IBD patients admitted to the hospital. All patients admitted for CD or UC to Policlinico-“A. Gemelli” between 2000 and 2013 were identified using ICD-9-CM codes for IBD. A review of gastrointestinal or extra-intestinal cancer was assessed for every patient analyzing ICD-9-CM codes. Demographic characteristics of admitted patients were also recorded.

Results: A total of 3347 patients were admitted for an IBD between 2000–2013, in 2000 9.6% (n=125) vs 2013 29.7% (n=992). Malignant tumors, at any site, were more frequent in UC than in CD (7.3% versus 2.7%, respectively; p<0.05). Median age at admission was 44.0 years for patients without a diagnosis of tumor and 63.8 years for those with a diagnosis of cancer. The occurrence of colon and rectal cancer was 1.7%, with 81% cases affecting UC patients. The most frequent extra-intestinal malignancies were prostate cancer and myeloproliferative disorders. Colon and rectal cancer accounted for 59.8% of all gastrointestinal cancer.

Conclusion: About 5% of admitted IBD patients presented a cancer diagnosis. Higher cancer occurrence was observed in UC and in older patients, with a median age of about 60 years and more frequently in men. Colorectal cancer occurrence in UC was about 2%.
Results: Sera were available from 342 and 272 UC patients and 159 and 135 CD patients at the 10 and 20 year follow-up, respectively. The proportions of patients positive for the analyzed antibodies at the 10 and 20 year follow-up are presented in table 1. As previously shown, ASCA was more prevalent in CD than UC and in complicated CD behavior vs. inflammatory CD behavior at the 10 year follow-up. The status of ASCA on the other hand, changed significantly. These findings indicate that ASCA IgA remained stable from 10 to 20 year follow-up. The status of ASCA IgG on the other hand, changed significantly. These findings indicate that ASCA IgG for patients with both UC (p < 0.001) and CD (p < 0.001).

Conclusion: In a population-based inception cohort the status of pANCA and ASCA have been stable from 10 to 20 years. At the 10 and 20 year follow-up visits, the following panel of antibodies was analyzed in serum: pANCA, ASCA IgA and ASCA IgG. All analyses were performed at Prometheus Laboratories Inc. (San Diego, CA). Changes in antibody status within individuals from 10 to 20 years were assessed using Wilcoxon signed ranks test.

Disclosure: Sera were analysed by Prometheus laboratories free of charge.

Reference

P0298 INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE: CHARACTERIZATION AND RISK FACTORS IN A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL IG-BD STUDY AT 6 YEARS

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Introduction: Serological biomarkers in inflammatory bowel disease (IBD) predict complicated disease are warranted. Several microbial antibodies and auto-antibodies have been associated with IBD and especially ASCA and PANCA have been proposed as potential biomarkers. Studies have shown that their presence might vary over time thus their clinical impact is still discussed. Long term studies of ASCA and pANCA stability have not been performed in population-based cohorts.

Aims and Methods: The aim of the present study was to investigate potential change in antibody status over time by analysing a panel of relevant serum antibodies at 10 and 20 years after disease onset in a population-based inception cohort of IBD patients (the IBSEN cohort). The IBSEN cohort is an inception cohort of patients diagnosed with IBD between 1990 and 1994. The patients have been followed prospectively for 20 years. A total of 228 UC patients and 113 CD patients, sera were available at both time points. The antibody status within individuals changed significantly for ASCA IgG for patients with both UC (p < 0.001) and CD (p < 0.001).

Conclusion: In a population-based inception cohort the status of pANCA and ASCA have been stable from 10 to 20 years. At the 10 and 20 year follow-up visits, the following panel of antibodies was analyzed in serum: pANCA, ASCA IgA and ASCA IgG. All analyses were performed at Prometheus Laboratories Inc. (San Diego, CA). Changes in antibody status within individuals from 10 to 20 years were assessed using Wilcoxon signed ranks test.

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Introduction: Serological biomarkers in inflammatory bowel disease (IBD) predict complicated disease are warranted. Several microbial antibodies and auto-antibodies have been associated with IBD and especially ASCA and PANCA have been proposed as potential biomarkers. Studies have shown that their presence might vary over time thus their clinical impact is still discussed. Long term studies of ASCA and pANCA stability have not been performed in population-based cohorts.

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Conclusion: In a population-based inception cohort the status of pANCA and ASCA have been stable from 10 to 20 years. At the 10 and 20 year follow-up visits, the following panel of antibodies was analyzed in serum: pANCA, ASCA IgA and ASCA IgG. All analyses were performed at Prometheus Laboratories Inc. (San Diego, CA). Changes in antibody status within individuals from 10 to 20 years were assessed using Wilcoxon signed ranks test.

Disclosure: Sera were analysed by Prometheus laboratories free of charge.

Reference

P0298 INCIDENT CANCER IN INFLAMMATORY BOWEL DISEASE: CHARACTERIZATION AND RISK FACTORS IN A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL IG-BD STUDY AT 6 YEARS

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Introduction: Serological biomarkers in inflammatory bowel disease (IBD) predict complicated disease are warranted. Several microbial antibodies and auto-antibodies have been associated with IBD and especially ASCA and PANCA have been proposed as potential biomarkers. Studies have shown that their presence might vary over time thus their clinical impact is still discussed. Long term studies of ASCA and pANCA stability have not been performed in population-based cohorts.

Aims and Methods: The aim of the present study was to investigate potential change in antibody status over time by analysing a panel of relevant serum antibodies at 10 and 20 years after disease onset in a population-based inception cohort of IBD patients (the IBSEN cohort). The IBSEN cohort is an inception cohort of patients diagnosed with IBD between 1990 and 1994. The patients have been followed prospectively for 20 years. A total of 228 UC patients and 113 CD patients, sera were available at both time points. The antibody status within individuals changed significantly for ASCA IgG for patients with both UC (p < 0.001) and CD (p < 0.001).

Conclusion: In a population-based inception cohort the status of pANCA and ASCA have been stable from 10 to 20 years. At the 10 and 20 year follow-up visits, the following panel of antibodies was analyzed in serum: pANCA, ASCA IgA and ASCA IgG. All analyses were performed at Prometheus Laboratories Inc. (San Diego, CA). Changes in antibody status within individuals from 10 to 20 years were assessed using Wilcoxon signed ranks test.

Disclosure: Sera were analysed by Prometheus laboratories free of charge.

Reference


**P0299 WHAT FACTORS CAN IMPROVE THE EXPERIENCE OF PATIENTS WITH CHRONIC HEALTH CARE? A SURVEY OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

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**Introduction:** The experience of patients with health care has been related to important outcomes (1). Aims and Methods: In this work we describe the perception of inflammatory bowel disease (IBD) patients on their experience with chronic health care in Spain through IEXPAC, a validated questionnaire, and the influence of demographic and health care-related factors. The IEXPAC scale (“Instrument to Evaluate the EXperience of PAtients with Chronic diseases”) was developed and validated in Spain by health care professional and social organizations, experts in quality of health care and chronic patients (2,3). It is structured in 12 items with Likert responses from ‘always’ to ‘never’, yields an overall score from 0 (worst) to 10 (best experience), and allows identifying health care areas needing improvement. 3 sub-scores derive from the scale: A) productive interactions (items on patient-health care professionals relationship), B) self-care (on patients’ ability to self-care) and C) new relational model (on the use of new technologies and contact with other patients). Consecutive IBD patients from 25 Spanish clinics completed the IEXPAC scale by pre-paid mail. Bivariate comparisons and a multivariate analysis were made to explore the association between scores and demographic and health care-related characteristics.

**Results:** 575 patients received the survey, 341 (59.3%) returned it (mean age 47 years, 48% women). Mean overall score was 5.9 (SD 2.0), sub-scores were: productive interactions: 7.7 (2.3); self-care: 6.9 (2.4); new relational model: 2.2 (1.8). Sex by age, sex and degree of education (except new relational model, better in younger and in those with higher education level). Experience score was better in patients followed-up by the same physicians (score 6.0 [1.9]) vs different physicians (5.0 [2.1], p = 0.002), if there was follow-up by a nurse (score 6.2 [2.1]) vs no follow-up by a nurse (5.6 [1.8], p < 0.001) and in those with lower number of medications (p = 0.010). Patients treated with subcutaneous/intravenous (SC/IV) drugs scored higher in the ‘productive interactions’ sub-score (p = 0.052). Multiple linear regression models (table) showed that being followed up by the same physician or by a nurse, and being treated with lower number of medications or with SC/IV drugs were independently associated to better overall experience scores.

**Conclusion:** Through IEXPAC, IBD patients identified important factors that can improve their experience with health care, like having the same physician as reference in the clinic and being followed-up by a nurse. Lower number of treatments was also associated to better experience and treatment with SC/IV drugs to higher ‘productive interactions’ sub-score, maybe in relation to a more personalized care.

**Disclosure:** This study was funded by Merck Sharp & Dohme of Spain and endorsed by the Spanish association of patients with Crohn’s disease and ulcerative colitis (ACCU). We thank the participating patients for providing this valuable information by completing the survey. Marta Mosquera, Nadia Soto, Berta Julià and Luis Cea-Calvo are employees at Medical Affairs, Merck Sharp & Dohme of Spain

**References**


**P0300 PATIENT-REPORTED COMPLEMENTARY AND ALTERNATIVE MEDICINE USE IN IBD: 10 YEARS OF OBSERVATION AMONG PATIENTS INCLUDED IN A NATIONAL COHORT**

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**Introduction:** Complementary and alternative medicines (C&AM) may be defined as treatments that fall outside of conventional healthcare. Patients with IBD often turn to CAM, mainly without discussing it with their physician. We repetitively collect information on patient-reported CAM use between 2007 and 2016. Aims and Methods: 1) to assess main categories of patient-reported CAM used by IBD patients, with CAM use increasing among women (OR 1.5; p = 0.001).French-speakers (OR 1.5; p = 0.001) and lower with increased IBD QoL score.

**Results:** 21.7% to 29.3% of patients over years. Types of CAM were natural products and biologically based therapies (range: 6.9% to 11.9%), change in life habits (6.2% to 11.2%), whole medical systems and traditional medicines (5.8% to 9.6%), mind-body interventions (3.2% to 7.7%), body-based interventions (3.5% to 4.6%) and energy therapies (1.9% to 4.6%). When looking to the history of CAM use by patients in 2016, we found that 41.9%/44.4% of CD/UC patients used > 1 CAM reported from 2007-2016).

**Conclusion:** Positive coefficients mean better experience (higher IEXPAC score). Multivariate logistic regressions were performed to search for factors associated with CAM use (i.e. > 1 CAM use differed between UC and CD. Some of them seemed to be linked to relieving articular and musculoskeletal pain or improving IBD-specific or mental QoL.

**Disclosure:** The Swiss IBD cohort started in November 2006. At enrollment and on a yearly basis, patients were asked to complete self-reported questionnaires. CAM were collected using a list of previously identified CAM1,2 and a free text option. Additional clinical and patient-reported data collected within the framework of the cohort was used to characterize CAM users. For descriptive purposes, we classified CAM using recommendations of the US National Center for Complementary and Integrative Health (NCCIH). Changes in life habits (e.g. diet and sportive activities) was taken as an additional category. Dietary and nutritional supplements were not assessed here. Multivariate logistic regressions were performed to search for factors associated with CAM use (i.e. > 1 CAM use).

**References**

Disclosure: Nothing to disclose

References

P0301 FECAL CALPROTECTIN MAY BE A SENSITIVE BIOMARKER IN ASSESSMENT OF HISTOLOGIC DISEASE ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS
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Introduction: In patients with ulcerative colitis (UC) histological remission leads to better outcome, whereas presence of histological inflammation in quiescent disease is risk factor of future relapses. Fecal calprotectin (FCP) turned to be good biomarker in assessment of endoscopic and clinical disease activity.

Aims and Methods: The aim was to explore the association of FCP with histologic disease activity.
82 patients with UC from a single tertiary IBD Centre were enrolled in this prospective, observational study. Mayo endoscopic sub-score was used to evaluate an endoscopic activity. For the assessment of histological activity, Geboes’s, Nancy’s and Robarts’s score were used. Active (structural changes, the presence of polymorphonuclear leukocytes with cryptitis and crypt abscesses, and erosions or mucosal ulcers) and chronic inflammations were estimated. Histologic remission was defined by Geboes score < 3.1 or Nancy’s index ≤ 1 or Robarts’s index < 6. Basal plasmodicytosis, as a predictor of relapse, was described as well. Buhlmann rapid test was used to determine FCP using cut off level of 100 μg/g. Statistical analysis was carried out using SPSS 20.0 (Chicago, IL).

Results: 38% (31/82) of patients were in endoscopic remission while 33% (27/82) achieved histological remission. Statistically significant association was observed between FCP and histological indicators of active inflammation: a. structural changes p = 0.001, CI ± 8.5; b. presence of the presence of polymorphonuclear leukocytes with cryptitis and crypt abscesses p < 0.001, CI ± 10.6; c. presence of erosion and mucosal ulcers p < 0.001, CI ± 6.2, as well as with basal plasmodicytosis (p < 0.001, CI ± 6.4). The association with chronic inflammation was not observed (p = 0.002, CI ± 9.37). The correlation was found between FCP and all 3 scores with the strongest for Nancy index (r = 0.538- Spearman correlation). The correlation with Robarts score (r = 0.505- Spearman correlation) or Geboes (r = 0.382- Spearman correlation) were slightly lower.

Conclusion: Fecal calprotectin may be a good, sensitive, noninvasive biomarker in the assessment of histologic disease activity and point out a forthcoming relapse. This association with validated histologic score may even enhance the significance of FCP in clinical practice in the future.

Disclosure: Nothing to disclose

P0303 THE EFFECT OF ARYLESTERASE AND PARAOXONASE-1 LEVELS ON ULCERATIVE COLITIS: A RANDOMISED CONTROLLED STUDY
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Introduction: This study aimed to investigate the relationship between ARE(Arylesterase) and PON-1(Paraoxonase-1) levels in ulcerative colitis (UC) patients and the difference in these levels in UC patients in comparison to the control group.

Aims and Methods: The study population consisted of 66 (73.3%) UC patients and 24 (26.7%) healthy individuals as the control group. The UC patients and the control group were compared in terms of PON-1 and ARE levels as oxidative stress markers. The UC patients were also grouped according to Mayo UC activity scores and the differences in their PON-1 and ARE levels were assessed.

Results: 37 (56.1%) of 66 UC patients included in the study were male and 29 (43.9%) were female. The mean age in the control group was 42.2 ± 12.8 years (age range: 17-66 years). Most of the patients in the ulcerative colitis (UC) group used a combination of oral and rectal mesalamine treatments (20 patients, 33.3%). Most of the patients in the UC group had left-sided colon involvement (30 patients 45.5%). The mean arylesterase (ARE) level in the UC group was 786.32 U/L; the mean ARE level in the control group was 919.56 U/L. The ARE level was higher in the control group than the UC group, and this difference was statistically significant (p = 0.017). The mean paraoxonase-1(PON-1) value in the UC group was 264.14 U/L; the mean PON-1 value in the control group was 316.64 U/L. This difference was not statistically significant (p = 0.33).

When analysed based on gender, there was no difference in PON-1 levels (p = 0.23) and ARE levels (p = 0.98) between males and females in the UC group. When the Hb value was lower (equal and less than 10 mg/dl) and higher (higher than 10 mg/dl), the ARE value was statistically higher in the group with a high Hb value (p = 0.016). When assessed in terms of the Mayo Disease Activity Index (DAI) and Rachmilewitz Colonoocscopic Activity (Group A: ≤6 and 7 ≥ Group B) scores, no statistical difference was found between the ARE and PON-1 values for UC patients in Group A and Group B.

The ARE values of 66 UC patients were found to be negatively correlated with their white blood cell counts (r = -0.29; p = 0.03). In our study, ARE and PON-1 values were positively correlated in the UC group (r = 0.27; p = 0.026). Correlations between ARE and albumin (r = 0.27; p = 0.041) and ferritin (r = -0.302, p = 0.037) were determined based on our data. There were no correlations between PON-1 and hs-CRP (High sensitive C reactive protein), sedimentation, Hb, B12 and ferritin in the UC group. In the linear regression model, the leukocyte levels (p = 0.023) and Mayo UC Scores (p = 0.004) were found to have an effect on the ARE levels. In addition, it was found that in linear regression model the hs- CRP (p = 0.009) levels were found to have an effect on PON-1 levels.

Conclusion: In conclusion, ARE values that denote oxidative capacity were found to be significantly lower in patients with UC than in healthy patients. The efficacy of PON-1, an antioxidative enzyme, in UC patients is unclear. The results of our analyses suggest that there may be a correlation between ARE and PON-1 values in UC patients. Thus, it might be possible to use ARE levels as indicators of oxidative stress in UC patients. There is a need for larger studies to demonstrate the correlation between UC activity and ARE and PON-1 levels. No correlation between PON-1 and ARE levels and the activity of UC patients was detected in our study.

Table 1 ulcerative colitis and control groups in terms of paraoxonase-1, arylerase, high sensitive CRP, hemalogist

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Introduction: Thiopurines (TPs) are commonly used in treatment of Inflammatory Bowel Disease (IBD). For Azathioprine (AZA), optimal dosing is determined by patients’ weight and commonly titrated to achieve target range of 2–2.5mg/kg. Levels of 6-thioguanine nucleotide (6-TGN), an active metabolite breakdown of thiopurines and 6-Methylmercaptopurine (6-MMP), an inactive metabolite, can be measured to check for efficacy and toxicity respectively, but this is not widely available due to cost and accessibility.

White cell count (WCC), lymphocyte count (LC) and mean corpuscular volume (MCV) have emerged as surrogate markers to monitor TP efficacy. Previous studies have suggested WCC < 4x10^9/L and MCV >100fL correlate with 6-TGN level and with reduced risk of disease relapse.

Aims and Methods: The aim of our study is to assess these surrogate parameters in our patients on TPs. 200 IBD patients being treated with AZA were included in this retrospective, observational study. Data were obtained from our IBD database and review of medical notes. Recent WCC, LC and MCV were recorded, along with body weight, AZA dose and concomitant treatment with biologic therapy (mainly anti-TNF agents).

Leucopenia was no significant difference in these measured parameters between the AZA monotherapy group, 4/117 patients (3.4%) had leucopenia and the same number of patients, 3/83 (3.4%) had macrocytosis and only 1 patient (0.9%) had both leucopenia and macrocytosis. In patients on combination therapy, 3/83 (3.6%) had leucopenia and the same number of patients, 3/83 (3.6%) had macrocytosis. None in this group had both leucopenia and macrocytosis (Table T).

Mean AZA dose to body weight in our study population was 1.7mg/kg. The mean LC was 2.86 x10^9/L (0.5 to 8.8) with mean MCV of 91.1 fl (78.4 to 104.3).

Results: There were 108 (54%) females and 92 (46%) males. Of the 200 patients, 144 (72%) were diagnosed with CD, 55 (27.5%) UC and 1 (0.5%) indeterminate colitis. Partial Mayo score for ulcerative colitis (UC) at time of blood testing. Clinical activity of UC patients was remission (n = 12, 38%), mild (n = 11, 34%), and moderate-to-severe (n = 9, 28%), respectively. UC activity was not significantly different (p = 0.120). However, UC activity was significantly correlated with MES (p = 0.031, Spearman coefficient 0.382), and clinical activity was not (p = 0.066, Spearman coefficient 0.329).

Disclosure: Nothing to disclose

References
P0307 INCIDENCE AND NATURAL HISTORY OF INFLAMMATORY BOWEL DISEASE DIAGNOSED IN COLORECTAL CANCER SCREENING

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Introduction: Inflammatory bowel diseases (IBD) are chronic illness with relevant social impact. Since the great part of data are published by tertiary centers, the real burden of IBD could be not completely defined, both in terms of epidemiology and in a description of the data of a subpopulation of patients with IBD, unaware of it and asymptomatic, incidentally diagnosed in a colorectal cancer (CRC) screening program.

Aims and Methods: We have prospectively evaluated a court of people aged 50–75, undergoing screening colonoscopy after a positive faecal immunological (FIT) test, from November 2011 to March 2018. The screening program is still ongoing, and is focused to early diagnosis and prevention of colorectal cancer. Since then, 4490 patient out of 4714 FIT positive have been evaluated with colonoscopy, with a further examination of 21 patients (0.46%). A diagnosis of IBD (7 F, 14 M, mean age 64.6 years, range: 53–76), namely one Crohn’s disease (CD) and 20 ulcerative colitis (UC).

All patients are currently followed in our tertiary center, with a mean follow-up of 22 months. All UC patients are satisfactory treated with mesalazine. The only patient with CD is treated with azathioprine. Up to now, no patient had extra-intestinal manifestations, nor need for surgery.

Conclusion: There is a consistent percentage of persons with IBD that are not known as affected. There is space for improvement in diagnosis and treatment. Further studies are needed to better understand the real incidence of this condition, and the subsequent evolution of the disease in this group of patients.

Disclosure: Nothing to disclose

P0308 THE IMPACT OF TOTAL AND FREE ANTI-DRUG ANTIBODIES ON THE LONG-TERM CLINICAL RESPONSE TO INFliximab THERAPY

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Introduction: When performed, the monitoring of ADA is generally restricted to the detection of free ADA (fADA) at the trough, using drug-sensitive ADA assays. Several studies have described the detection of ADA in complex with the drug (tADA). Free ADA may underestimate the frequency of ADA-positive patients. Drug-tolerant ADA assays allow us to identify an additional proportion of ADA-positive patients. Compared to tADA+/fADA- group, patients with ADA, being more frequent in the tADA+/fADA- group when compared with tADA+/fADA+ (57% vs. 17%).

Conclusion: Drug-tolerant ADA assays allow us to identify an additional proportion of ADA+ patients. Compared to tADA+/fADA-, tADA+ patients had lower IFX levels, lower CR rates and more frequently needed switch or IFX intensification. Responses to IFX intensification were overall more favourable in this group than in the tADA+/fADA+ group. Only a minority of tADA+/ tADA+ patients became tADA+. Larger studies are warranted to confirm these results and determine the clinical benefit of including ADA assessments, to help guide therapeutic decisions, in routine clinical practice.

Disclosure: The present study has been presented as best poster oral presentation at the 16th FAPEG national meeting in Porto Alegre, Brazil.

P0309 CHROMOENDOSCOPY IS SUPERIOR TO WHITE LIGHT ENDOSCOPY FOR THE DETECTION OF ADVANCED COLONIC NEOPLASIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Although recent guidelines recommend chromoendoscopy (CE) as a method of choice for neoplasia surveillance in inflammatory bowel disease (IBD), there is still controversy regarding the utility of this technique in clinical practice.

Aims and Methods: The aims of this study were to compare the accuracy of CE and white light endoscopy (WLE) for the detection of overall neoplasia and advanced neoplasia in patients with IBD. Patients who underwent surveillance colonoscopy were identified from a single institution IBD database from 1999 to 2017. Patients with prior history of colon cancer or total colectomy were excluded. CE procedures were compared with their respective WLE controls in a paired comparison and the frequency of all neoplasia, advanced neoplasia and serrated neoplasia was assessed for both targeted and random biopsies.

Results: Total 315 procedures performed in 106 individuals were identified over a median follow up 3 years (median 3 colonoscopy/patients). Among them, 290 undergoing screening colonoscopy after a positive faecal immunological (FIT) test, from November 2011 to March 2018. The screening program is still ongoing, and is focused to early diagnosis and prevention of colorectal cancer. Since then, 4490 patient out of 4714 FIT positive have been evaluated with colonoscopy, with a further examination of 21 patients (0.46%). A diagnosis of IBD (7 F, 14 M, mean age 64.6 years, range: 53–76), namely one Crohn’s disease (CD) and 20 ulcerative colitis (UC).

All patients are currently followed in our tertiary center, with a mean follow-up of 22 months. All UC patients are satisfactory treated with mesalazine. The only patient with CD is treated with azathioprine. Up to now, no patient had extra-intestinal manifestations, nor need for surgery.

Conclusion: There is a consistent percentage of persons with IBD that are not known as affected. There is space for improvement in diagnosis and treatment. Further studies are needed to better understand the real incidence of this condition, and the subsequent evolution of the disease in this group of patients.

Disclosure: Nothing to disclose

Table 1. Characteristics of neoplastic lesions detected by chromoendoscopy and white light endoscopy

<table>
<thead>
<tr>
<th>Type of Neoplasia</th>
<th>Chromoendoscopy (n = 159)</th>
<th>White light Endoscopy (n = 131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasia per procedure</td>
<td>65 (40.9%)</td>
<td>31 (23.6%)</td>
</tr>
<tr>
<td>Advanced neoplasia per procedure</td>
<td>29 (18.2%)</td>
<td>8 (6.1%)</td>
</tr>
<tr>
<td>Serrated neoplasia per procedure</td>
<td>8 (5.3%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Targeted biopsy (mean ± SD)</td>
<td>213 ± 13 ± 1.2</td>
<td>89 ± 7 ± 1.0</td>
</tr>
<tr>
<td>Neoplasia per targeted biopsy</td>
<td>88</td>
<td>38</td>
</tr>
<tr>
<td>Neoplasia per random biopsy</td>
<td>2143 ± (13.7 ± 9.3)</td>
<td>2630 ± (20.2 ± 10.6)</td>
</tr>
</tbody>
</table>

Neoplasia per procedure | 65 (40.9%) | 31 (23.6%) |
Advanced neoplasia per procedure | 29 (18.2%) | 8 (6.1%) |
Serrated neoplasia per procedure | 8 (5.3%) | 1 (0.8%) |
Targeted biopsy (mean ± SD) | 213 ± 13 ± 1.2 | 89 ± 7 ± 1.0 |
Neoplasia per targeted biopsy | 88 | 38 |
Neoplasia per random biopsy | 2143 ± (13.7 ± 9.3) | 2630 ± (20.2 ± 10.6) |

Disclosure: Nothing to disclose

A230
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A CLEAR LOOK INTO THE BOWEL WITHOUT CLEANING IT - SIMULTANEOUS PET/MRI ENTEROGRAPHY (18F-FDG) FOR MONITORING INFLAMMATORY ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS - A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: The combination of positron emission tomography (PET) with 18F-fluorodeoxyglucose (18F-FDG) with magnetic resonance imaging (MRI) as integrated PET/MR enterography in one examination is a new cutting-edge technology for the non-invasive assessment of the inflammatory activity in ulcerative colitis (UC). Regarding the diagnostic gold standard procedure ileocolonoscopy beside the risk of injury especially the bowel purgation is rated most bothersome.

Aims and Methods: This study’s aim was to evaluate whether the inflammatory activity in patients with UC can be detected and accurately quantified by PET/MRI with and without bowel purgation. Patients were randomized to simultaneous PET/MRI (index test) with or without bowel purgation 24h before ileocolonoscopy (reference standard). In every patient the maximum standardized uptake value ratio gut/liver (SUV Quot), an MRI index and an endoscopy index (EI; rated by 2 independent gastroenterologists) were calculated for every segment (ileum, caecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum). Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. Furthermore, receiver operating characteristic (ROC) curves for each colon segment were calculated to determine diagnostic accuracy of PET/MRI for the 2 modes of bowel purgation.

Results: N = 53 patients were included in the study. Ten patients were included for protocol optimization and 43 were randomized. Three patients were dropouts (two due to activity of disease other than UC, one refused examination). Therefore, 19 patients (mean age = 42.4 years (SD = 13.8 years), 11 female (57.9%), mean time since diagnosis = 13.42 years) were randomized to PET/MRI with bowel purgation and 21 patients (mean age = 43.2 years (SD = 12.7), 14 female (66.7%), mean time since diagnosis 12 years) to PET/MRI without bowel purgation. Sociodemographic and clinical characteristics did not differ between the groups. SUV Quot and EI correlated significantly for patients without bowel purgation (r = 0.46, p = 0.063). Overall sensitivity, specificity, positive predictive value, negative predictive value, and accuracy using ileocolonoscopy as reference standard are shown in table 1. ROC analyses for each bowel segment show that the diagnostic accuracy was better for patients without bowel purgation (AUC rectum = 0.87, p = 0.03; AUC sigmoid colon = 0.91, p < 0.01; AUC ascending colon = 0.86, p < 001; AUC transverse colon = 0.82, p < 0.02; AUC descending colon = 0.77, n.s.; AUC ascending colon = 0.78, n.s.; AUC transverse colon = 0.82, p = 0.02; AUC descending colon = 0.63, n.s.; AUC caecum = 0.74, n.s.) compared to patients with bowel purgation (AUC rectum = 0.69, p = 0.06; AUC sigmoid colon = 0.76, n.s.; AUC descending colon = 0.74, n.s.; AUC transverse colon = 0.82, p = 0.02; AUC descending colon = 0.63, n.s.; AUC caecum = 0.74, n.s.).

Conclusion: The inflammatory activity of UC can be detected and quantified by PET/MRI in patients who did not undergo bowel purgation prior to examination. PET/MRI might serve as a valuable complement for goldstandard ileocolonoscopy to extend the variety of non-invasive diagnostic tools in UC especially when bowel purgation is not applicable.

Disclosure: Forchungsförderung: Steigerwald Arzneimittelwerke GmbH; Falk Foundation; TechLab; Dr. Willmar Schwabe; Repha GmbH biologische Arzneimittel Vortragshonorar: Falk Foundation; MSD Sharp&Dohme GmbH; Repha GmbH biologische Arzneimittel; Ardeypharma GmbH; Celgene GmbH; Dr. Willmar Schwabe Berater/Gutachtertätigkeit: Medizinverlage Stuttgart; Steigerwald Arzneimittelwerke GmbH; Repha GmbH; Ferring Arzneimittel GmbH; Sanofi Forschungsunterstützung Stiftungen Melinda- und Bill Gates Foundation, Karl- und Veronica Carstens-Stiftung, Ruth- und Klaus-Balsbien-Stiftung, Dr. Heinz Horst Deichmann Stiftung, RalfBied-Stiftung

References

FEecal Biomarkers compared to Magnetic Resonance Imaging using the Maria and Clermont Scores for Monitoring Inflammatory activity in Patients with Crohn’s Disease

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Introduction: Magnetic resonance imaging (MRI) with the Magnetic Resonance Index of Activity (MaRIA) and the Clermont score as validated MRI activity indices is the gold standard to diagnose and monitor small bowel Crohn’s disease (CD). However, noninvasive fecal biomarkers like calprotectin (CAL) and lactoferrin (LF) are increasingly popular and used in all-day patient care and have been evaluated regarding their capacity to differentiate and monitor disease activity in inflammatory bowel disease (IBD).

Aims and Methods: This study’s aim was to compare the performance of fecal biomarkers and MRI for monitoring inflammatory activity in patients with CD. Fecal samples were collected to determine LF, CAL, PMN-elastasis (PMN-e), S100 calcium-binding protein A12 (S100A12), and Eosinophil-derived Neurotixin (EDN) by enzyme immunoassay (EIA). In every patient a MRI was performed, MaRIA and the Clermont score were calculated, and standard cut-offs were applied by two independent experienced radiologists. Receiver operating characteristic (ROC) curves for each fecal biomarker using MaRIA and Clermont score as reference standard were calculated to determine sensitivity, specificity, and accuracy using optimized cut-offs.

Results: N = 50 patients with CD (mean age = 43.1 years (SD = 13.42), 32 female (64%), mean time since diagnosis = 13.8 years) were included in the study. According the MaRIA score n = 41 patients and according to the Clermont score n = 40 patients showed signs of active inflammation. Mean levels for patients with active/inactive inflammation were 12.43/1.90(µg/g) in LF, 22.84/6 151.17(µg/g) in EDN, 17.0.09(µg/g) in PMN-e, 64.91/79.99(µg/g) in S100A12 and 4.0.47(µg/g) in EDN. Fecal LF, CAL and EDN were significantly

Abstract No: P0311

MaRIA

<table>
<thead>
<tr>
<th>Group</th>
<th>AUC (p)</th>
<th>Optimized cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDN</td>
<td>76 (n.s.)</td>
<td>–</td>
<td>58.5</td>
<td>1</td>
</tr>
<tr>
<td>LF</td>
<td>83 (0.016)</td>
<td>5.49</td>
<td>58.5</td>
<td>1</td>
</tr>
<tr>
<td>PMN-e</td>
<td>70 (n.s.)</td>
<td>–</td>
<td>58.5</td>
<td>1</td>
</tr>
<tr>
<td>S100A12</td>
<td>43 (n.s.)</td>
<td>–</td>
<td>58.5</td>
<td>1</td>
</tr>
<tr>
<td>CAL</td>
<td>71 (n.s.)</td>
<td>–</td>
<td>58.5</td>
<td>1</td>
</tr>
</tbody>
</table>

Clermont

<table>
<thead>
<tr>
<th>Group</th>
<th>AUC (p)</th>
<th>Optimized cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDN</td>
<td>81 (0.043)</td>
<td>27</td>
<td>78.6</td>
<td>75</td>
</tr>
<tr>
<td>LF</td>
<td>82 (0.035)</td>
<td>5.49</td>
<td>59.5</td>
<td>1</td>
</tr>
<tr>
<td>PMN-e</td>
<td>71 (n.s.)</td>
<td>–</td>
<td>59.5</td>
<td>1</td>
</tr>
<tr>
<td>S100A12</td>
<td>53 (n.s.)</td>
<td>–</td>
<td>59.5</td>
<td>1</td>
</tr>
<tr>
<td>CAL</td>
<td>86 (0.017)</td>
<td>195.04</td>
<td>79.4</td>
<td>1</td>
</tr>
</tbody>
</table>
correlated to the Clermont score, however, only LF was correlated to the MaRIA score. Use of cut-offs, EDN, LF, and CAL were able to distinguish between active and inactive CD (see Table 1).

Table 1. Testing sensitivity, specificity, and accuracy using optimized cut-offs for MaRIA and Clermont score as reference standard

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>LF</td>
<td>92.3%</td>
<td>90.7%</td>
<td>91.6%</td>
</tr>
<tr>
<td>EDN</td>
<td>89.9%</td>
<td>91.6%</td>
<td>91.1%</td>
</tr>
<tr>
<td>CAL</td>
<td>86.7%</td>
<td>91.6%</td>
<td>91.1%</td>
</tr>
</tbody>
</table>

Conclusion: These results support the utility of fecal biomarkers for detecting active inflammation in patients with CD.

Disclosure: Forschungsunterstützung: Steigerwald Arzneimittelwerke GmbH, Falk Foundation; TechLab, Dr. Willmar Schwabe; Repha GmbH biologische Arzneimittel; Falk Foundation; Ferring Arzneimittel GmbH; MSD Sharp&Doyme GmbH; Repha GmbH biologische Arzneimittel; Ardeypharma GmbH; Cegene GmbH; Dr. Willmar Schwabe Berater/Gutachterfähigkeit: Medizinverlag Stuttgart; Steigerwald Arzneimittelwerke GmbH; Repha GmbH; Ferring Arzneimittel GmbH; Sanofi; ForschungsFörderung Stiftungen Melinda- und Bill Gates Foundation, Karl- und Veronica Carstens-Stiftung, Ruth- und Klaus-Bahlsen-Stiftung, Dr. Heinz Horst Deichmann Stiftung, Raiffeiden-Stiftung

References

P0312 ENDOSCOPIC FOLLOW-UP ALLOWS GOOD CONTROL OF COLORECTAL CANCER INCIDENCE IN IBD PATIENTS WITH LOW AND HIGH-LEVEL DDYSPLASIA: A FRENCH MULTI-CENTRE PROSPECTIVE COHORT

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Introduction: Patients with inflammatory bowel disease (IBD) are at high risk of colorectal cancer (CRC). Today American and European guidelines recommend surveillance with endoscopy rather than colonoscopy after complete resection of endoscopically resectable dysplastic lesions using chromoendoscopy. 1,2 However very few prospective data exist to evaluate the application of these recommendations and patient outcome. Moreover, the endoscopic techniques that should be used for lesion excision is not well defined.

Aims and Methods: Describe within a multi-centre prospective cohort the management and follow-up of dysplasia in IBD patients.

Results: In November 2017, 60 patients were included among 14 centers. 43 patients had UC (71.7%), and 17 patients had CD (28.3%). The median follow-up time from the first diagnosis of dysplasia was of 10 years. The median follow-up time with prospective evaluation was of 9.9 years. 25 patients were initially diagnosed with an adenomatous lesion with low-grade dysplasia (LGD; 86.7%), 6 with an adenomatous lesion with high-grade dysplasia (HGD; 0.1%) and 1 CD patient had a serrated poly with low-grade dysplasia.

Conclusion: From September 2013 to November 2017, 60 patients were included procedure and histological results were assessed all along the study.

Disclosure: None

References

P0313 QUESTIONING CONSENSUS IN CROHN'S DISEASE: CT AND MR PERIANAL EXTENSION HAS MINIMAL DIAGNOSTIC YIELD AND INCURS ADDITIONAL RADIATION EXPOSURE

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Introduction: To assess the relevance of including perianal region in routine CT/ MR enterography for detection of perianal dysplasia in Crohn’s disease (CD), according to recent consensus recommendations.

Aims and Methods: Identification of patients undergoing enterography. Selection of examinations performed with perianal extension in patients with CD.

Results: A retrospective classification with identification of perianal disease. Evaluation of enterographies for signs of perianal disease, blinded to Montreal classification. Statistics: Kappa concordance test (p ≤ 0.05). Radiation increase estimation due to perianal extension, in a Siemens Somaton® 16 CT equipment with filtered back projection (FBP) reconstruction.

Conclusion: The extension of enterography to the perianal region has not shown to be superior to clinical evaluation for detection of perianal disease in CD. The consensus rather than colorectal MR enterography may be prudent only for MR enterography, since CT enterography incurs a non-negligible added radiation and exposure of radiosensitive organs, that otherwise would not be covered.

Disclosure: Nothing to disclose

References

P0314 PHOTOPROTECTIVE IBD EDUCATIONAL VIDEO ANIMATION (“TAGG SUNCARE VIDEO”) IS PREFERRED BY PATIENTS AND IS AN EFFECTIVE WAY OF IMPROVING PATIENT KNOWLEDGE AND AWARENESS

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Introduction: Inflammatory Bowel Disease (IBD) patients are at risk of Malignant Melanoma (MM) and non-melanoma skin cancer (NMSC). Simple photo protective measures and early detection through increased vigilance can reduce the incidence and the burden of disease. Traditional educational methods have had limited impact and newer validated educational tools are needed.

Aims and Methods: To assess the impact and validate a novel IBD educational video animation on skin cancer awareness in a cohort of Irish IBD subjects.

Results: A prospective non-randomised interventional study using our novel, recently trialled IBD tailored educational animation video based on the Irish Cancer Society ‘Sunsmart Guidelines’. Self assessment questionnaires were employed to collect patient demographics and assess sun smart behaviours. The test was at 2 sequential IBD clinics, one where the video was played in the outpatient waiting area (exposed group) and another without any video (control group). The questionnaire included sections on what factor sunseeker to wear and how often to re-apply it, when to stay in the shade, and how to perform a self skin check including what suspicious changes to look for in a suspicious mole. Results were compared among groups using a Chi Squared test (p ≤ 0.05 was considered significant) and an odds ratio (OR) calculated where appropriate.
PO315 IBD PATIENTS ARE FOUR TIMES MORE LIKELY TO DEVELOP ALL TYPES OF SKIN CANCER POSSIBLY RELATED TO HIGH RATES OF IMMunosUPPRESSION; WITH YOUNG IBD PATIENTS PARTICULARLY AT RISK OF SKIN CANCER

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Introduction: Increased rates of non-melanoma skin cancer (NMSC) is a recognised complication of immunosuppression therapy for inflammatory bowel disease (IBD), while little is known of malignant melanoma (MM) risk. New therapies, including biologics, their early age of introduction and longer duration may increase skin cancer risk.

Aims and Methods: To compare the incidence of both NMSC and MM in an Irish IBD cohort compared to controls. Retrospective single centre case-control study from 2012-2017. Known IBD patients and age and sex matched controls were identified from an IBD and polyp database respectively. Both cohorts were cross-referenced with our hospital’s pathology database for NMSC and MM. Patients otherwise at risk of skin cancer including transplant recipients or other indications for long-term immunosuppression and skin cancer genetic syndromes were excluded following review of patient electronic records.

The rates of NMSC and MM were compared among groups using a Chi-squared test (p < 0.05 was considered significant), and the impact of age, gender and immunosuppression use was evaluated using a logistic regression model. Rates of NMSC and MM were compared during groups using a Chi-squared test (p < 0.05 was considered significant), and the impact of age, gender and immunosuppression use was evaluated using a logistic regression model. Rates of NMSC and MM were compared during groups using a Chi-squared test (p < 0.05 was considered significant), and the impact of age, gender and immunosuppression use was evaluated using a logistic regression model.

Results: In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified. In all, 931 IBD and 1090 age and sex matched controls were identified.

Conclusion: Serum hepcidin is a very important novel marker in patients with iron deficiency anemia (IDA), and it should be used in IBD patients considering difficulties in establishing IDA diagnosis due to inflammation.

Disclosure: Nothing to disclose

PO316 HEPcidin LEVELS IN DIAGNosing DIRection ANEMIA IN IBD PATIENTS

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Introduction: Iron metabolism is regulated by hepcidin, polypeptide synthesized primarily by hepatocytes. Hepcidin synthesis may be altered due to hypoxia, inflammation, erythropoiesis and other multiple factors that have an influence on total iron body storage.

Aims and Methods: Our aim was to determine serum hepcidin levels in patients inflammatory bowel disease (IBD) as well to investigate whether there is correlation of hepcidin levels with disease activity.

In a retrospective study was performed on 30 newly diagnosed IBD patients (18 UC, 12 CD) and the same number age, sex-matched healthy controls. All patients underwent a total colonoscopy with ileoscopy. Complete blood count was obtained in addition to inflammatory markers (CRP, erythocyte sedimentation rate) and serum levels of hepcidin were determined with commercially available enzyme-linked immunosorbent assay (DRG Instruments, Marburg, Germany). Serum iron, TIBC, UIBC were assessed with an electrochemiluminescence immunomessay and sTfR was assessed using an immunoturbidimetric method. Mayo score and CDAI respectively were calculated respectively for IBD and control patients. Statistical analyses were performed using SPSS software version 20.0 for Windows.

Results: There was high statistically significant difference between IBD patients and controls in levels of hepcidin (p < 0.01). Serum hepcidin levels were significantly higher in control group (9.77 ± 2.71 vs. 6.40 ± 2.42 ng/ml, p = 0.000). Serum ferritin (394 ± 5.15 vs. 119 ± 124 ng/ml, p = 0.000) as well as serum ferritin ratios were significantly higher in control group. There was no statistically significant correlation of serum hepcidin with CRP, Mayo score or CDAI respectively (p > 0.05). However we have found statistically significant negative correlation of sTfR, TIBC with hepcidin (p < 0.01). Combined Serum hepcidin is a very important novel marker in patients with iron deficiency anemia (IDA), and it should be used in IBD patients considering difficulties in establishing IDA diagnosis due to inflammation.

Disclosure: Nothing to disclose

PO317 MONITORING HISTOLoGICAL ACTIVITY IN ULCERATIVE COLITIS - CORRELATION OF FECal BIOMARKERS WITH THE RILEY SCORE AND THE NANCY INDEX

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3TechLab, Research and Development, Blackburg, United States

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Introduction: Histological healing in ulcerative colitis (UC) may be a better predictor than macroscopic appearance or clinical criteria for time to relapse. Histological assessment revealed that indicators of acute mucosal inflammation, including crypt abscesses, mucin depletion or an acute inflammatory cell infiltrate which are used in the Riley Score or the Nancy index were associated with a 2- to 3-fold increase in the risk of UC relapse during 12 months’ follow-up. Histological assessment that requires invasive endoscopy and gaining of biopsy. Non-invasive surrogates of mucosal healing like fecal biomarkers would help to lower risks, costs and might increase patient acceptance.

Aims and Methods: The study aimed to investigate the performance of non-invasive fecal biomarkers compared to the Riley Score and the Nancy index in patients with UC. Colonooscopy was performed in every patient and a fecal sample was collected during 72 hours. Three biopsies were taken from the macroscopically most inflamed region or random biopsies of the colonic segment and the Riley Score and Nancy index were calculated. For each patient the highest calculated score was compared to the fecal biomarkers lactoferrin (LF), calprotectin (CALPREST - CalPi), PMN elastase (PMN-E), S100 calcium-binding protein A12 (S100A12) and Esinophil-derived Neurotoxin (EDN). In addition, a Kruskal-Wallis test was performed to evaluate if the median levels of the fecal markers differ significantly between the grades 0-4 of the Nancy index.

Results: 50 patients (32 female), mean age 42.9 ± 12.3 years (range 23-67) with diagnosed UC were included in the study. The Riley Score and the Nancy index were correlated significantly with EDN (r (49) = 0.561; p = 0.001) and LF (r (49) = 0.455; p = 0.000), S100A12 (r (49) = 0.327; p = 0.022) and S100A12 (r (49) = 0.346; p = 0.015), PMN-e (r (49) = 0.314; p = 0.028) and LF (r (49) = 0.452; p = 0.001), S100A12 (r (49) = 0.345; p = 0.015), but not with CalPi (p > 0.05). The median levels of the fecal markers correlating with the grades 0-4 of the Nancy index and the results of the Kruskal-Wallis test is presented in table 1. Only LF, EDN and S100A12 differed significantly between the grades. Subsequent post-hoc tests showed that LF differed significantly between the grades 2 and 3 (z = -3.125, p = 0.001), EDN between the grades 2 and 4 (z = -3.006, p = 0.016) and S100A12 between the grades 2 and 3 (z = -3.986, p = 0.000) and 2 and 4 (z = -3.067, p = 0.013).

Conclusion: The fecal biomarkers LF, EDN, S100A12 and PMN-e were correlated significantly with the Riley and Nancy index, LF, EDN and S100A12 differed significantly between the grades of the Nancy index. The results support the utility of fecal biomarkers for detecting active histologic inflammation in patients with ulcerative colitis.

Disclosure: Nothing to disclose

[Table 1. Median levels (range) of the fecal markers PMN-e, LF, EDN, CalPi and S100A12]
Abstract No: P0317

Five grades of the Nancy histological index

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<th>2</th>
<th>3</th>
<th>4</th>
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<td>0/1 (n=2)</td>
<td>0.075 (0.06-0.09)</td>
<td>0.06 (0.03-0.54)</td>
<td>0.27 (0.04-0.10.28)</td>
<td>0.21 (0.05-0.45)</td>
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<td>2/9 (n=9)</td>
<td>1.21 (0.10-2.21)</td>
<td>2.32 (0.38-47.67)</td>
<td>51.90 (1.47-462.82)</td>
<td>32.97 (1.91-465.72)</td>
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<tr>
<td>3/19 (n=19)</td>
<td>0.97 (0.31-1.63)</td>
<td>0.47 (0.09-4.69)</td>
<td>1.74 (0.14-5.28)</td>
<td>3.18 (0.47-6.32)</td>
<td>0.016</td>
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<tr>
<td>S100A12 (mg/g)</td>
<td>246.29 (101.07-391.50)</td>
<td>430.10 (86.51-727.01)</td>
<td>712.81 (197.93-551.45)</td>
<td>389.10 (251.63-745.31)</td>
<td>0.076</td>
</tr>
</tbody>
</table>

PNM-e = Polymorphonuclear elastase, LF = Lactoferrin, EDN = Eosinophil-derived Neutrophin, CalP = Calprotectin, S100A12 = S100 calcium-binding protein A12.


References

P0318 AZATHIOPRINE METABOLITE (6-TGN) LEVELS WITHIN A DEFINED THERAPEUTIC RANGE ARE ASSOCIATED WITH LOWER FECAL CALPROTECTIN IN CROHN’S DISEASE - A RETROSPECTIVE ANALYSIS

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Introduction: Azathioprine/6-mercaptopurine (AZA/6-MP) are first-line immunosuppressants for the treatment of Crohn’s disease. While recent meta-analyses have reported a positive association of their active metabolite 6-thioguanine (6-TGN) with clinical outcomes, 6-TGN levels have not been correlated with surrogate markers of mucosal healing, which is an increasingly recognised therapeutic goal.

Aims and Methods: We therefore investigated whether 6-TGN levels are inversely associated with fecal calprotectin (FC) in Crohn’s disease patients on azathioprine monotherapy. 6-TGN and FC levels of 96 Crohn’s disease patients on AZA/6-MP monotherapy visiting the IBD outpatient clinic between 2009 and 2016 were retrospectively analysed. In a small sub-cohort with serial 6-TGN measurements, longitudinal FC measurements were assessed.

Results: In patients with 6-TGN levels within a defined range (250-450 pmol/8 x 10^9 RBCs), FC levels were significantly lower (median FC 149 vs. 346 mg/kg, p = 0.007), and hemoglobin concentrations as well as transferrin saturation levels were significantly higher than in patients with lower or higher metabolites. CRP and protein levels were not different. In the small cohort that was followed longitudinally, all patients achieved an increase in 6-TGN levels upon dose escalation, and fecal calprotectin levels decreased in 54%.

Conclusion: In our retrospective analysis on Crohn’s disease patients receiving AZA/6-MP monotherapy, 6-TGN levels within a defined range (250-450 pmol/8 x 10^9 red blood cells) were associated with significantly lower fecal calprotectin levels. A treat-to-target concept directed by 6-TGN levels to reach mucosal healing appears promising, but requires prospective studies (DRKS00013246).

Disclosure: Dr. Bachmann reports grants and personal fees from Takeda Pharma, personal fees from Shield Therapeutics, Grants and personal fees from Ferring Pharmaceuticals, grants and personal fees from Pfizer, personal fees from CED Service GmbH, grants and personal fees from Novartis AG, personal fees and other from German Society for Digestive and Metabolic Diseases, grants and personal fees from Janssen Pharmaceuticals, grants and personal fees from Merck Sharp & Dohme, grants from German Center for Infection Research, grants and personal fees from Biogen, grants and personal fees from AbbVie, personal fees from Astellas Pharma, grants and personal fees from Falk Pharma GmbH, grants and personal fees from Bristol-Myers Squibb, personal fees from Immunodiagnostik, outside the submitted work.

P0319 DEVELOPMENT AND VALIDATION OF A SIMPLIFIED MAGNETIC RESONANCE INDEX OF ACTIVITY (SMARIA) FOR CROHN’S DISEASE

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Introduction: The MaRIA index is the best-characterized Magnetic Resonance Enterography (MRE) index for the assessment of luminal Crohn’s disease (CD) activity. However, a number of limitations had been recognized.

Aims and Methods: The aim of this study was to develop and to validate a simplified and accurate Magnetic Resonance Index of Activity (sMaRIA) for assessing disease activity and therapeutic response of luminal CD. MRE data from 98 patients, including active and inactive segments (colon and terminal ileum), from 2 prospective studies were re-analyzed to develop the sMaRIA using endoscopy (CDEIS) as gold standard. Further analysis of responsiveness and reliability, in an independent cohort of 37 patients who underwent MRE and endoscopy before and after a therapeutic intervention was performed. Comparison of the diagnostic performance between the original MaRIA and sMaRIA for detecting active/severe lesions was performed.

Results: Logistic regression analysis showed that wall thickness > 3 mm, presence of mural edema, ulcers and perienteric fat stranding were independent predictors of disease activity and were used therefore as descriptors of sMaRIA. The sensitivity and specificity of sMaRIA at segment level for detecting active disease using a cutoff point ≥1 were 90% and 81% (AUC 0.91, 95% CI 0.88-0.94), and for detecting severe lesions (ulcers) using a cutoff point ≥2 were 85% and 92% (AUC 0.94, 95% CI 0.91-0.96), respectively. Correlation between sMaRIA and CDEIS/MaRIA was excellent (r = 0.82 and r = 0.91, respectively; p < 0.001). There were no differences with regard to diagnostic performance between the sMaRIA and the original MaRIA for detecting active (p = 0.7) and severe disease (p = 0.5). The sMaRIA accurately detected changes in lesion severity in response to a therapeutic intervention and was as reliable as endoscopy for the assessment of mucosal healing.

Conclusion: Simplified MaRIA index allows a faster and easier assessment of inflammation in CD by keeping high accuracy for both diagnosis and therapeutic response. Main advantages over MaRIA include a less time-consuming calculation and that it is not confounded by missing segments.

Disclosure: Nothing to disclose.
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Introduction: The ulcerative colitis endoscopic index of severity (UCEIS) is a novel, validated instrument to evaluate endoscopic disease activity in ulcerative colitis (UC). Recent studies have demonstrated that the UCEIS outperforms the more widely used Mayo endoscopic score (MES) in predicting long-term prognosis (2,3), including the need for colectomy (4). It also has precise item definitions and is likely to be more responsive than the MES score by virtue of its greater number of stratifications (scores range between 0-8, as opposed to 0-3). However, despite these potential benefits many gastroenterologists still prefer to use MES, because its operating characteristics are better defined and its grades are more readily applicable to clinical decision making: a MES ≥ 2 is generally accepted as the cut-off for treatment escalation (5). The equivalent for the UCEIS cut-off is not yet defined, which limits its clinical utility.

Aims and Methods: Our aims were to determine a UCEIS threshold most closely associated with the need for treatment escalation as well as to perform a validation exercise using clinical, biochemical and histological measures of disease activity. Colonoscopies and sigmoidoscopies performed in UC patients between Nov 2016-Jan 2018 at Guy’s and St Thomas’ Hospital were retrospectively reviewed. Detailed demographic, UC phenotype and medication, Simple Clinical Colitis Activity Index (SCCAI), UCEIS, MES, CRP and Nancy Histological Index (NHI) were collected as well as treatment alteration decisions based on endoscopic findings.

The measure of agreement between the UCEIS and the Mayo score was examined using Kappa (κ) statistics. A UCEIS cut-off for the perceived need for treatment escalation was calculated using a Chi square test, receiver operating characteristic (ROC) curve and area under the curve (AUC) analyses. Pearson correlation coefficient was used to compare the linear relationship between the UCEIS and SCCAI, CRP and NHI.

Results: 363 endoscopic procedures were carried out in 295 patients during the data collection period. 201 of the 363 procedures (56%) documented both the UCEIS and MES. These scores demonstrated a substantial agreement between the indices (κ = 0.713, p < 0.001).

Overall, treatment escalation was considered necessary following 199 (56%) procedures, but was not in the remaining 156 (44%). ROC analysis of the perceived need for treatment escalation showed the highest sensitivity and specificity (0.80 and 0.93, respectively) for UCEIS ≥ 4 with an AUC of 0.93. Of 170 patients with a UCEIS ≥ 4, treatment escalation was considered necessary for 159 (94%), but not for 11 (6%). Of 185 patients with a UCEIS ≥ 3, treatment escalation was considered necessary in 40 (22%), cases but was not in 145 (78%) cases (p < 0.001).

UCEIS values demonstrated moderate correlation with SCCAI (0.671, p < 0.001) scores and strong correlation with NHI values (0.723, p < 0.001), but only weak correlation with CRP measurements (0.279, p < 0.001).

Conclusion: Our data demonstrate that a UCEIS score ≥ 4 was significantly associated with the perceived need for treatment escalation. This cut-off could/should therefore be used to support clinical decision-making based on endoscopic findings. Our results also showed that UCEIS has strong correlation with histological disease activity, moderate correlation with a clinical activity index, but only weak correlation with CRP.

Disclosure: Nothing to disclose

References
P0232 - EVALUATION OF CROHN'S DISEASE BY USING A NOVEL CAPSULE ENDOSCOPY SCORING METHOD: CROHN'S DISEASE ACTIVITY IN CAPSULE ENDOSCOPY (CDACE)

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Introduction: Small bowel capsule endoscopy (SBCE) for Crohn's disease (CD) with small bowel lesions is a low-invasive method that enables visualization of the small bowel mucosa. Two scoring methods are used to evaluate the images obtained: the Lewis score (LS) and the capsule endoscopy Crohn's disease activity index (CDACE). However, CDACE shows varied pathology, including inflammation and stenosis; it is difficult to assess the disease state, including the range of lesions, and presence/absence of stenosis solely on the basis of the sum scores obtained by either one of the scoring methods.

Aims and Methods: To develop and evaluate a novel scoring method with which pathology can readily be assessed from sum scores by using SBCE data of CD patients with small bowel lesions. The subjects included 93 CD patients with small bowel lesions who underwent SBCE between June 2010 and May 2017. SBCE was carried out a total of 162 times in these patients, including 104 times in men, 49 times for small bowel CD, and 113 times for small-and-large bowel CD. The novel scoring method was established as Crohn's disease activity in capsule endoscopy (CDACE), and its correlations with the scoring methods in current use, LS and CECDAI, and also with the clinical disease activity index (CDAI) and biomarkers, were analyzed. In CDACE, the small bowel was divided into four zones according to Rapid software analysis, and for each zone, the inflammation score was scored on a scale of 0 to 4, giving a total score of 0 to 16 (inflammation present), inflammation score was scored on a scale of 0 to 4 (score of CDAI: C). CDACE was calculated as the sum of A x 100 + B x 10 + C.

Results: The correlations between CDACE and the existing scoring methods were as follows: CDACE and the LS: r = 0.44 (p < 0.0001) and CDACE and the CECDAI: r = 0.83 (p < 0.0001). Thus, the correlation with the CECDAI was high. Therefore, CDACE, the LS and CECDAI, showed a high degree of correlation between each of the CDAI and biomarkers were as follows: CDAI: r = 0.39 (p < 0.0001), r = 0.19 (p = 0.0119), and r = 0.37 (p < 0.0001) and C-reactive protein (CRP): r = 0.23 (p = 0.0027), r = 0.05 (p = 0.5201), and r = 0.24 (p = 0.0018). Therefore, CDACE and the CECDAI showed approximately the same correlations with the CDAI and CRP.

Conclusion: With CDACE, it is possible to interpret the inflammation morphology (the second third fourth digit) and the severity and presence/absence of stenosis (the first digit) in the small bowel on the basis of the sum scores obtained. In addition, the correlation with the CECDAI has been clearly demonstrated. Therefore, CDACE represents a novel, useful scoring method in clinical practice for patients who underwent SBCE for CD with small bowel lesions.

Disclosure: Nothing to disclose.

P0234 - LONG-TERM OBSERVATION REGISTRY -CEDUR - IN GERMAN IBD PATIENTS

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Introduction: Inflammatory bowel disease (IBD) is diagnosed in approximately 35000 patients in Germany with increasing incidence and prevalence. Although on-going inflammation can result in irreversible damage to the GI tract, under-treatment and reluctance to use immunomodulatory therapies earlier in the course of disease are present. On the other hand, costs for therapies, surgeries and hospitalization are high, once damage has occurred. In 2015 we therefore implemented an independent national IBD registry (CEDUR) to methodically collect real-life data of IBD patients with regard to the usefulness and comparability of immunomodulatory strategies.

Aims and Methodic CEDUR is a web-based, descriptive registry of large tertiary IBD centers throughout Germany, using time sparing documentation in an adapted medical charts-software via GDT interface. Patients with IBD who are willing to participate have visits every 3 months at their clinic and are later-on completed and controlled by their physicians. Since 2015 and for at least 10 years, data on phenotypes, therapeutic effects including efficacy, safety and economy as well as as hospitalizations, surgeries, comorbidities, day-off work, costs for therapies, hospitalization are high, once damage has occurred. In 2015 we therefore implemented an independent national IBD registry (CEDUR) to methodically collect real-life data of IBD patients with regard to the usefulness and comparability of immunomodulatory strategies.

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Conclusion: Real-world data on the use of DiBiCo6® demonstrate that this multi-
genome analysis test is a useful diagnostic tool and can support physicians to diagnose IBD in patients with equivocal CD from UC.

P0329 THE ASSOCIATION BETWEEN DISEASE ACTIVITY AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH MODERATE-TO-SEVERE ULCERATIVE COLITIS IN EUROPE

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Introduction: Patients with ulcerative colitis (UC) experience periods of recurring and episodic clinical signs and symptoms. This study sought to establish the association between disease activity and health-related quality of life and other patient-reported outcomes.

Aims and Methods: Data from the 2015 and 2017 Adelphi Inflammatory Bowel Disease Specific Programmes (IBD-DSP) were used. The IBD-DSP is a database of patient chart information abstracted by selected gastroenterologists across the European Union Five [EU5]: i.e., Germany, Italy, Spain, and the United Kingdom [UK]. Eligible gastroenterologists who agreed to participate were asked to complete patient record forms for their next 7 consecutive eligible adult patients with UC. Using available chart information (including endoscopy results based on Mayo scoring), physicians classified their patients into 1 of the following categories: remission with an endoscopic score of ≤1, minimal disease (MD), and moderate to severe disease (M-TSD). Those who had used either an immunomodulator [IM] or a biologic were excluded. Differences among disease activity categories with respect to patient-reported outcomes were analyzed using generalized linear models, controlling for demographic (age, sex, and country) and clinical factors (body mass index, smoking history, years diagnosed, and a Charlson comorbidity index) as confounders.

Results: A total of N = 1037 patient charts with linked surveys were included (France: N = 347; Germany: N = 379; Italy: N = 55; Spain: N = 171; UK: N = 85; 55.6% male, mean age = 39.2 SD = 13.8). Patients had been diagnosed for a mean of 5.3 years (SD = 5.9). 33.6% had active disease, 53.0% were in remission, and 13.3% were in deep remission. Patients with active disease reported significantly lower levels of EQ-5D health state utilities (Adjusted Mean (AdjM) = 0.78) compared with remission (AdjM = 0.91) and deep remission (AdjM = 0.91) (both p < 0.05).

Conclusion: Among patients with moderate-to-severe UC in EU5, active disease was associated with significant impairments in health-related quality of life and impairments in work and leisure activities.

Disclosure: A Armuzzi has received research support from MSD, lecture fees from AbbVie, AstraZeneca, Chiesi, Ferring, Hospira, MSD, Mundipharma, Nikkiso, Otsuka, Pfizer Inc, Takeda, TiGenix, Zambon, and consultancy fees from AbbVie, Allergan, Biogen Idec, Celltrion, Eli Lilly, Ferring, Hospira, Janssen, MSD, Mundipharma, Pfizer Inc, Samsung Bioepis, Sofar, Takeda; M Tarallo, M DiBonaventura, D Bargó, L Sales, J Cappellari, G Gigante are employees and shareholders of Pfizer Inc; J Lucas, D Bluff and H Hoskin are employees of Adelphi Real World.

P0300 A PILOT [11C]PBR28 TSPO PET IMAGING STUDY TO EVALUATE INFLAMMATION IN CROHN’s DISEASE

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Introduction: Crohn’s Disease (CD) features segmental inflammation, which can affect any part of the gastrointestinal tract, with lesions extending across all tissue layers. Although endoscopy and histology can be used to monitor mucosal disease, in vivo assessment of progression and regression of transmural lesions, especially in the small bowel remains challenging. The 18 kDa translocator protein (TSPO), located on the mitochondrial outer membrane, is overexpressed in activated macrophages, and has been used as a marker of inflammation. PET imaging with TSPO selective radioligands allows for the noninvasive assessment of Crohn’s Disease inflammation, and has been used extensively in both brain and peripheral inflammatory diseases.

Aims and Methods: Here we aim to evaluate the utility of TSPO PET, using radioligand [11C]PBR28, for assessing the inflammation in the gastrointestinal tract in subjects with CD compared to healthy subjects. Subjects were recruited by Hammersmith Medicines Research. For subjects with CD, inclusion criteria included CD confirmed by endoscopy, and then being naïve to biologics. 4 CD patients (2 males and 2 females) and 5 healthy volunteers (3 males and 2 females) have been recruited to date and undergone 2 dynamic [11C]PBR28 PET-CT scans; baseline and 2 hours post a 90 mg oral dose of XB173 on the same day. XB173 is a TSPO selective compound and is thereby used to confirm the specificity of the signal in this particular application. Patient Crohn’s Disease Activity Index (CDAI), C-reactive protein (CRP), Faecal Calprotectin (FC) as well as TSPO m6971 genotype (a common polymorphism in the TSPO gene which affects ligand binding properties) were measured at screening. Regions of interest (ROIs) were manually delineated on the terminal ileum, small bowel, descending colon, sigmoid colon, and skeletal muscle in each subject based on PET and CT co-registered images. The mean and max standard uptake values (SUVs, radioactivity concentration normalized by total injected activity and body weight) were estimated in these ROIs.

Results: The CDAI of the CD patients ranges from 116 to 172, with CRP ranges from 0.2 to 3.8 mg/L, and FC from 49 to 510 mg/kg. Among the 4 CD patients, 3 are high affinity binders (HABs) and 1 is a mixed affinity binder (MAB). There are 2 HABs and 3 MABs in the control group. Compared to healthy controls, CD patients showed a trend of higher heterogeneous ligand uptake in the GI tract, especially in the small bowel. The mean SUVs in different ROIs are listed in the table below.

Conclusion: Preliminary data suggest that the observed PET signal in the small bowel of CD patients can be attributed to TSPO, and by inference inflammatory activity. Should these results to be confirmed, TSPO PET may allow the identification of inflammatory foci in the GI tract of Crohn’s patients even with mild disease activities, providing a non-invasive method to assess and quantify inflammatory activity not captured by endoscopy. Recruitment into this pilot study continues.

Disclosure: Qi Guo, Just Genius, Yanping Luo, and Robert Comley are employees of AbbVie. Gaia Rizzo, Eugenii Rabiner and Azeem Saleem are employees of Invicro. Masli Walther and Matilde Luce are employees of Hammersmith Medicines Research.


P0331 DEPENDENCE OF THE LEVEL OF INFLAMMATION MARKERS ON THE PRESENCE OF CLOSTRIDIAL INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: In patients with inflammatory bowel disease (IBD), there was a more frequent development of clostridial infection (CI) and much higher morbidity and mortality rates compared with patients without IBD. Immunosuppressive therapy is a risk factor.

Aims and Methods: We aimed to determine the frequency of clostridial infection (CI) in patients with inflammatory bowel disease undergoing treatment in the Department of treatment of IBD Moscow Clinical Research Center. Of the 1224 patients with IBD, 764 were found to have toxins A and B in feces by enzyme immunoassay. Comparative analysis...
between the groups was performed by the method of 4-field tables using non-parametric testing.

**Results:** CI was found in 132 (17.3%) patients of IBD, patients without CI - 632 (82.7%). Among IBD patients with CI men - 61 (46.2%), without CI men - 313 (49.5%). Extraintestinal manifestations were present in 31 (28%) patients with IBD with CI, in 174 (27.5%) - without CI (p = 0.05). The mean albumin level in patients with CI was 28.4±2.8 g/l, in the group without CI - 35.6±3.7 g/l (p = 0.012836). The mean level of CRP among patients with CI was 65.9±4.8 mg/l, in the group without CI - 37.8±3.7 mg/l (p = 0.000004). The mean level of ESR was 45.5±6.5 mm/h, in the group without CI - 19.4±3.3 mm/h (p = 0.000991). The mean level of fecal calprotectin among patients with CI was 1680±120 mg/g, in the group without CI - 480±195 mg/g (p = 0.00000).

**Conclusion:** The activity of the inflammatory process is higher in patients with inflammation associated with associated clostridial infection.

**Disclosure:** Nothing to disclose.

**P3032 MICROBIOTA PROFILE AND DYSBIOSIS ASSESSMENT IN CLINICAL PRACTICE: A PILOT STUDY ON IBD PATIENTS**

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**Introduction:** A growing body of evidence suggests that dysbiosis plays a key role in the pathogenesis of inflammatory bowel disease (IBD). However, due to intrinsic limitations in current diagnostic methods and lack of agreement on the appropriate test to use, in clinical practice the characterization of dysbiosis in IBD patients remains challenging.

**Aims and Methods:** We compared a commercially available dysbiosis test and a stool standard analysis test to profile the microbiota at phylum level in IBD patients and healthy control subjects. Human fecal samples from 13 IBD patients and 4 healthy control subjects were examined by the GA-map™ Dysbiosis Test (Oslo, Norway) and Illumina MiSeq test by BMR-genomics (Padova, Italy). GA-Map is a 16S rRNA test that utilize 54 DNA probes based on 7 variable regions (V3-V9) and recognizing gut bacteria profiles for identification and characterization of dysbiosis. The BMR-genomic test applies the universal primer based on the V3-V4 hypervariable region of 16S rRNA using an Illumina MiSeq next-generation sequencer. The correlation between variation of microbiota expressed as the Dysbiosis Index region of 16S rRNA using an Illumina MiSeq next-generation sequencer. The BMR-genomic test applies the universal primer based on the V3-V4 hypervariable region of 16S rRNA using an Illumina MiSeq next-generation sequencer. The correlation between variation of microbiota expressed as the Dysbiosis Index (DI) and fecal calprotectin (FC) levels in IBD patients was also investigated.

**Results:** BMR-GENOMICS reports on the relative abundance (%) of the major phyla on IBDs microbiota. So far, we compared the trend of BMR-genomics reports on the relative abundance (%) of the major phyla with normalized signal

**References:**

**P3034 TARGET GOLDMANUM LEVELS TO ACHIEVE MUCOSAL HEALING IN PATIENTS WITH INTESTINAL DISEASES**

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**Introduction:** Golimumab is approved as a therapy for ulcerative colitis (UC) patients. Recently data also demonstrated efficacy and mucosal healing in Crohn’s disease (CD); however, little is known regarding target drug levels. Our aim is to identify trough golimumab levels in IBD associated with endoscopic remission.

**Aims and Methods:** This was a retrospective analysis of patients on maintenance golimumab for a minimum of 4 months. Concomitant therapies, disease status at the time of levels, endoscopic and clinical response (significant reduction in symptoms and biochemical markers with weaning of steroids) were recorded. Endoscopic and radiology records approximate to the date of the assay were reviewed. Primary outcome was mucosal healing defined as Mayo 0-1 or SES-CD score < 5. Secondary outcomes included clinical remission and endoscopic improvement. Drug levels were measured with Dynasure assay, mean trough levels compared using Kruskal-Wallis test, and used logistic regression to construct a probabilistic model determining sensitivity and specificity of levels predicting mucosal healing.

**References:**
1. Varela N, Yáñez-Barquín P, Lilley BN, Liu Y, Liu D, Mokler S, Gleichmann C, Zeligman J, Liu X, Maloney L, et al. Quantitation of adalimumab within the clinically relevant 0.5–25 µg/mL concentration range. The RIDA®QUICK ADM Monitoring allows accurate and precise quantification of adalimumab within the clinically relevant 0.5–25 µg/mL concentration range. The RIDA®QUICK ADM Monitoring shows excellent agreement with the RIDASCREEN® ADM Monitoring, which uses the same highly specific antibody clone to adalimumab. The RIDA®QUICK ADM Monitoring is easily accessible and supports timely dose adjustments of patients receiving adalimumab treatment in routine clinical practice.

**Disclosure:** Chris Barthel, Karin Wagenhäuser, Daniela Fichtner, Steffen Rameil, Thomas Van Stappen are employees of R-Biopharm AG (Darmstadt, Germany).
mean level was higher in patients with mucosal healing (n = 8, mean 5.9 μg/mL) vs non-response (n = 5, mean 2 μg/mL, p = 0.06) although analysis was limited by lower numbers in this cohort.

Conclusion: Treatment with golimumab was associated with mucosal healing in 45% IBD patients. Higher golimumab levels were associated with mucosal healing in CD and trough levels > 6.1 μg/mL were associated with endoscopic remission.

Disclosure: Nothing to disclose

P0335 EFFICACY AND SAFETY OF ADALIMUMAB IN CHINESE PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN’S DISEASE
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6 Shanghai TenPth People’s Hospital, Shanghai, China
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Introduction: The efficacy and safety of adalimumab induction and maintenance treatment in Chinese patients with moderately and severely active Crohn’s disease (CD) were assessed in a 26-week, phase 3, randomized, double-blind, placebo-controlled, multicenter study.

Aims and Methods: Adult patients naïve to anti-TNF therapy (CD Activity Index [CDAI] 220–450, hs-CRP≤3 mg/L) were stratified by CDAI (>300 ≥300) and corticosteroid use (yes/no) at baseline and randomized (1:1) to double-blind adalimumab 160 mg at weeks 0, 2, 40 mg at weeks 4/6 or placebo at weeks 0/2 followed by blinded adalimumab 160/80 mg at weeks 4/6. At week 8, all patients received open label (OL) 40 mg adalimumab every other week for up to 18 weeks. The primary endpoint (clinical remission [CDAI < 150]) and key secondary endpoints (Table) were assessed at week 4 between adalimumab and placebo using the Cochrane-Mantel-Haenszel (CMH) test and stratified by the randomization factors. Clinical remission at week 26 was assessed in patients with response (decrease CDAI ≥70 points from baseline) at week 8 and compared with a clinically meaningful threshold of 30% using the 1 sample Exact test.

Adverse events (AE) were collected throughout the study.

Results: Of 205 randomized patients (65 [31.7%] female, 32.9 [9.9] mean [SD] years of age and 2.7 [3.0] years disease duration), 196 (95.6%) completed the induction period and 159 (77.6%) completed OL treatment to week 26. The primary endpoint and key secondary endpoints were met (Table). Serious AEs and serious infections, respectively, were reported in 2/102 (2.0%) and 0 patients with adalimumab, 1/103 (1.0%) and 0 patients with placebo during double-blind treatment and in 36/200 (18.0%) and 7/200 (3.5%) patients receiving any adalimumab during the trial.

Conclusion: Adalimumab induced and maintained clinical remission and response in Chinese patients with CD who failed conventional therapy. The safety profile of adalimumab was generally comparable with placebo and consistent with the known safety profile of adalimumab.

Disclosure: B Chen: has nothing to disclose X Gao: has nothing to disclose J Zhong: has nothing to disclose J Ren: has nothing to disclose X Zhu: has nothing to disclose Z Liu: has nothing to disclose K Wu: has nothing to disclose M Chen: has nothing to disclose J Kalabic, B Huang, T Doan, AM Robinson are AbbVie employees; may own AbbVie stock and/or options

Reference

P0336 IMPROVED PATIENT-REPORTED OUTCOMES WITH UPADACITINIB AS AN INDUCTION THERAPY FOR PATIENTS WITH ULCERATIVE COLITIS: DATA FROM U-ACHIEVE
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2 Icahn School of Medicine at Mount Sinai, New York, United States
3 University Hospital Gasthuisberg, Leuven, Belgium
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Introduction: Upadacitinib (UPA) is an oral, selective Janus kinase 1 inhibitor that is being assessed in patients with ulcerative colitis (UC). The effects of UPA on patient-reported outcomes (PRO) were evaluated in the double-blind placebo-controlled dose-ranging 8-week induction portion of the phase 2b/3 study (U-ACHIEVE [NCT02819635]).

Aims and Methods: Adult patients with moderately to severely active UC (Adapted Mayo score [Mayo score without Physician Global Assessment] 5–9 points and centrally-read endoscopy subscore 2–3) who had inadequate response or intolerance to immunosuppressants, corticosteroids, or biologics were randomly assigned in a 1:1:1:1 ratio to double-blind induction therapy with placebo (PBO) or the modified-release formulation of UPA at 7.5, 15, 30, or 45 mg once daily (QD) for 8 weeks. Patients answered the following PRO questionnaires at baseline, and Week 2, 4, and 8: Inflammatory Bowel Disease Questionnaire (IBDQ), EuroQol–5 dimensions (EQ-5D), 36-Item Short Form Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-F), and Work Productivity and Activity Impairment (WPAI).

Mean change from baseline to Week 2 was assessed using analysis of covariance; missing data were reported using last observation carried forward. The percentage of patients with IBDQ response, defined as increase ≥16 points from baseline to Week 8, was determined; comparisons between UPA dosage groups and PBO were based on Cochran-Mantel-Haenszel tests and missing data were reported using non-responder imputation.

Results: A total of 250 patients with mean age 42.3 years, 60% male, and mean UC duration 8 years were analysed. At baseline, mean IBDQ was 125. EQ-5D visual analogue scale (VAS) was 53. SF-36 Physical Component Summary (PCS) was 42, SF-36 Mental Component Summary (MCS) was 41, FACT-F was 29, WPAI activity impairment was 52%, and overall work impairment was 51%.

Significant improvements in all PROs were consistently observed as early as Week 2 in patients receiving 45 mg QD (p < 0.05). At Week 8, IBDQ response was reported by significantly more patients taking UPA (67%, 62%, and 77% for 15, 30, and 45 mg QD, respectively) than PBO (35%) (all p < 0.05). For patients treated with UPA compared to PBO, significant improvements from baseline to Week 8 were reported in IBDQ score, EQ-5D VAS, and SF-36 PCS for all UPA doses (all p < 0.05; Table). Significant improvements were also shown for FACT-F and overall work impairment and activity impairment in 15, 30, and 45 mg QD (Table).

Disclosures: Financial support for the study and medical writing services (Joann Hettsch, Fishawack) was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. Ghodd: Steering committee: Pfizer, Janssen, AbbVie, BMS, Celgene, Boehringer-Ingelheim; Speaker: AbbVie, Janssen, Takeda, Shield, Ferring, Falk. Colombel: Consultant/advisory board: AbbVie, Amgen, Boehringer-Ingelheim, Celgene, Celltrion, Enteromé, Ferring, Genentech, Janssen and Janssen, Medimmune, Merck & Co, Pfizer, Protagonist, Second Genome, Seres, Shire, Takeda, Theradiag; Speaker: AbbVie, Ferring; Speaker’s bureau: Amgen; Stock options: Intestinal Biotech Development, Genefit; Research grants: AbbVie, Takeda, Janssen and Janssen. Vermeire: Consulting: AbbVie, MSD, Takeda.
IBDQ response (Δ≥16) 34.8% 46.8% 67.3%*** 61.5%* 76.8%**
Mean change from baseline
IBDQ score 11.4 (n = 45) 30.8* (n = 44) 42.9** (n = 48) 42.8*** (n = 49) 48.9*** (n = 55)
EQ-5D VAS -1.0 (n = 44) 11.5* (n = 44) 16.4*** (n = 48) 14.3*** (n = 48) 21.5*** (n = 54)
SF-36 PCS 0.5 (n = 44) 5.4# (n = 44) 5.8*** (n = 48) 6.8*** (n = 48) 7.8*** (n = 54)
FACT-F 3.2 (n = 44) 6.9 (n = 44) 9.2** (n = 48) 10.4*** (n = 48) 10.5*** (n = 53)
WPRA: % activity impairment -7.7 (n = 44) -14.8 (n = 44) -17.1* (n = 48) -24.2*** (n = 48) -27.2*** (n = 54)
WPRA: % overall work impairment# -0.8 (n = 27) -10.5 (n = 27) -22.6** (n = 30) -19.1* (n = 33) -23.0* (n = 39)

***, **, * statistically significant at 0.001, 0.01, 0.05, and 0.1 level for treatment group vs PBO. # Only employed subjects.

References

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Introduction
5-aminosalicylic acid (5-ASA) is the mainstay of treatment of patients with ulcerative colitis (UC). 5-ASA acts locally in the colonic mucosa and its mucosal concentrations inversely correlated to disease activity (1–4). Previous studies suggest that treatment with Asacol (pH-dependent formulations) (1, 2) is more effective than Mezavant and Pentasa (time-dependent release formulation) (1, 5). However the different 5-ASA formulations (1–4) were included. 8 hours after ingestion of mesalazine, mean mucosal concentration of 5-ASA and its inactive metabolite acetyl-5-ASA were measured. Disease activity was assessed by Mayo score (MS) and IBDQ improvement was assessed using a mixed model repeated measures (MMRM) analysis. The percentage of patients at Week 12 with clinical response, endoscopic healing, and IBDQ improvement ≥16 were also assessed.

Results
Aims and Methods: In this cross-sectional non-randomized study, we have measured mucosal concentration of 5-ASA and its inactive metabolite acetyl-5-ASA in the left hemicolon of patients with quiescent ulcerative colitis using the Inflammatory Bowel Disease Questionnaire (IBDQ) and evaluated using a mixed model repeated measures (MMRM) analysis. The percentage of patients at Week 12 with clinical response, endoscopic healing, and IBDQ improvement ≥16 were also assessed.

Conclusion: Patients using Mezavant had significantly higher mucosal 5-ASA concentrations than patients using Pentasa, despite higher endoscopic MS. There was small intra-individual variations, but large inter-individual variations in mucosal 5-ASA concentrations in the left hemicolon of patients with UC using oral mesalazine preparations.

Disclosure: Nothing to disclose.

References
P0309 COMPARATIVE FREQUENCY OF CLOSTRIDIAL INFECTION IN PATIENTS WITH ULCERATIVE COLITIS RECEIVING MESENCHYMAL STROMAL CELLS AND BIOLOGICAL PREPARATIONS

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Introduction: Patients with inflammatory bowel disease (IBD) experienced more frequent development of Clostridial infection and much higher rates of morbidity and mortality compared to patients without IBD. Risk factors are immunosuppressive therapy.

Aims and Methods: The aim is to compare the frequency of Clostridial infection (CI) in patients with ulcerative colitis (UC) receiving bone marrow mesenchymal stromal cells (MSC) and biological therapy.

Materials and methods. The patients were divided into 3 groups: the first group (n = 23) received the MSCs culture according to the scheme (0-12 weeks), then every 26 weeks; the second group of patients with UC (n = 23) received infliximab (IFX) in combination with azathioprine (AZA) according to the recommended scheme, the third group received only IFX according to the scheme. The toxins A and B of Clostridium difficile were determined by the enzyme immunoassay in the stools. The comparative analysis was carried out using the method of 4-field tables using nonparametric statistical criteria.

Results: In patients of the 1st group, toxin A was detected in 2/23 patients (4.3%), in the 2nd group - in 2/23 patients (9.5%) (RR - 0.44, 95% CI 0.06-4.3, x2 - 0.06, p > 0.05), in the third - in 2/23 patients (9.5%) (RR - 0.44, 95% CI 0.06-4.3, x2 - 0.06, p > 0.05). In patients of the 1st group toxins A and B were not detected - 0/23 (0.0%), in the 2nd group toxins A and B were detected in 1/21 (3%) patients (x2 - 0.59, p > 0.05, and x2 - 0.52, p > 0.006) respectively.

Conclusion: The frequency of Clostridial infection in patients with ulcerative colitis receiving mesenchymal stromal cells is significantly lower than in patients with ulcerative colitis receiving biological immunosuppressive preparations.

Disclosure: Nothing to disclose.
INTRODUCTION

We demonstrated similarity of efficacy, safety and pharmacokinetics of CT-P13 and INX in phase 2 randomized control trial in moderate to severe Crohn's disease (CD) patients (1). Recent studies suggested an association between higher infliximab trough concentrations and better clinical outcomes in the treatment of inflammatory bowel disease (2), which has to be examined in a prospective observation. Note. Lower limit of quantitation of serum Infliximab concentration was 0.55 µg/ml.

Aims and Methods: This post-hoc analysis of the CT-P13 3.4 study (NCT02098681) aimed at determining whether earlier Ctrough might be used as a predictor of subsequent clinical remission. A total of 198 patients who underwent efficacy analysis at Week 54 and had PK parameters at Week 6 (pre-dose concentration at Week 14) and Week 14 (pre-dose concentration at Week 22) were included in this analysis. All PK parameters were analyzed while the patients received INX or CT-P13 at 5 mg/kg with no dose escalation until week 22. Mann-Whitney U test was used to analyze the difference of Ctrough levels in patients achieving or not achieving clinical response at Week 54, and between CT-P13 and INX treatment groups among responders. Receiver operating characteristic (ROC) curves were constructed for sensitivity (S) and specificity (Sp) analyses of Ctrough levels at Week 54.

RESULTS: Median Week 6 Ctrough levels were 3.7 and 3.6 µg/ml, and Week 14 Ctrough levels were 2.6 and 2.2 µg/ml in the CT-P13 and INX groups, respectively. Ctrough levels were significantly higher (p < 0.01) in Week 54 responders (CDAI < 150) than in non-responders in both CT-P13 and INX treatment groups. Since overall Ctrough levels in responders were not significantly different between CT-P13 and INX treatment groups (p > 0.05), both groups were pooled for further analysis. While Week 6 Ctrough could be much more sensitive to predict clinical success (specificity > 90%) than Week 6. Suggested diagnostic cut-offs to predict clinical remission were Ctrough > 4.5 µg/ml at Week 6, and Ctrough level > 4.0 µg/ml at Week 14 as a predictor of subsequent clinical remission. In addition, Week 14 levels appear to be more specific to predict one year outcome than Week 6 levels.

Conclusion: Cheon J.H.; Consultancies and/or lecture fees from CELLTRION, Lee K.-M.; Consultancies and/or lecture fees from Celltrion, Takeda, AbbVie, Janssen, Ferring and Korea, Shire, Takeda Korea, Celltrion. Choi C.; Consultancies and/or lecture fees from Celltrion, Takeda, AbbVie, Janssen, Ferring and Korea, Shire, Takeda Korea, Celltrion, Janssen, Roche, HAC Pharma, Cornerstone Health, IQVIA, Celltrion. Cheon J.H.; Consultancies and/or lecture fees from CELLTRION, Lee S., Lee S.G, Lee JH; Consultancies and/or lecture fees from Celltrion, Abbvie Korea, Ferring Korea, Janssen Korea, Kangstem Biotech, Kuhl Pharm, Shire Korea, Takeda Korea, Cornerstones Health, IQVIA, Celltrion.

Note. Lower limit of quantitation of serum Infliximab concentration was 0.55 µg/ml.

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<table>
<thead>
<tr>
<th>Week 6 Ctrough</th>
<th>CTR-P13: Median(IQR)(µg/ml)</th>
<th>Non-Responder</th>
<th>p-value</th>
<th>INX: Median(IQR)(µg/ml)</th>
<th>Non-Responder</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>CDAD-70</td>
<td>3.90 (2.65-7.07)</td>
<td>2.42 (0.55-5.93)</td>
<td>0.088</td>
<td>3.76 (2.15-6.95)</td>
<td>1.72 (0.76-4.85)</td>
<td>0.026</td>
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<tr>
<td>CDAD-100</td>
<td>3.96 (1.80-7.30)</td>
<td>2.88 (0.55-5.56)</td>
<td>0.038</td>
<td>4.02 (2.15-7.16)</td>
<td>2.17 (0.91-4.20)</td>
<td>0.018</td>
</tr>
<tr>
<td>Clinical remission</td>
<td>4.9 (2.32-8.06)</td>
<td>1.72 (0.55-4.39)</td>
<td>0.001</td>
<td>4.45 (2.5-8.49)</td>
<td>2.17 (0.91-3.71)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Week 14 Ctrough</td>
<td>Responders</td>
<td>Non-Responders</td>
<td>p-value</td>
<td>Responders</td>
<td>Non-Responders</td>
<td>p-value</td>
</tr>
<tr>
<td>CDAD-70</td>
<td>2.98 (0.74-6.14)</td>
<td>0.61 (0.55-1.42)</td>
<td>0.020</td>
<td>2.47 (0.88-4.14)</td>
<td>0.55 (0.55-2.35)</td>
<td>0.012</td>
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<tr>
<td>CDAD-100</td>
<td>2.98 (0.74-6.14)</td>
<td>0.61 (0.55-2.13)</td>
<td>0.016</td>
<td>2.85 (0.94-4.6)</td>
<td>0.61 (0.55-2.11)</td>
<td>0.004</td>
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<tr>
<td>Clinical remission</td>
<td>3.40 (1.14-6.56)</td>
<td>0.68 (0.55-2.54)</td>
<td>0.0002</td>
<td>3.11 (0.94-6.03)</td>
<td>1.17 (0.55-2.68)</td>
<td>0.001</td>
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</table>
(FX: 5mg/kg every 8 weeks, ADA: 40mg every other weeks) and confirmed tolerability of ED were allocated to ED group. All administered elemental diet 9000kcal/day or more. Other patients were allocated to Non-ED group. Primary endpoint was the cumulative remission rate at 2 years after baseline. CDAI was calculated at each visit during 2 years after baseline. Clinical relapse defined as ≥20 points in CDAI and/or need for additional treatment including dose escalation of Anti-TNF and surgery. Adherence of ED was confirmed by clinician’s interview to patients at each visit and amount of prescriptions.

Results: 88 patients were enrolled and 16 patients were excluded due to no response of Anti-TNF induction therapy. Of the 72 patients, 37 were allocated to ED group and 35 subjects were allocated to Non-ED group. As for clinical features, previous enteral nutrition was more frequent observed in ED group (p = 0.03). The cumulative remission rate at 2 years was no significant difference between ED group (60.9% in ED group, 56.7% in Non-ED group, p = 0.98). By a multivariate analysis, intestinal stricture (HR: 5.0, 95% CI: 1.6–15.2), previous steroid therapy (HR: 4.0, 95% CI: 1.1–14.9) and CRP > 5mg/L (HR: 6.5, 95% CI: 1.8–24.4) at baseline were risk factors of clinical relapse. Adherence of ED in ED group was relatively low and only 11 patients had been kept 9000kcal/day or more of ED.

Conclusion: Additional power of ED for CD patients who responded to initial Anti-TNF induction therapy could not be confirmed. Efficacy of concomitant ED in clinical settings such as loss of response need to be clarified in the future. Moreover, improvement of adherence might be important in order to obtain clinical efficacy of ED.

Disclosure: Nothing to disclose.

P0343 EARLY OPTIMIZATION OF GOLUMUMBDE DOSES INDUCES DELAYED RESPONSE AND LONG-TERM CLINICAL BENEFIT IN ULCERATIVE COLITIS

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Introduction: Data assessed outcomes of glucocorticoid monotherapy (GLM) dose optimization in patients with ulcerative colitis (UC) are lacking. According to the summary of product characteristics by the European Medicines Agency (EMA) patients with body weight less than 80 kg received GLM maintenance doses of 50 mg q2wk at week 2, followed by week 6 (3). The benefit of GLM dose escalation from 50 mg q4wk to 100 mg q4wk has not been evaluated in clinical practice.

Aims and Methods: The aim of this study was to evaluate outcomes of early optimization of GLM from 50 mg q4wk to 100 mg q4wk in UC patients with adequate response to GLM induction treatment. This observational multicentre cohort study included consecutive UC patients without response to GLM induction doses, in which weight-based GLM maintenance doses of 50 mg q2wk were administered (57.1%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naive patients and for 10.4 months in steroid dependent (57.1%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naive patients and for 10.4 months in steroid dependent cohort. Mucosal biopsies revealed that infiltrating leukocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leukocytes in the biopsies from the responder patients. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were non-responders. Patients with the first UC episode were identified as the best responder (4). Patients' demographic features should guide to select responder patients.

Results: We evaluated 24 UC patients with body weight below 80 kg, 18 (75%) were female, 18 (75%) had extensive colitis and 5 (20%) left-sided colitis. The mean age of the patients was 47 (standard deviation 14), and the median disease duration was 9.5 years (interquartile range [IQR] 4–14). 14 patients (58%) had previous anti-TNF failure (4 infliximab, 2 adalimumab and 8 both). All patients received induction with GLM 200 mg/100 mg at weeks 0 and 0 and 2. In all patients GLM 50 mg q4wk was optimized to 100 mg q4wk, starting at week 6 in 10 patients and at week 10 in 14 patients. At week 14, 16 of 24 patients (67%; 12 with corticosteroid-free) recovered clinical response. Of these, 4 patients (%) achieved corticosteroid-free remission. After a median follow-up of 12 months (IQR 10–22), 13 of 24 patients (54%) avoided GLM failure. 13 of 16 patients (81%; all but 1 were corticosteroid-free) who achieved delayed response at week 14 recovered clinical benefit with GLM 100 mg q4wk at last follow-up. Eleven of 24 patients (46%) had GLM failure. Reasons for GLM discontinuation were nonresponse at week 14 in 8 patients (37%) and secondary loss of response in 3 patients (27%) who had delayed response at week 14. None of the patients experienced adverse events leading to GLM withdrawal. All 24 patients avoided colectomy at last follow-up. None of the patients were dose-de-escalated to GLM 50 mg q4wk.

Conclusion: Early optimization of GLM from 50 mg q4wk to 100 mg q4wk induces delayed response (by partial Mayo score) at week 14 in two thirds of UC patients with body weight below 80 kg who were non-responders to GLM induction. Continuing GLM 100 mg q4wk in patients who do not demonstrate an early clinical response to GLM induction but achieve a delayed response was safe and leads to long-term clinical benefit.

Disclosure: CT has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, and Gebro Pharma. The remaining authors declare that they have nothing to disclose.

Reference

P0344 BASELINE DEMOGRAPHIC FEATURES OF ULCERATIVE COLITIS PATIENTS AS PREDICTORS OF CLINICAL RESPONSE TO ADSORPTIVE DEPLETION OF MYELOID LINEAGE LEUKOCYTES AS REMISSION INDUCTION THERAPY

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Introduction: Inflammatory bowel disease (IBD) is associated with elevated myeloid lineage leukocytes, which show activation behaviour (1) including the CD14+CD16+DR++ phenotype known as proinflammatory monocytes and a major source of tumour necrosis factor-a (2). Accordingly selective depletion of myeloid leukocytes by granulocyte/monocyte apheresis (GMA) with a CDAI has been expected to promote remission and enhance drug efficacy. However, hitherto studies in IBD have reported contrasting efficacy outcomes, ranging from an 85% (3) to a statistically insignificant level (4). Patients’ demographic features should guide to select responder patients.

Aims and Methods: In a single-centre retrospective setting, we looked at the baseline clinical and endoscopic features of responders and non-responders to adsorptive GMA in 145 consecutive ulcerative colitis patients who had undergone GMA as remission induction therapy. 73 patients were steroid naive, 70 were steroid dependent, and 2 were steroid refractory. Patients had received up to 11 GMA sessions over 10 weeks. At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control. Clinical activity index (CAI) >4 was defined as remission. Biopsies from endoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.

Results: At entry, the average CAI was 12.8, range 10–17; 93 patients (64.1%) had responded to GMA, 52 of 73 steroid naive (71.2%), 40 of 70 steroid dependent (57.1%), and 1 of the 2 steroid refractory cases. On average remission was sustained for 8.6 months in steroid naive patients and for 10.4 months in steroid dependent cohort. Mucosal biopsies revealed that infiltrating leukocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leukocytes in the biopsies from the responder patients. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were non-responders. Patients with the first UC episode were identified as the best responder (4). Patients’ demographic features should guide to select responder patients. Patients with extensive deep ulcers, with long duration of UC refractory to multiple pharmacologics are unlikely to benefit from GMA. In therapeutic settings, knowing baseline features, which may identify responder patients should help to avoid futile use of medical resources.

Disclosure: Nothing to disclose.

References
Introduction: Anti-tumour necrosis factor alpha (anti-TNF) therapies are effective and widely used in the management of patients with inflammatory bowel disease (IBD). However, they may induce a drug-induced lupus ‘syndrome’, recently termed anti-TNF induced lupus (ATIL). The widely accepted diagnostic criteria for this syndrome being (1) a temporal relationship between symptoms and anti-TNF therapy and resolution of symptoms following cessation of the offending medication, (2) at least one serologic American College of Rheumatology criteria of systemic lupus erythematosus (SLE), either a positive ANA or anti-dsDNA, and (3) at least one non-serological criteria such as arthritis, serositis or rash (1). ATIL is increasingly recognised and described in the rheumatology literature, however, data on the true prevalence of ATIL in IBD populations due to lack of recognition of the condition as well as difficulty making a diagnosis as there is significant overlap in symptoms with the extraintestinal manifestations of IBD.

Aims and Methods: To evaluate the incidence, clinical and serological markers, as well as risk factors for developing ATIL, in an IBD population. A retrospective observational cohort study of all IBD patients that completed induction as well as at least one maintenance dose of anti-TNF therapy (infliximab or adalimumab) at Royal Perth Hospital between January 2008 and December 2017. A diagnosis of ATIL was confirmed based on the criteria outlined above. Demographic, clinical and serological parameters were obtained from electronic and paper records.

Results: 154 ATIL treatment courses with anti-TNF therapy (30 infliximab and 124 adalimumab) were included. 17 (5.7%) patients that received infliximab and 1 patient (0.6%) on adalimumab developed ATIL. Patients that developed ATIL were more likely to be older at commencement of anti-TNF (46.47 years ± 13.79 years vs. 43.75 years, p = 0.027) and were more likely to be female (72.2%), antidi-SLE (21.1%), anti-Smith antibodies (marker for idiopathic SLE) (16.7%), anti-Ro/SSA antibodies (marker for systemic lupus erythematosus) (10.5%) and anti-dsDNA (marker for drug induced lupus) (10.5%). ANA was positive in 22 patients (46.9%) with results ranging from 7 to 30 IU/ml. In those patients who had a baseline ANA performed prior to commencing anti-TNF therapy (14 patients), the ANA level increased compared with their baseline level. Other serological markers that developed ATIL included anti-dsDNA in 105 (67%), anti-histone antibodies (marker for drug induced lupus) 2/15 (13%), anti-Smith antibodies (marker for idiopathic SLE) 0/15 (0%), Rheumatoid Factor (autoimmune arthritis) 0/8 (0%) and anti-CCP (Rheumatoid arthritis) 0/5 (0%).

Conclusion: Our study suggests, IBD patients with varying doses and durations during their anti-TNF course. The mean duration of anti-TNF therapy till development of ATIL was 19.78 months ± 15.76 months. The most common clinical symptom was polyarthitis in 15 patients (83.3%) with rash occurring in 5 patients (27.8%). All patients with a diagnosis of ATIL demonstrated an elevated ANA with results ranging from 7 to 30 IU/ml. In those patients who had a baseline ANA performed prior to commencing anti-TNF therapy (14 patients), the ANA level increased compared with their baseline level. Other serological markers that developed ATIL included anti-dsDNA in 105 (67%), anti-histone antibodies (marker for drug induced lupus) 2/15 (13%), anti-Smith antibodies (marker for idiopathic SLE) 0/15 (0%), Rheumatoid Factor (autoimmune arthritis) 0/8 (0%) and anti-CCP (Rheumatoid arthritis) 0/5 (0%).

Disclosure: Nothing to disclose.

References:

Disclosure:

Unification of IBD Management Across Countries: Are There Differences Among China, India, and the United States

Aim: To compare the differences in medical and surgical management of inflammatory bowel disease (IBD) across China, India, and the United States.

Methods: This study included IBD patients recruited from three major IBD centers in China, India, and the United States. Demographic, clinical, and medication use data were collected using a standardized questionnaire. Logistic regression analyses were performed to determine the factors associated with differences in medical and surgical management.

Results: The study included 300 IBD patients from China, 200 from India, and 300 from the United States. There were significant differences in the use of medications and surgical interventions across the countries. For example, the use of biologics was higher in the United States compared to China and India. The odds of undergoing surgery for Crohn’s disease were higher in India compared to the United States. The odds of using corticosteroids were similar across the three countries.

Conclusion: There are significant differences in the medical and surgical management of IBD across China, India, and the United States. Further research is needed to identify the underlying reasons for these differences and to develop strategies to improve the management of IBD worldwide.
Endoscopic remission subscore (RBS) S Ghosh

DATA FROM U-ACHIEVE

ABDOMINAL PAIN FOR PATIENTS WITH ULCERATIVE COLITIS: WITH IMPROVED SYMPTOMS IN BOWEL URGENCY AND

P0348 INDUCTION THERAPY OF UPADACITINIB IS ASSOCIATED with the abstract. All authors are AbbVie employees and may hold AbbVie stocks or

Disclosure: The study was funded by AbbVie. AbbVie contributed to the study design, research, and interpretation of the data, writing, reviewing and approving the abstract. All authors are AbbVie employees and may hold AbbVie stocks or options.

P0348 INDUCTION THERAPY OF UPADACITINIB IS ASSOCIATED WITH IMPROVED SYMPTOMS IN BOWEL URGENCY AND ABDOMINAL PAIN FOR PATIENTS WITH ULCERATIVE COLITIS: DATA FROM U-ACHIEVE

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Introduction: Upadacitinib (UPA) is an oral selective Janus kinase 1 inhibitor that is being assessed in patients with ulcerative colitis (UC). In addition to the symptoms captured in the Mayo score, the effects of UPA on other patient-reported UC symptoms including bowel urgency and abdominal pain were evaluated in the double-blind placebo-controlled dose-ranging 8-week induction portion of the phase 2b/3 study (U-ACHIEVE [NCT02819635]).

Aims and Methods: Adult patients with active UC (Adapted Mayo score [Mayo score without Physician Global Assessment] ≤ 5–9 points and centrally-read endoscopy subscore 2–3) who had inadequate response or intolerance to corticosteroids, immunosuppressants, or biologics were randomized to the modified-release formulation 7.5, 15, 30, or 45 mg once daily (QD) UPA or PBO (1:1:1:1:1) for 8 weeks. UC symptoms including bowel urgency (yes/no) and abdominal pain (0–none, 1–mild, 2–moderate, 3–severe) were collected in the patient daily diary. The total number of days with bowel urgency, average score of abdominal pain, Mayo rectal bleeding subscore (RBS), and stool frequency subscore (SFS) over the most recent 3-consecutive days prior to the study visits were calculated. The proportion of patients who reported no bowel urgency and abdominal pain score = 0 (which were considered the most stringent endpoints), along with RBS = 0 and SFS ≤ 1 at week 8, respectively, were compared between UPA and PBO groups using the Cochran-Mantel-Haenszel test adjusted for previous biologic use, baseline corticosteroid use, and baseline Adapted Mayo score ≤7 and >7. Non-responder imputation was used for missing values. Sensitivity analyses were conducted by excluding patients with no bowel urgency or those with none to mild abdominal pain (average abdominal pain score ≤1) at baseline.

Results: A total of 250 patients with mean age 42.3 years, 60% males, and mean UC duration 8 years were analysed. At baseline, 83% of subjects reported 3 days with bowel urgency and 41% of subjects had an average abdominal pain score ≤ 1. As early as week 2, more UPA-treated patients reported no bowel urgency over the 3 days and less abdominal pain compared with PBO. At week 8, significantly higher proportions of patients reported no bowel urgency over the 3 days; abdominal pain score = 0, RBS = 0, and SFS ≤ 1 in most UPA groups compared with the placebo group with a potential dose effect across the 7.5 mg, 15 mg, 30 mg, and 45 mg QD dose groups (Table). In the sensitivity analyses, the risk difference between UPA groups and PBO was similar to the primary analyses when excluding patients with no bowel urgency, or excluding those with none to mild abdominal pain at baseline.***, **, *, *statistically significant at 0.001, 0.01, 0.05, and 0.1 level for treatment vs PBO.

Patients with no bowel urgency at baseline were excluded.

Results: Financial support for the study was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content. S Ghosh: Dr. Ghosh is a steering committee member for Pfizer, Janssen, AbbVie, BMS, Celgene and receives speaker honorarium from AbbVie, Janssen, Takeda, Shield, and Falk Pharma. E Louis has received Educational Grants from MSD, Abbvie, Takeda; and speaker fees from Abbvie, Ferring, MSD, Chiesi, Mitsubishi Pharma, Hospira, Janssen, Takeda. Advisory Board: Abbvie, Ferring, MSD, Takeda, Hospira, Mitsubishi Pharma, Celtrion, Prometheus. S Lee has received grant and research support from AbbVie, Arena, Atlantic, Celgene, Gilead Sciences, Janssen, Pfizer, Salix, Shield, Takeda, Tetherex, UCB Pharma and has performed consulting for Arena, Celgene, Celtrion Healthcare, Cornerstones, Eli Lilly and Company, Janssen, Mesoblast, Pfizer, Salix, Takeda, and UCB Pharma. EV Loftus Jr: Consulting for AbbVie, Takeda, Janssen, UCB, Agen, Pfizer, Eli Lilly, Celgene, Celltrion Healthcare. Research support from AbbVie, Takeda, Janssen, UCB, Agen, Pfizer, Genentech, Receptos, Gilead, Celgene, Seres, MedImmune, Robarts Clinical Trials, F Cataldi, B Huang, WJ Lee: employees of AbbVie and may own AbbVie stock.

Abstract No: P0347

<table>
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<th>Endpoint</th>
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<th>15 mg QD</th>
<th>30 mg QD</th>
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<tr>
<td>Clinical Remission per Adapted Mayo</td>
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<td>7 (4–10)</td>
<td>12 (9–14)</td>
<td>16 (14–20)</td>
<td>19 (16–22)</td>
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<tr>
<td>Endoscopic Improvement</td>
<td>2 (9–4)</td>
<td>15 (13–18)</td>
<td>23 (20–27)</td>
<td>32 (28–36)</td>
<td>35 (31–38)</td>
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<tr>
<td>Clinical Remission per Full Mayo</td>
<td>12 (9–17)</td>
<td>28 (25–31)</td>
<td>38 (34–42)</td>
<td>47 (44–51)</td>
<td>52 (48–56)</td>
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<tr>
<td>Endoscopic Remission</td>
<td>2 (1–4)</td>
<td>3 (2–5)</td>
<td>4 (3–6)</td>
<td>9 (7–12)</td>
<td>19 (16–22)</td>
<td></td>
</tr>
</tbody>
</table>

NRI: Non-responder imputation

Clinical remission per adapted Mayo: stool frequency subscore ≤ 1, rectal bleeding subscore of 0, and endoscopic subscore ≤ 1

Endoscopic improvement: endoscopic subscore ≤ 1

Clinical remission per full Mayo: full Mayo score ≤ 2 with no subscore > 1

Clinical response per adapted Mayo: decrease from baseline in the adapted Mayo score ≥ 2 points and ≥ 30% from baseline, PLUS a decrease in rectal bleeding subscore (RBS) ≥ 1 or an absolute RBS ≤ 0

Endoscopic remission: endoscopic subscore of 0.

[Table Exposure-Response Model-Predicted Efficacy Endpoints at Week 8 In Subjects with UC for Different Upadacitinib Regimens*]

*Simulation for 200 replicates, each with 600 subjects (400:200 upadacitinib:placebo) per dosing regimen. The 90% prediction intervals (5th/95th percentile) reflect the impact of random sampling of subjects and model parameters point estimates (i.e. prediction intervals do not reflect the model parameter uncertainty.).

Disclosure: The study was funded by AbbVie. AbbVie contributed to the study design, research, and interpretation of the data, writing, reviewing and approving the abstract. All authors are AbbVie employees and may hold AbbVie stocks or options.

Abstract No: P0348
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Introduction: Genome-wide association studies revealed that single nucleotide polymorphisms within the gene encoding protein tyrosine phosphatase non-receptor type 2 (PTPN2) are associated with the onset of inflammatory bowel diseases (IBD) and other chronic inflammatory disorders. PTPN2 is involved in maintaining intestinal homeostasis in vivo via regulating inflammatory signalling pathways and protecting intestinal epithelial barrier function. Previously, we have shown that spermidine, a naturally occurring polyamine, exerts anti-inflammatory effects in mouse colitis models and treated in the same manner. mRNA expression of IFNG, PTPN2, ICAM1 (which encodes for intercellular adhesion molecule 1) and NOD2 (encoding for nucleotide-binding oligomerization domain-containing protein 2) was analysed in both experiments by performing quantitative-PCR.

Results: IFN-γ treatment resulted in increased mRNA expression of ICAM1, PTPN2 and NOD2 genes in all cells. Of interest, however, in cells expressing CT genotype, basal mRNA expression of those genes was already elevated, and their mRNA expression level following IFN-γ treatment was clearly higher than those observed in PTPN2 wild-type cells. In line with this, cells carrying the CT variant showed reduced PTPN2 activity in basal and IFN-γ treated conditions. Activation of PTPN2 by spermidine clearly reduced IFN-γ-induced elevation of ICAM1, IFNG and NOD2 expression in T84 and HT29 cell lines (p < 0.05). Despite initially elevated IFN-γ responses, spermidine treatment was more effective in HT29 cells expressing the CT variant (p < 0.05), resulting in elevated activation of PTPN2, and more pronounced reduction of ICAM1, INFG and NOD2 mRNA expression in all cell types (TT; n = 5), as well as from healthy controls (all TT; n = 5) and treated in the same manner. mRNA expression of IFNG, PTPN2, ICAM1 (which encodes for intercellular adhesion molecule 1) and NOD2 (encoding for nucleotide-binding oligomerization domain-containing protein 2) was analysed in both experiments by performing quantitative-PCR.

Conclusion: Spermidine treatment effectively reduced inflammatory response in T84 and HT29 cell lines and in PBMC from IBD patients. Reduction of the inflammatory responses is more pronounced in case of the presence of C (variant) allele in PTPN2 SNP rs1893217 carriers. Taken together our data indicates that spermidine might be a new promising therapeutic agent in IBD treatment, furthermore the presence of the PTPN2 C allele might serve as a good prediction marker for treatment response.

Disclosure: Nothing to disclose

P0350 VEDOLIZUMAB IN REFRACTORY MICROSCOPIC COLITIS: AN INTERNATIONAL CASE SERIES

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5University of California, Division of Gastroenterology, San Diego, United States

Aims and Methods: We solicited gastroenterologists in Europe and Canada for cases of MC treated with vedolizumab. All patients had histologically proven MC. Vedolizumab 300 mg IV was administered at weeks 0, 2 and 6, and then every 8 weeks. Clinical remission and histological remission were defined as < 3 stools per day and normalization of histology, respectively.

Results: Eleven cases were evaluated for analysis from 4 referral centers in 4 different countries [9 females, median age at diagnosis 49 years, lymphocytic colitis (LC) n = 5, collagenous colitis (CC) n = 6]. Median (IQR) disease duration at vedolizumab initiation was 51 (29–70) months and median stool frequency was 8 (6–10) per day. All patients had previously failed second-line therapy. Patients had also been exposed to mesalamine (5/11), cholestyramine (5/11), azathioprine (6/11), methotrexate (3/11) and 10/11 had failed at least 1 anti-TNF agents (8/11 infliximab, 5/11 adalimumab, 1/1 golimumab). Reasons for anti-TNF cessation were inefficacy (8/10), loss of response (1/10) and delayed infusion reaction (1/10). After 3 infusions of vedolizumab, clinical remission was observed in 5/11 patients (2 LC and 3 CC) of whom 3 remained well with maintenance therapy (median duration of 13 months). Vedolizumab was stopped due to intolerance in 1 patient (post-infusion hypertensive crisis) and loss of response for 1 patient. Biopsies after induction were obtained from 9/11 patients. Histological remission was observed in 3/4 patients with clinical remission 2/3 CC, 1/1 LC and 0/5 patients without clinical improvement. Rescue therapies in failure were budesonide (n = 1), systemic steroids (n = 1), methotrexate (n = 1), experimental drug (n = 1) and loop-ileostomy (n = 1).

Conclusion: In a series of highly refractory microscopic colitis patients, vedolizumab induced clinical remission in 5/11 subjects and disappearance of histological inflammation in 3/4. Larger randomized trials are needed to assess the efficacy of vedolizumab in patients with MC.

Disclosure: Nothing to disclose

P0351 DEFINING ‘EARLY DISEASE’ IN INFLAMMATORY BOWEL DISEASE: THE RESULTS OF A SYSTEMATIC LITERATURE REVIEW

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Aims and Methods: The Cochrane library, MEDLINE and EMBASE were searched using key words and indexing terms. Eligible papers reported the characteristics and/or treatment (ts) of adult pts (≥18 years) with ‘early’ inflammatory bowel disease (IBD) from clinical or observational studies published January 2008 - March 2018. There was no intervention or comparator restriction and no assumption on the definition of ‘early’. Papers published before 2008, not in English, in paediatric or non-IBD pts were excluded. Uncertainty as to study eligibility was reconciled by a second independent reviewer.

Results: The SLR returned 1,742 abstracts; 107 papers (16 clinical studies; 91 observational studies) met inclusion criteria. A mean 6.2 papers per year (yr)
were published 2008–2012 and 16.0/yr in 2013–2017. ‘Early disease’ was explicitly defined in 33 papers (19 CD; 7 UC; 1 CD and UC; 6 IBID overall) 22 (67%) used time since diagnosis (DX) only; 9 (27%) combined this with DX history; 1 (3%) DX history and symptom duration; and 1 (3%) DX history and time since first IBID prescription. Definitions in UC used time since DX only (6 papers), combined with DX history and symptom duration (1 paper). Cut-off points for time since DX were applied in 30 papers: ≤3 months (20%), 3–6 months (17%), 6–12 months (27%), 1–2 yrs (17%) and >2 yrs (20%). Definitions based on DX history specified pts should be immunomodulator (IMM) and biologic naive (7 papers) or additionally corticosteroid (CS) naive (4 papers). ‘Early disease’ pt characteristics were stratified by CD and UC. Median disease duration ranged between 0.2–10.6 yrs in CD and 1.1–5.4 yrs in UC. CD cohorts included pts with stricturing (max 64%), penetrating (max 48%) or fistulising disease (max 14%). Disease and prior surgery (max 51%); UC cohorts included pts with pancolitis (max 100%) and prior surgery (max 69%) (see Table). ‘Early’ CD cohorts met the consensus criteria (disease duration <18 months and IMM and biologic naive) in only 2 papers published since 2012. Conclusion: The characteristics of ‘early’ CD and UC pts have increasingly come under focus as the concept of early intervention in IBID has gained traction. Early disease has predominantly been defined by time since DX (± other variables) but the disease duration of ‘early’ cohorts can be very long. Often ‘early’ pts already have complex disease, which may mean the ‘window of opportunity’ for intervention is missed. The consensus definition of ‘early’ CD has not been consistently applied since being developed. Robust definitions of early CD and UC are required to accurately evaluate the potential of early biologic tx to improve outcomes.

References

P0352 LACK OF EARLY RESPONSE AND MUCOSAL HEALING IS ASSOCIATED WITH COLEYTECTOMY IN PATIENTS WITH MODERATE TO SEVERE UC. A MULTICENTRIC REAL-WORLD OUTCOME STUDY

Data from ulcerative colitis (UC), uncontrolled inflammation may result in disease progression requiring colectomy. Mucosal healing (MH) has been associated with avoidance of colectomy (1). The pursuit of mucosal healing (MH) has been associated with a reduction in disease progression requiring colectomy. Mucosal healing (MH) was defined in 33 papers (19 CD; 7 UC; 1 CD and UC; 6 IBID overall) 22 (67%) used time since diagnosis (DX) only; 9 (27%) combined this with DX history; 1 (3%) DX history and symptom duration; and 1 (3%) DX history and time since first IBID prescription. Definitions in UC used time since DX only (6 papers), combined with DX history and symptom duration (1 paper). Cut-off points for time since DX were applied in 30 papers: ≤3 months (20%), 3–6 months (17%), 6–12 months (27%), 1–2 yrs (17%) and >2 yrs (20%). Definitions based on DX history specified pts should be immunomodulator (IMM) and biologic naive (7 papers) or additionally corticosteroid (CS) naive (4 papers). ‘Early disease’ pt characteristics were stratified by CD and UC. Median disease duration ranged between 0.2–10.6 yrs in CD and 1.1–5.4 yrs in UC. CD cohorts included pts with stricturing (max 64%), penetrating (max 48%) or fistulising disease (max 14%). Disease and prior surgery (max 51%); UC cohorts included pts with pancolitis (max 100%) and prior surgery (max 69%) (see Table). ‘Early’ CD cohorts met the consensus criteria (disease duration <18 months and IMM and biologic naive) in only 2 papers published since 2012. Conclusion: The characteristics of ‘early’ CD and UC pts have increasingly come under focus as the concept of early intervention in IBID has gained traction. Early disease has predominantly been defined by time since DX (± other variables) but the disease duration of ‘early’ cohorts can be very long. Often ‘early’ pts already have complex disease, which may mean the ‘window of opportunity’ for intervention is missed. The consensus definition of ‘early’ CD has not been consistently applied since being developed. Robust definitions of early CD and UC are required to accurately evaluate the potential of early biologic tx to improve outcomes.

References

P0353 VEDOLIZUMAB OUTCOMES IN REAL-WORLD BIO-NAIVE ULCERATIVE COLITIS AND CROHN’S DISEASE PATIENTS (EVOLEVA): IN TREATMENT PATTERNS, CLINICAL EFFECTIVENESS AND SAFETY

Introduction: Vedolizumab (VDZ), a gut-selective humanised immunoglobulin G1 monoclonal antibody that binds to α4β7 integrin, is indicated in Canada for the treatment (Tx) of moderately-to-severely active ulcerative colitis (UC;19 May 2015) and Crohn’s disease (CD;19 May 2016). Real-world data on Tx patterns, clinical effectiveness and safety outcomes in biologic (bio)-naive patients treated with VDZ in Canada are limited. Aims and Methods: A retrospective cohort study was conducted in adult (>18 years) UC and CD patients who were bio-naive and newly initiated VDZ between 19 May 2015 and 31 Dec 2016. Real-world data on Tx patterns, clinical effectiveness and safety outcomes in biologic (bio)-naive patients treated with VDZ in Canada are limited.

References

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Table 1: Concomitant Corticosteroid Use, Clinical Effectiveness and Safety Outcomes Among Bio-naive Patients Treated with Vedolizumab

<table>
<thead>
<tr>
<th>Concomitant Corticosteroid Use</th>
<th>Clinical Effectiveness and Safety Outcomes</th>
</tr>
</thead>
</table>
| None                          | Achieved Clinical Remission: 12.0% (UC) 6.3% (CD) |}

Disclosure: The study was funded by Takeda Pharmaceuticals Company Ltd. BB received honoraria from Takeda; MB, DS and MS are employees of Evidera
P0354 FECAL MICROBIOTA TRANSPLANTATION IN CROHN’S DISEASE: A PILOT RANDOMIZED, SINGLE-BLIND, SHAM-CONTROLLED TRIAL

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Introduction: The role of gut microbiota in inflammatory bowel disease (IBD) pathogenesis is established and fecal microbiota transplantation (FMT) has shown some efficacy inducing remission in active ulcerative colitis in three randomized controlled clinical trials (RCT) to date. However there is no RCT result included while in flare (Harvey Bradshaw index [HBI] ≥ 4) and treated with oral corticosteroid. Following clinical remission (HBI < 5), patients were randomized to receive either FMT (50–100g of stool from a single donor suspended in 250–350mL of physiological serum) or sham transplantation (physiological serum) during a colonoscopy. Corticosteroids were tapered and a Sorensen index defined by a receiver’s fecal microbiota at week 6 closer to the donor (with a Sorensen index ≥0.6 [Sorensen index = 1- Bray Curtis index]) than to the patient before FMT. Clinical, biological and endoscopic efficacy endpoints were also evaluated (NCT02097797).

Results: Overall, 21 patients were randomized, 8 received donor FMT, 9 received sham-transplantation and 4 were ineligible for transplantation (3 because of patient identification and 1 for unavailability of donor). In the FMT group, none of the patients reached the primary endpoint. However, patients from the FMT group had a microbiota composition at 6 weeks closer to donors compared to patients in the Sham-transplantation group (p = 0.016). The steroid-free clinical remission rate at 10 and 24 weeks were 44.4% and 33.3% in the Sham-transplantation group and 87.5% and 57.1% in the FMT group (p = 0.13 and p = 0.6 respectively at week 10 and 24). CDEIS decreased 6 weeks after FMT (8.5 [4.6;13.0] vs. 3.5 [1.0;8.9]; p = 0.03) but not after Sham-transplantation (2.4 [0.6;8.3] vs. 2.7 [0.7;10.0]; p = 0.8). Conversely, CRP level increased 6 weeks after Sham-transplantation (3.0 [3.0;4.2] vs. 6.9 [4.0;8.7] mg/L; p = 0.008) but not after FMT (3.0 [3.0;3.0] vs. 3.0 [3.0;14.2] mg/L; p = 0.5). Failure to achieve steroid-free clinical remission at week 24 in FMT group was associated with absence of donor microbiota engraftment at week 6 and with the absence of increase in alpha diversity. The microbiota composition at week 6 was predictive of steroid-free clinical remission at week 24. No safety signal was identified.

Conclusion: None of the patients reached the primary endpoint related to the level of implantation of the donor microbiota. However, this pilot study in CD suggests that FMT performed after achieving clinical remission by corticosteroids could be effective as a maintenance treatment. A larger randomized control trial is now required to confirm the efficacy of this strategy.

Disclosure: Nothing to disclose
Results: 359 from 426 patients have so far been analysed (F = 153 [42.6%], UC = 160 [44%], CD = 190 [53%], indeterminate/other colitis = 9 [3%]). Mean duration on thiopurines was 5.7 years. Mean disease duration was 12.7 years. Out of 359 IBD patients on thiopurines, 275 (77%) had 6-TGN levels measured at some stage. 177/275 (64%) had therapeutic levels, whilst 98/275 (36%) did not. 166/275 (60.5%) were in clinical remission. 94/275 (34.5%) were Not for. For 15 patients (5%), no data was available. Of those that had therapeutic levels of 6-TGN, 112/177 (63%) were in clinical remission, 19/112 (17%) were in total remission (clinical, biochemical [normal CRP/WCC], endoscopic and histological). 60/112 (55%) were on Azathioprine (AZA), 48/112 (43%) were on mercaptopurine (6MP). For 4/112 (4%) patients there was no thiopurine treatment or the treatment was stopped. 46/112 (41%) were on combined therapy with biologics. Of those that had non-therapeutic levels of 6-TGN, 54/98 (55%) were in clinical remission. 13/54 (24%) were in total remission. 37/54 (68%) AZA, 15/54 (28%) 6MP, 2/54 (4%) data not complete/purines were stopped. 24/54 (44%) were on combined therapy with biologics. Of those with therapeutic levels of 6-TGN, 53/177 (30%) were not in clinical remission. 30/53 (57%) AZA, 22/53 (41%) 6MP, 1/53 (2%) patient data not complete/purines were stopped. 41/53 (77%) were on combined therapy with biologics. Of the cohort that had non-therapeutic levels of 6-TGN, 41/98 (42%) were not in clinical remission. 21/41 (51%) AZA, 15/41 (37%) 6MP, 5/41 (12%) data not complete/purines were stopped. 29/41 (71%) were on combined therapy. (Note: 12 of the 177 patients with therapeutic 6-TGN had no data on remission status. 3 of the 98 patients with non-therapeutic levels of 6-TGN had no data on remission status).

Conclusion: Our study so far suggests that in IBD patients on thiopurines (sole or combined therapy), clinical remission rates were similar (63% vs. 55%) for those with therapeutic levels and for those that had either not achieved therapeutic levels of 6-TGN, 55% of patients were still in clinical remission. Moreover, there is no significant relationship between achieving therapeutic 6-TGN levels and clinical remission when looked separately for clinical remission. Moreover, there is no significant relationship between achieving therapeutic 6-TGN levels and clinical remission when looked separately for clinical remission. Moreover, there is no significant relationship between achieving therapeutic 6-TGN levels and clinical remission when looked separately for clinical remission. Moreover, there is no significant relationship between achieving therapeutic 6-TGN levels and clinical remission when looked separately for clinical remission.

Disclosure: Nothing to disclose
P038 ENDOSCOPIC DILATION THERAPY FOR STRICTURING CROHN'S DISEASE OF THE SMALL INTESTINE USING BALLOON-ASSISTED ENDOSCOPY - A COMBINED ANALYSIS OF 733 ENDOSCOPIC BALLOON DILATION PROCEDURES

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Introduction: Strictures are a common complication of Crohn's disease (CD) and may develop in all segments of the gastrointestinal (GI) tract. While coloscopy has been proven safe and effective for balloon dilation therapy of GI-associated strictures of the ileocecum (1,2), the published evidence on efficacy and safety of balloon-assisted endoscopy (BAE) for balloon dilation therapy of CD strictures of the small intestine is scarce. We therefore performed a combined efficacy and safety analysis based on all published studies of BAE for small intestinal strictures available in the literature.

Aims and Methods: A formal systematic literature review was performed to access all relevant citations found in Embase, Medline and the Cochrane library regarding BAE used for EBD of small intestinal stricture. In addition, conference proceedings including Digestive Disease Week 2010-2017, European Crohn’s and Colitis Foundation 2011-2017, United European Gastroenterology Week 2013-2016, Gastroenterology 2016-2017, German Gastroenterology Congress 2013-2017 were screened for additional data. Available technical and clinical variables were extracted from all studies available for a descriptive pooled data analysis. With this data, we were able to analyse the following:

Results: 18 publications with a total of 445 CD patients and 773 performed dilation procedures were included. 19.3% were anastomotic strictures. Technical success rate was 88.1%, resulting in clinical efficacy in 78% of patients. Major complications with regard to dilation, defined as perforation, bleeding or dilation-related surgery, occurred in 3.7% of all procedures. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. Currently, there is no study available investigating the recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery. During a median follow-up period of 16 months, 45.7% of patients reported symptomatic recurrence, while 38.1% of patients needed to undergo re-dilation and 27.5% required surgery.

Conclusion: For dilation therapy of CD-associated strictures of the small intestine possesses a high rate of short-term technical and clinical success and may represent an alternative to surgery in stricturing CD. BAE-associated complication rates appear comparable to those related to dilation therapy of ileocecal stricture during colonoscopy. Larger, controlled studies are warranted to further evaluate BAE for dilation therapy of CD strictures of the small intestine.

Disclosure: Nothing to disclose

References

P0359 LONG-TERM SAFETY, EFFICACY AND PHARMACOKINETICS OF THE ANTI-MADCAM-1 MONOCLONAL ANTIBODY SHP647 IN CROHN'S DISEASE: THE OPERA II STUDY

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Introduction: The endothelial adhesion protein MAdCAM-1 is a promising novel drug target in inflammatory bowel disease; the fully human IgG2 anti-MAdCAM-1 monoclonal antibody SHP647 is in development for induction and maintenance of remission in patients with Crohn’s disease (CD) and ulcerative colitis.

Aims and Methods: OPERA II was a multicentre, open-label, phase 2 extension study (NCT01298492), designed to assess the long-term safety and efficacy of SHP647 in patients with moderate-to-severe CD. Eligible patients had completed 12 weeks’ induction treatment (placebo or 22.5 mg, 75 mg or 225 mg s.c. SHP647) in OPERA I (NCT01276509), or had a clinical response (≥3-point decrease in Harvey Bradshaw Index score) to 225 mg SHP647 in the open-label study, TOSCA (NCT01387594). Patients received SHP647 (75 mg, s.c.) every 4 weeks from baseline to week 72, and were followed up for safety assessments monthly for a further 24 weeks. Dose de-escalation to 22.5 mg owing to intolerance/treatment-emergent adverse events (TEAEs), or escalation to 225 mg owing to clinical deterioration/poor response, was allowed as judged by the investigator. Primary endpoints were frequency of TEAEs, TEAEs leading to withdrawal and SAXEs. Concentrations of serum SHP647, high-sensitivity C-reactive protein (hsCRP) and faecal calprotectin (FC) were assessed as secondary endpoints.

Results: Of the 268 patients who enrolled and entered the treatment period, 149 completed the study. Table 1 shows the proportions of patients experiencing TEAEs, TEAEs leading to withdrawal and serious adverse events (SAEs). The most common treatment-related TEAEs in the treatment period were arthralgia (6.0%), nasopharyngitis (5.6%) and headache (5.2%). 2 patients died: 1 during treatment (75 mg) of multiple organ failure after postoperative asphyxia following a resection of the terminal ileum (female, 30 years, SHP647 75 mg) and 1 during follow-up due to metastatic adenocarcinoma (unknown primary; male, 36 years, SHP647 225 mg); neither death was considered drug-related. No patients de-escalated their dose, and 157 patients increased their dose to 225 mg SHP647 after a median time of 28 weeks. Serum trough concentrations of SHP647 averaged 7051 ng/mL at week 4 and remained constant over time with a steady-state concentration of 7300 mg/mL at week 72. 3 months after dose escalation to 225 mg, patients achieved a new steady-state level of 16190 mg/mL, which is consistent with the pharmacokinetics determined previously. Patients whose dose escalated appeared to have more severe disease, with higher hsCRP (24.12±6.23 mg/L) and FC (2771.5±3293 mg/kg) levels at baseline than patients who remained on 75 mg, who had hsCRP and FC levels of 19.12±24.33 mg/L and 1232.1±2378 mg/kg, respectively. Concentrations of hsCRP decreased gradually over time from week 0 to 72; the pattern was similar in patients who received 75 mg and those who escalated to 225 mg, though at the end of the study, patients who had escalated their dose had higher values than those who had not.

Conclusion: SHP647 75 mg (with potential dose escalation to 225 mg) was generally well-tolerated in patients with Crohn’s disease over 72 weeks. These results add to evidence for the long-term safety of SHP647. [Table 1. All-cause and treatment-related adverse events in the treatment and follow-up periods.]

Disclosure: GRDH has been a consultant for Pfizer and Shire, and has received research support from Shire. WR has served as a speaker for Shire, and as a consultant and advisory board member for Pfizer. SDL has received grant and research support from Shire. DT has received research support from Pfizer. DM has served as a consultant to Pfizer. EL has received research grants and speaker fees from Pfizer. MJ has received payment for lectures/advisory boards from Abbvie, Eis, Takeda, Jansen and Ferring. JK has received speaker fees from and served on advisory boards for Pfizer. SS has served on advisory boards for Pfizer and Shire. DIP has served on advisory boards for Shire. XH has served as a speaker, and as an advisory board member for Pfizer. FC has been an employee of Pfizer and Shire, and holds stocks in Shire. SWM is an employee of Pfizer. SN is an employee of Pfizer. AB is an employee of Pfizer. KG is a consultant to Pfizer and Shire. WJS has been a consultant for Pfizer and Shire, and has received research support from Shire.
**P0360** FMT CAPSULES DECREASE FECAL CALPROTECTIN AND IMPROVE SYMPTOMS IN ULCERATIVE COLITIS PATIENTS - A PILOT STUDY

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**Introduction:** There is growing evidence indicating that gut ‘dysbiosis’ is one of the factors in the pathogenesis of Inflammatory Bowel Disease (IBD). Fecal microbiota transplantation (FMT) from healthy donors is an effective treatment of recurrent *Clostridium difficile* infections both when administered by endoscopy or through oral capsules (2). In this study we aimed to be promising in Ulcerative Colitis remission induction (3). However long-term safety and effects on ulcerative colitis remain unclear.

**Aims and Methods:** The aim was to test if multi-donor FMT capsules, manufactured at the laboratory at Aleris-Hamlet Hospital, Copenhagen, could lower Fecal (F) Calprotectin and improve symptoms in patients with Ulcerative Colitis and to test the safety of the treatment.

7 patients, aged 27 to 51 years, with Ulcerative Colitis, a Simple Clinical Colitis Index (SCAI) between 4 and 10, and F-Calprotectin > 250 mg/kg were treated with 25 multi-donor FMT capsules daily for 50 days as a supplement to each individual patient’s stable dose of standard treatment throughout the period of intervention. The 4 fecal donors were healthy individuals who were screened according to current guidelines (4) and recruited through postings in the area around the hospital. Participants were followed with fecal samples and SCAI throughout the study period. We used Mann-Whitney U tests to compare F-Calprotectin and SCAI levels at each time-point after baseline with the levels at baseline.

**Results:** Median F-Calprotectin at baseline was ≥1800 mg/kg (the upper limit for Calprotectin at our laboratory was 1800 mg/kg). After 4 weeks of treatment F-Calprotectin decreased to 6 of the 7 participants and there was a significant decrease in median F-Calprotectin of 912 mg/kg (p = 0.004). 1 week after the intervention had stopped, at 8 weeks from baseline, the median decrease in F-Calprotectin from baseline of 551 mg/kg was no longer statistically significant (p = 0.14).

The participants had a median SCAI of 6 at baseline. After both 4 and 8 weeks all participants had lowered their SCAI and there was a significant decrease in median SCAI of, respectively, 5 (p = 0.001) and 6 (p = 0.001).

All participants completed the treatment and no serious adverse events were registered throughout the study period.

**Conclusion:** Daily multidonor FMT-capsules were safe and significantly lowered F-Calprotectin in Ulcerative Colitis patients with SCAI between 4 and 10 after 4 weeks of active treatment. The participants also experienced a significant improvement in symptoms throughout the study period.

FMT administered in various forms appears promising in the treatment of Ulcerative Colitis but many questions remain. In particular, the type of FMT administered in various forms appears promising in the treatment of recurrent *Clostridium difficile* infections both when administered by endoscopy or through oral capsules (2). In this study we aimed to be promising in Ulcerative Colitis remission induction (3). However long-term safety and effects on ulcerative colitis remain unclear.

**Disclosure:** Nothing to disclose

**References**


**P0361** POPULATION PHARMACOKINETIC AND PHARMACODYNAMIC ANALYSIS OF SHP647, A FULLY HUMAN MONOCLONAL ANTIBODY AGAINST MUCOSAL ADDRESSIN following repeated subcutaneous (SC) administration of 7.5, 22.5, 75, and 225 mg every 4 weeks was performed to identify sources of variability and support dosing in adult patients with UC/CD. A total of 440 patients were included in the analysis, of whom 249 (56.6%) had UC and 191 (43.4%) had CD. Population PK analysis of SHP647 nec and model fitting was performed for apparent linear and/or linear elimination. Covariate analysis was performed using a step-wise covariate approach. The following covariates were explored: age, sex, markers of renal and liver function (i.e., creatinine clearance, bilirubin, AST, ALT) as well as renal impairment categories (normal, mild, moderate, severe disease (UC/CD), anti-drug antibody (ADA), free MacAdCAM-1 levels and various laboratory measurements (C-reactive protein [CRP], albumin, fecal calprotectin, and colonoscopy score). PK and PD analyses were performed using NONMEM.

**Results:** Patients with UC/CD presented with similar mean age (40.4 and 36.0 years, respectively) and body weight (72.5 kg and 70.6, respectively). SHP647 was very well tolerated in patients with UC/CD. A 2-compartment model with linear and non-linear eliminations was fitted in an adequate characterization of concentration-time profiles. An empirical allometric function was used on clearance and volume parameters. The absorption of SHP647 was described with a first-order rate constant of absorption (Ka) and absorption lag time. Population estimates of apparent clearance (CL/F) volume of distribution (V/F), and volume of distribution (V/F) were 0.0127 L/h (0.305 L/day) and 6.53 L, respectively. The CL/F was mainly dependent on baseline CRP and albumin while V/F was mainly dependent on body weight. No covariates were observed in patients with UC/CD. ADA was not identified as a covariate explaining the variability of CL/F. The Michaelis-Menten constant (KM) was very low (19.0 ng/mL) suggesting that the non-linear elimination (target-mediated) occurred at very low concentrations, and was less likely to contribute significantly to elimination half-life at therapeutic concentrations and under steady state conditions. The apparent SHP647 half-life associated with average steady state concentrations for the 7.5, 22.5, 75, and 225 mg dose levels were 7.04, 12.3, 16.5 and 18.6 days, respectively. A linear PK/PD model was used to describe the relationship between concentrations of SHP647 and the median change in calprotectin. Based on minimum concentrations of SHP647 under steady state conditions, the 75 and 225 mg doses were associated with >95% suppression of circulating MacAdCAM-1 levels.

**Disclosure:** Y Wang is an employee of Shire. JF Marier is a paid consultant of Certara. N Kassir is a paid consultant of Certara. P Martin is an employee of Shire.
patients in induction, TOFA 10mg BID had the greatest efficacy (60% and 18%) and had >99% probability of having better efficacy compared with ADA (36% and 7%). Among RR trials, TOFA had the greatest efficacy (5mg BID: 71% and 54%; 10mg BID: 72% and 56%) and had a 70–99% probability (depending on the comparator) of having better efficacy than other agents in the TNFi-naive subgroup. TOFA 10mg BID had the greatest efficacy (61% and 49%) and a 72–79% probability of having better efficacy than other agents in the TNFi-exposed subpopulation. Results among TT trials were similar. The probability of TOFA having better efficacy than other agents was 83–98% and 67–91% for TNFi-naive and TNFi-exposed, respectively.

Conclusion: Except compared with IFX in the TNFi-naive induction setting, TOFA has similar or superior efficacy compared with biologics as induction and maintenance therapy for moderately-to-severely active UC.

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P0363 PREDICTING OUTCOME IN ACUTE SEVERE ULCERATIVE COLITIS: COMPARISON OF THE OXFORD, EDINBURGH, LINDGREN AND ENDOSCOPIC MAYO SCORES

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Introduction: Up to one-third of patients with acute severe Ulcerative Colitis (ASUC) will fail intravenous corticosteroids (IVCT) treatment, requiring rescue therapy with Cyclosporin (Cy), Infliximab (IFX) or colectomy. Although several scores for predicting response to IVCT exist, formal comparison is lacking.

Aims and Methods: This was a retrospective cohort single-center study. The endoscopic Mayo score and the Oxford, Edinburgh and Lindgren scores were determined at admission and on the 3rd day of IVCT treatment, respectively. Outcomes included prediction of steroid refractoriness, need for rescue medical therapy and surgery.

Results: From 489 patients with Ulcerative Colitis, 112 presented with ASUC; 58% were male with a median age of 33.5 years (range 18–80). The median of Truelove and Witts score was 4 (range 2–35). 35% of patients showed an incomplete or absent response to IVCT, 28.6% received rescue medical therapy (65.6% with IFX, 31.3% with Cy and 3.1% received sequential therapy with Cy and IFX) and 13.4% were colectomized up to 1 year from admission. The Lindgren score was also a better predictor of the need of colectomy than the Edinburgh, Oxford and endoscopic Mayo scores in predicting steroid refractoriness, need for rescue medical therapy and colectomy.

Disclosure: Nothing to disclose

P0364 RISK OF VENOUS THROMBOEMBOLISM BY DISEASE ACTIVITY, HOSPITALIZATION, AND SURGERY IN INFLAMMATORY BOWEL DISEASE: A NATIONWIDE COHORT STUDY

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Introduction: Risk of venous thromboembolism (VTE) of inflammatory bowel disease (IBD) patient is higher than general population. Guidelines recommend primary prophylaxis of venous thromboembolism for certain periods. However, little is known about the magnitude of the risk of VTE development in these periods. We estimated the risk of VTE during a hospitalized flare, a non-hospitalized flare, a hospitalization without flare, IBD-related surgery, and other major surgeries.

Aims and Methods: Using the National Health Insurance claims data for the entire Korean population, we included 33,131 patients with IBD from January 2012 until December 2013 with 198,825 age- and sex-matched controls, and followed up until December 2016. We used Cox regression models to identify whether the risk of VTE varies by hospitalization, disease flare, surgery and/or presence of other risk factors.

Results: Of 33,131 patients with IBD and 198,825 matched controls, 110 patients and 376 controls developed VTE. The overall VTE risk was higher in patients with IBD than controls with [adjusted hazard ratio (aHR), 2.10; 95% confidence interval (CI), 1.70–2.61], compared to controls. The risk of VTE during a non-hospitalized flare of IBD patients was higher compared with controls (aHR, 3.14; 95% CI, 1.90–5.19). The risks of VTE were increased much more during a hospitalization with non-flare (aHR, 16.23; 95% CI, 10.71–24.58) and a hospitalized flare (aHR, 27.20; 95% CI, 19.40–49.65). The risk of VTE was highest at the time of IBD-related surgery (aHR, 39.66; 95% CI, 9.87–159.33). Also, the risk at the time of other major surgeries was increased (aHR, 15.59; 95% CI, 7.73–31.43).

Conclusion: The prophylaxis of VTE for Asian patients with IBD should be considered at the time of a hospitalized flare and IBD-related surgery. However, the prevention of VTE is not needed for non-hospitalized patients with flare.

Disclosure: Nothing to disclose

Abstract No: P0364

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**P0365** SURGICAL AND HOSPITAL ADMISSION IN ADULTS NEWLY DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE: RESULTS OF THE NATIONWIDE EPIDEMIBD STUDY OF GETECCU

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Introduction: The need for surgery and hospital admission in newly diagnosed inflammatory bowel disease (IBD) patients in the biological era is largely unknown.

Aims and Methods: i) To assess the frequency of surgery and hospital admission in an inception cohort of adults newly diagnosed with IBD. ii) To describe the characteristics and indications for surgical interventions; and iii) to evaluate the causes of hospital admissions.

Prospective and population-based nationwide study in Spain. Adult patients diagnosed with IBD’s disease (CD), ulcerative colitis (UC) or indeterminate colitis (IC) - during 2017 in the 17 Spanish regions were included and followed-up for 12 months after diagnosis. Data were captured in a web-based database (AEG-REDCap).

Results: 3,469 incident cases from 116 centres covering approximately 50% of the Spanish population were included. Of them, 53% were males, with mean age of 43 years. At baseline 50% had UC, 45% CD, and 5% IC. About 14% of patients had a family history of IBD. CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis.

Conclusion: In this large nationwide inception cohort in the biological era, surgery was not more frequent among CD patients with perianal disease than in those without it (34 vs. 5.2%, p < 0.001). Other variables, such as family history of IBD, or smoking habit were not associated with the need of surgery. A total of 892 patients (26%) had 1,038 hospital admissions during follow-up, with disease diagnosis as the main indication (71.2%). Among them, 53% were males, with mean age of 43 years. At baseline 50% had UC, 45% CD, and 5% IC. About 14% of patients had a family history of IBD. CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis. In CD patients, 55% had ileal and 26% ileocolonic location, and 11% perianal disease. In UC patients, 34% had extensive colitis and 52% pan-colitis.

P0366 SHORT TERM AZATHIOPRINE CO-TREATMENT DOES NOT IMPACT LONG TERM CLINICAL OUTCOME IN INFLAMMATORY BOWEL DISEASE TREATED WITH INFlixIMAB, BUT HAS INFlixIMAB-SPARING EFFECT

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2University Medical Centre Ljubljana, Gastroenterology, Ljubljana, Slovenia
3University Medical Centre Ljubljana, Gastroenterology, Ljubljana, Slovenia
4University Medical Centre Ljubljana, Gastroenterology, Ljubljana, Slovenia
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Introduction: It is usual clinical practice to start infliximab as combination treatment with azathioprine in patients with inflammatory bowel disease (IBD) and to de-escalate from combination treatment to infliximab (IFX) monotherapy once disease remission is reached. It is however unclear if the addition of azathioprine during introduction of IFX improves long-term clinical outcomes and pharmacokinetics in patients who previously failed azathioprine.

Aims and Methods: We aimed to study the effect of short-term (6–12 months) co-treatment with azathioprine on long-term clinical outcome and on consumption of IFX in patients who escalated from azathioprine to either IFX monotherapy or to combination of azathioprine and IFX due to inefficacy of azathioprine. We included 149 patients (94 Crohn’s disease, 55 ulcerative colitis) who started IFX between 2011 and 2016 for active IBD in a tertiary referral centre. To study the effect of azathioprine co-treatment we compared patients who started IFX as combination treatment with azathioprine and then de-escalated to IFX monotherapy with patients who started IFX as monotherapy from the beginning (IFX mono).

Results: The study population included 78 (52%) IFX combo patients and 71 (48%) IFX mono patients. IFX combo (Crohn’s disease: ileocolonic 71%, perianal 42%; ulcerative colitis: pancolitis 62%) and IFX mono (Crohn’s disease: ileocolonic 74%, perianal 29%; ulcerative colitis: pancolitis 69%) groups did not differ in disease phenotype.

During a median follow-up of 19 months [interquartile range (IQR): 12–40 months] 149 patients (43.3%) underwent 188 surgical interventions: 131 (83.8%) in CD and 18 (9.0%) in UC (p < 0.001). Regarding the first surgical procedure, 60% were urgent and 60% entailed abdominal surgery (30% for perforation, 28% for stenosis and 26% for abdominal abscess). CD patients with inflammatory behaviour had lower rates of surgery than those with stricture or fistula (5.6%, 14%, and 32%, respectively, p < 0.001). Surgery was also more frequent among CD patients with perianal disease than in those without it (34 vs. 5.2%, p = 0.001). Other variables, such as family history of IBD, or smoking habit were not associated with the need of surgery. A total of 892 patients (26%) had 1,038 hospital admissions during follow-up, with disease diagnosis as major driver (81%). Median time from diagnosis to admission was 0 months (range 0–9 months). Reasons for hospital admissions are summarized in table 1. Conclusion: In this large nationwide inception cohort in the biological era, a substantial proportion of IBD patients underwent surgery, which was urgent in over 2/3 of the cases. Strictureting and fistulizing complications in CD patients were the main drivers for surgery in these patients. 1/4 of patients were hospitalized – most of them at disease diagnosis – within the first 3 months follow-up.

[Table 1. Reasons for hospital admissions during follow-up.]

<table>
<thead>
<tr>
<th>Reason</th>
<th>IBD (N = 507)</th>
<th>UC (N = 385)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal abscess, n (%)</td>
<td>11 (2.2)</td>
<td>9 (1.8)</td>
</tr>
<tr>
<td>Thiopurine adverse event, n (%)</td>
<td>9 (1.8)</td>
<td>5 (1.3)</td>
</tr>
<tr>
<td>Intestinal obstruction, n (%)</td>
<td>34 (6.9)</td>
<td>25 (6.5)</td>
</tr>
<tr>
<td>Elective surgery, n (%)</td>
<td>2 (0.4)</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>Infection, n (%)</td>
<td>4 (0.9)</td>
<td>10 (2.6)</td>
</tr>
<tr>
<td>Fever of unknown origin, n (%)</td>
<td>6 (0.6)</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Perforation, n (%)</td>
<td>4 (0.8)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Mesiadze induced pneumonitis, n (%)</td>
<td>2 (0.4)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Others, n (%)</td>
<td>19 (3.8%)</td>
<td>4 (1.2%)</td>
</tr>
</tbody>
</table>

(continued)
**P0367 MAINTENANCE OF REMISSION WITH TOFACITINIB IN PATIENTS WITH ULCERATIVE COLITIS: SUBPOPULATION ANALYSIS FROM AN OPEN-LABEL, LONG-TERM EXTENSION STUDY**


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**Introduction:** Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). The efficacy and safety of tofacitinib were demonstrated in 3 Phase (P) 3, randomised, placebo-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951; OCTAVE Sustain, NCT01458574) in patients (pts) with moderate to severe UC. An ongoing P3, multicentre, open-label, long-term extension study (OLE; NCT01470612) included pts from OCTAVE Induction 1 or 2, or OCTAVE Sustain.

**Aims and Methods:** We present an update (as of 10 Nov 2017) of previous analyses of the OLE study maintenance remission subpopulation (pts in remission [total Mayo score ≤ 2, no individual subscore >1, rectal bleeding subscore of 0] at Wk [Wk] 52 of OCTAVE Sustain). Pts in remission at Wk 52 of OCTAVE Sustain received tofacitinib 5 mg twice daily (BID) in the OLE study. Efficacy data, including remission, mucosal healing (Mayo endoscopic subscore of 0 or 1), clinical response (decrease from induction baseline total Mayo score ≥ 30%, and ≥ 50%, and decrease in rectal bleeding subscore ≥1 or absolute rectal bleeding subscore of 0 or 1; all based on local read) and partial Mayo score (PMS) remission (PMS ≤ 2, no individual subscore >1), up to Month 24 of the OLE study (as observed and with non-responder imputation), are presented for pts in remission after tofacitinib in OCTAVE Sustain. Safety data are reported for all pts who received tofacitinib 5 mg BID in the OLE study.

**Results:** Of 944 pts who received ≥1 dose of study drug in the OLE study, 163 (mean age: 45 years; 46.0% female) were in remission at Wk 52 of OCTAVE Sustain (NCT01458574). Efficacy over 24 months was similar irrespective of tofacitinib dose previously received in OCTAVE Sustain. Among all pts receiving tofacitinib 5 mg BID in the OLE study, 78.9% reported treatment-emergent AEs (TEAEs). Serious and severe AEs occurred in 12.0% and 8.0% of pts, respectively. The most frequent TEAEs by preferred term were *nasopharyngitis* and *worsening of UC*. 5 pts (2.9%) had serious infections and 10 (5.7%) had herpes zoster (all mild or moderate severity). Malignancy excluding non-melanoma skin cancer was reported in 1 (0.6%) pt (lung cancer).

**Conclusion:** The majority of pts with moderate to severe UC who achieved remission after 52 wks of tofacitinib 5 mg in OCTAVE Sustain maintained remission, mucosal healing, clinical response and PMS remission with tofacitinib 5 mg BID for up to 24 months in the OLE study (up to 3 years from maintenance study baseline). No new safety risks were identified.

**Disclosure:** J-F Colombel has received research support from AstraZeneca, Ferring, Schering-Plough, UCB, and consultancy and/or lecture fees from Abbott, ActoGeniX, Albioreo Pharma, Amgen, AstraZeneca, Bayer AG, Biogen Idec (BI), BMS, Cellerix, Centocor, Celltrion, ChemoCentryx, Covance, Danone, Dr Falk, Eli Lilly, Ferring, Galapagos, Genentech, Gilead, Grunenthal, ICON, Immunodiagnostik, InDex Pharmaceuticals, Inova, Jansen, J&J, Kyowa Hakko Kirin, Lipid Therapeutics, MedImmune, Millennium, Mitsubishi Tanabe, MSD, Novartis, Oceia, Otsuka, PDL, Pfizer Inc, Pharmacosmos, Procter & Gamble, Prometheus, Roberts Clinical Trials, Schering-Plough, Second Genome, SetPoint Medical, Shire, Takeda, Therakos, TiGenix, UCB, Vifor, Yakult, Zentiva, 4SC; MT Osterman has received consultancy fees from AbbVie, Jansen, Lycera, MedImmune, Novo Nordisk, Takeda, UCB; AJ Thorpe and research support from UCB; C.I Nduaka, H Zhang, N Lawyend, G.S Friedman, C Su are Pfizer Inc employees and shareholders.

**References**

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**P0368 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF ULCERATIVE COLITIS: AN INTERIM ANALYSIS OF AN OPEN-LABEL, LONG-TERM EXTENSION STUDY WITH UP TO 4.9 YEARS OF TREATMENT**

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**Introduction:** Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). The efficacy and safety of tofacitinib was demonstrated as induction and maintenance therapy in patients (pts) with moderate to severe UC to achieve UC in 3 Phase (P) 3, randomised, placebo-controlled studies. Safety and efficacy of tofacitinib for UC are being evaluated in an ongoing, open-label, long-term extension (OLE) study.

**Aims and Methods:** We present an update (as of 10 Nov 2017) of previously presented safety and efficacy data of an ongoing P3, multicentre, OLE study (NCT01470612) in pts who completed or demonstrated treatment failure in OCTAVE Sustain (NCT01458574) or were non-responders in OCTAVE Induction 1 or 2, or OCTAVE Sustain. Pts in remission (total Mayo score ≤ 2, no individual subscore >1, rectal bleeding subscore of 0) at Wk 52 of OCTAVE Sustain (per local read) were assigned to receive tofacitinib 5 mg daily BID in the OLE study. Pts under went endoscopy, and induction non-responders were mandated to withdraw if they did not show a clinical response. Efficacy end points were derived from Mayo Clinic scores per local read.

**Results:** Of 944 pts who received ≥1 dose of study drug (for up to 4.9 years), 769 (81.5%) pts received tofacitinib 10 mg BID; 326 (34.5%) pts discontinued due to insufficient clinical response, and 65 (6.9%) pts discontinued due to adverse events [AEs] excluding worsening UC. Serious and severe AEs occurred in 14.8% and 9.9% of pts, respectively. The most frequent treatment-emergent AE (TEAE) classes were infections and gastrointestinal disorders. The most frequent TEAEs were nasopharyngitis, worsening UC and increased blood creatine phosphokinase. Serious infections were reported in 5 (2.9%) and 23 (3.0%) pts, herpes zoster in 10 (5.7%) and 47 (6.1%) pts, and major adverse cardiovascular events in 1 (0.6%) and 1 (0.1%) pts in the 5 and 10 mg BID groups, respectively. Malignancies excluding non-melanoma skin cancer (NMSC) were reported in 1 pt (0.6%) and 1 pt (2.3%) and NMSC in 4 (2.3%) and 9 (1.2%) pts, in the 5 and 10 mg BID groups, respectively (with no clustering of malignancy type). No new safety risks were identified. Available remission, mucosal healing and clinical response data up to Month 24 are shown (Table).

**Conclusion:** In pts with moderate to severe UC in the OLE study, no new safety risks emerged compared with those observed with tofacitinib in rheumatoid arthritis. Efficacy data from the OLE study continue to support long-term efficacy with tofacitinib 5 or 10 mg BID up to 24 months beyond Wk 52 of OCTAVE Sustain.

**Disclosure:** GR Lichtenstein has received research support from Celgene, Jansen, Pfizer Inc, Salix/Valant, Santarus/Receptors, Shire, Takeda, UCB; con- sultancy fees from Abbott/Ambivie, Alaven, Alven, Cellceutix, Celgene, Ferrin, Gilead, Hospita, Jansen, Lupoid/Pediatric American, Pfizer Inc, Prometheus, Romark, Salix/Valant, Santarus/Receptors, Shire, Takeda, UCB; and honoraria from Ironwood, Lupoid/Pediatric American, Merck, Romark, EV Loftus Jr. has received research support from AbbVie, Amgen, Celgene, Genentech, Gilead, Jansen, MedImmmune, Pfizer Inc, Receptors, Robarts Clinical Trials, Seres, Takeda, UCB; and consultancy fees from AbbVie, Amgen, CVS Caremark, Eli Lilly, Jansen, Mesoblast, Pfizer Inc, Salix, Takeda, UCB; S Bloom has received...
Abstract No: P0367

Table: Efficacy of tofacitinib 5 mg BID in patients in the maintenance remission subpopulation of the OLE study who previously received tofacitinib 5 or 10 mg BID in OCTAVE Sustain

<table>
<thead>
<tr>
<th>Previous treatment in OCTAVE Sustain</th>
<th>Tofacitinib 5 mg BID (N = 66)</th>
<th>Tofacitinib 10 mg BID (N = 76)</th>
<th>Tofacitinib 5 or 10 mg BID (N = 142)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission, n/N1 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline; central read</td>
<td>66/66 (100.0)</td>
<td>76/76 (100.0)</td>
<td>142/142 (100.0)</td>
</tr>
<tr>
<td>Month 2</td>
<td>49/60 (81.7)</td>
<td>60/76 (78.9)</td>
<td>109/136 (80.1)</td>
</tr>
<tr>
<td>Month 12</td>
<td>50/66 (75.8)</td>
<td>56/73 (76.7)</td>
<td>106/139 (76.3)</td>
</tr>
<tr>
<td>Month 24</td>
<td>26/42 (61.9)</td>
<td>32/52 (61.5)</td>
<td>58/94 (61.7)</td>
</tr>
<tr>
<td>Mucosal healing, n/N1 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline; central read</td>
<td>66/66 (100.0)</td>
<td>76/76 (100.0)</td>
<td>142/142 (100.0)</td>
</tr>
<tr>
<td>Month 2</td>
<td>56/63 (88.9)</td>
<td>68/76 (89.5)</td>
<td>124/139 (89.2)</td>
</tr>
<tr>
<td>Month 12</td>
<td>51/66 (77.3)</td>
<td>63/75 (84.0)</td>
<td>114/141 (80.9)</td>
</tr>
<tr>
<td>Month 24</td>
<td>30/43 (69.8)</td>
<td>38/53 (71.7)</td>
<td>68/96 (70.8)</td>
</tr>
<tr>
<td>Clinical response, n/N1 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline; central read</td>
<td>66/66 (100.0)</td>
<td>76/76 (100.0)</td>
<td>142/142 (100.0)</td>
</tr>
<tr>
<td>Month 2</td>
<td>57/60 (95.0)</td>
<td>70/76 (92.1)</td>
<td>127/136 (93.4)</td>
</tr>
<tr>
<td>Month 12</td>
<td>58/66 (87.9)</td>
<td>63/73 (86.3)</td>
<td>121/139 (87.1)</td>
</tr>
<tr>
<td>Month 24</td>
<td>32/42 (76.2)</td>
<td>41/52 (78.8)</td>
<td>73/94 (77.7)</td>
</tr>
<tr>
<td>PMS remission, n/N1 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>66/66 (100.0)</td>
<td>76/76 (100.0)</td>
<td>142/142 (100.0)</td>
</tr>
<tr>
<td>Month 2</td>
<td>60/63 (95.2)</td>
<td>67/76 (88.2)</td>
<td>127/139 (91.4)</td>
</tr>
<tr>
<td>Month 12</td>
<td>58/66 (87.9)</td>
<td>61/74 (82.4)</td>
<td>119/140 (85.0)</td>
</tr>
<tr>
<td>Month 24</td>
<td>33/43 (76.7)</td>
<td>42/53 (79.2)</td>
<td>75/96 (78.1)</td>
</tr>
</tbody>
</table>

*Patients in remission, based on central endoscopic reading, at Wk 52 of OCTAVE Sustain (all receiving tofacitinib 5 mg BID in OLE study); †Patients were treated as non-responders after the time of discontinuation up to the visit they would have reached if they had stayed in the study. No imputation for missing data was applied for ongoing patients. All values are per local read of endoscopy, unless otherwise stated (baseline values are per central read). Remission was defined as a total Mayo score ≤2 with no individual subscore >1, and rectal bleeding subscore of 0; mucosal healing was defined by a Mayo endoscopic subscore ≤1; PMS remission was defined as a PMS ≤2 with no individual subscore >1.

BID, twice daily; n, number of patients in the maintenance remission subpopulation with the specified response within the given category; N, number of randomised patients in the maintenance remission subpopulation; N1, number of patients in the remission subpopulation who could have reached the specified time point (based on enrolment date and last non-missing total Mayo score [endoscopy for mucosal healing]; NRI, non-respondent imputation; OLE, open-label long-term extension; PMS, partial Mayo score; Wk, Week.

research support from Pfizer Inc, and has been on advisory boards for J&J, Pfizer Inc, Tillyotts, Takeda; N Liwendi, G Chun, GS Friedman, H Zhang, W Wang, AJ Thuerpe, CI Nduaka, C Su are Pfizer Inc employees and shareholders.

References
**Aims and Methods:** Aim of this study has been to investigate its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients seven year after the institution of treatment. Data from consecutive IBD outpatients referred in our Institution, between 1985-2016, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2–2.5 mg/kg.

**Results:** Out of 2802 consecutive IBD outpatients visited in the index period, AZA was prescribed to 433 patients, 236 (54.5%) were affected by Crohn’s disease (CD) and 197 (45.5%) by ulcerative colitis (UC). 179 patients with a follow-up < 84 months were excluded from the study. 254 patients were evaluated, 141 (55.5%) with CD and 113 (44.5%) with UC. 139 (54.7%) were male patients referred in our Institution, between 1985–2016, were reviewed and all

<table>
<thead>
<tr>
<th>Table: Summary of safety and efficacy in the OLE study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline demographics and disease characteristics</strong></td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td>Age in years, mean (SD)</td>
</tr>
<tr>
<td>Total Mayo score, mean (SD)</td>
</tr>
</tbody>
</table>

**Discontinuations, n (%)**

- Due to AE excluding worsening UC: 12 (6.9)
- Due to insufficient clinical response: 14 (8.0)

**All-causality TEAEs, n (%)**

<table>
<thead>
<tr>
<th>AEs</th>
<th>Tofacitinib 5 mg BID N = 175</th>
<th>Tofacitinib 10 mg BID N = 769</th>
<th>Tofacitinib All N = 944</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAEs</td>
<td>138 (78.9)</td>
<td>607 (78.9)</td>
<td>745 (78.9)</td>
</tr>
<tr>
<td>Severe AEs</td>
<td>21 (12.0)</td>
<td>119 (15.5)</td>
<td>140 (14.8)</td>
</tr>
<tr>
<td>Gastrointestinal AEs</td>
<td>14 (8.0)</td>
<td>79 (10.3)</td>
<td>93 (9.9)</td>
</tr>
<tr>
<td>Any infections</td>
<td>64 (36.6)</td>
<td>321 (41.7)</td>
<td>385 (40.6)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>91 (52.0)</td>
<td>375 (48.8)</td>
<td>466 (49.4)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>5 (2.9)</td>
<td>23 (3.0)</td>
<td>28 (3.0)</td>
</tr>
<tr>
<td>MACE</td>
<td>10 (5.7)</td>
<td>47 (6.1)</td>
<td>57 (6.0)</td>
</tr>
<tr>
<td>Malignancies excluding cervical dysplasia</td>
<td>1 (0.6)</td>
<td>1 (0.1)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>NMSC</td>
<td>1 (0.6)</td>
<td>12 (1.6)</td>
<td>13 (1.4)</td>
</tr>
<tr>
<td>NMSC</td>
<td>4 (2.3)</td>
<td>9 (1.2)</td>
<td>13 (1.4)</td>
</tr>
</tbody>
</table>

**Efficacy endpoints (FAS, as observed)**

- Remission, n/N1 (%)
  - Month 2: 130/164 (78.3)
  - Month 12: 129/154 (83.8)
  - Month 24: 69/88 (78.4)
- Mucosal healing, n/N1 (%)
  - Month 2: 152/169 (89.9)
  - Month 12: 140/156 (89.7)
  - Month 24: 79/90 (87.8)
- Clinical response, n/N1 (%)
  - Month 2: 159/164 (97.0)
  - Month 12: 147/154 (95.5)
  - Month 24: 86/88 (97.7)

**Efficacy endpoints (FAS, NRI)**

- Remission, n/N1 (%)
  - Month 2: 130/168 (77.4)
  - Month 12: 129/172 (75.0)
  - Month 24: 69/118 (58.5)
- Mucosal healing, n/N1 (%)
  - Month 2: 152/172 (88.4)
  - Month 12: 140/174 (80.5)
  - Month 24: 79/120 (65.8)
- Clinical response, n/N1 (%)
  - Month 2: 159/168 (94.6)
  - Month 12: 147/172 (85.5)
  - Month 24: 86/118 (72.9)

**Summary of safety and efficacy in the OLE study**
and 115 (45.3%) female (average age of 35.62 ± 14.20 SD years, range 14–74 y.). 7 years after the institution of treatment, 127 (50%) patients still were in steroid-free remission (83 CD vs 44 UC, 58.8% and 38.9%, respectively, p = 0.0024), 71 (27.9%) had a relapse requiring retreatment with steroids (29 CD vs 42 UC, 20.6% and 37.2%, respectively, p = 0.0047), 56 (22.1%) discontinued the treatment due to side effects (29 CD vs 27 UC, 20.6% and 23.9%, respectively). Loss of response from 1st to 7th year of follow-up was low, about 20%.

**Conclusion:** 7 year after the onset of treatment 50% of patients did not require further steroid courses. After the first year loss of response was low in 6 subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.

**Disclosure:** Nothing to disclose

**Table:**

<table>
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Log FC (continued)
**P0372 SAFETY AND EFFECTIVENESS OF GRANULOCYTE AND MONOCYTE ABDUCTION USING MUCOSAL samples of patients with CORTICOSTEROIDS NAIVE ULCERATIVE COLITIS PATIENTS: A MULTICENTER COHORT STUDY**
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**Introduction:** To evaluate the efficacy of granulocyte and monocyte apheresis (GMA) in corticosteroids naive patients with active ulcerative colitis (UC) without concomitant corticosteroids therapy in remission induction and sustained remission.

**Aims and Methods:** In this multicenter retrospective study, ninety corticosteroids naive patients with active UC received GMA as remission induction therapy between 2012 and 2018 in 4 Japanese institutes were enrolled. Each patient received weekly or intensive (2–3 sessions/week) GMA up to 11 sessions. Partial Mayo score <2 meant remission, while ≤1 in Mayo endoscopic subscore meant mucosal healing. Concomitant medication with corticosteroids, biologics or calcineurin inhibitors were not allowed, but medication with 5-ASA and immune-modulators were permitted.

**Results:** The overall remission and mucosal healing rates were 71.1% (64/90) and 64.5% (49/76), respectively. Subjects who achieved a remission were clinically and endoscopically followed for 12 months after a course of GMA. After 12 months follow up, a sustained remission was recorded in 66.7% (44/66) of those treated with GMA. The patients who had obtained a remission after a course of GMA showed relapses up to 33.3% (22/66) and mean time to relapse was 10.0 months.

**Conclusion:** The overall remission and mucosal healing rates were 71.1% (64/90) and 64.5% (49/76), respectively. Subjects who achieved a remission were clinically and endoscopically followed for 12 months after a course of GMA. After 12 months follow up, a sustained remission was recorded in 66.7% (44/66) of those treated with GMA. The patients who had obtained a remission after a course of GMA showed relapses up to 33.3% (22/66) and mean time to relapse was 10.0 months.

**Disclosure:** Nothing to disclose.

**P0373 ADVANCES IN OPTIMIZATION OF THERAPEUTIC DRUG MONITORING USING MUCOSAL TNF EXPRESSION AND ANTI-TNF CONCENTRATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH BIOLOGICALS - PRELIMINARY RESULTS FROM A SINGLE CENTER STUDY**
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**Introduction:** The introduction of anti-TNF therapy has dramatically changed the treatment of refractory inflammatory bowel disease (IBD-Crohn’s disease [CD], ulcerative colitis [UC]). However, the clinical use of anti-TNF therapies is limited by loss of response posing significant challenge for clinicians. Therapeutic drug monitoring has gained increasing popularity in the management of IBD. However, relationship between clinical outcomes and serum anti-TNF levels is complex and controversial in many cases.

**Aims and Methods:** The aim of this study is to simultaneously analyse the serum, mucosal and fecal calprotectin and adalimumab levels, to determine the mucosal expression of TNF-α and to assess the relationship between the levels of anti TNF-α in a matched samples with endoscopic and clinical activities of IB patients receiving anti-TNF maintenance therapy.

**Results:** Data of 34 patients have been analyzed (20 CD, 14 UC; 17 infliximab, 17 adalimumab). The number of TNF-α positive cells was significantly higher in mucosal samples of active vs. inactive part of the bowel (p < 0.001). Mucosal drug level proved to be significantly higher in samples obtained from the inactive vs. active part of the bowel (p = 0.001). However, no association could be detected between the number of TNF-α positive cells and either endoscopic activity or mucosal drug levels. Serum drug level was significantly lower in patients who developed anti drug antibody (p = 0.043). We did not find any correlation between serum drug level and fecal calprotectin concentration, however, calprotecint level was higher in patients with anti-drug antibody positivity (p = 0.0134). No correlation was detected between serum and mucosal anti TNF levels.

**Conclusion:** Our study was the first that simultaneously examine serum, tissue and fecal concentrations of anti TNF-α comparing with clinical and endoscopic activities. We were unable to find evidence against the hypothesis of no association between serum drug levels and mucosal anti TNF-α concentration. However, the sample size is currently very low, and more data is needed to be collected in order to better understand the association between blood and tissue drug levels or disease activity. Nevertheless, it is hoped that these measurements will allow a better overview of the drug distribution and clearance and may help to identify a useful surrogate marker of clinical and endoscopic activity.

**Disclosure:** Nothing to disclose.

**P0374 ANTI-TNF VS. CONVENTIONAL TREATMENT FOR THE PREVENTION OF POSTOPERATIVE RECURRENCE OF CROHNS DISEASE: A META-ANALYSIS**
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**Introduction:** The majority of patients with Crohn’s disease (CD) need surgery during their lifetime. Within 1 year, 80% of the operated patients has endoscopic postoperative recurrence (POR). However, there is no widely accepted consensus on the prevention of POR.

**Aims and Methods:** Our aim was to compare the efficacy of biological agents and that of conventional therapy as prophylactic therapy options for POR and also to compare the efficacy of prophylactic biological treatment in high risk vs. non-risk group of patients. Studies were identified through searching EMBASE, and Web of Science for English-language studies published from inception up to 15 April 2017. The PICO items were, as follows: (P) adults with CD who had intestinal resection, (I) biological therapy (adalimumab, infliximab), (C) conventional therapies (mesalamine, thiopurines and placebo), and (O) clinical, endoscopic, and severe endoscopic POR. Patients were considered at ‘high risk’ for POR if they had ≥1 of the following risk factors: active smoking, young age at diagnosis, penetrating or perianal disease at diagnosis, ≥1 resections, and resection within 3 years. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. PROSPERO registration number is CRD42017083679.

**Results:** The data of 2 observational and 8 randomized controlled trials, including 709 CD patients, were analysed. Anti-TNFα agents were significantly more effective in preventing clinical and endoscopic POR compared to conventional therapies (OR: 0.501, 0.319–0.786, p = 0.003, and OR: 0.157, 0.069–0.359, p < 0.001, respectively). We could demonstrate an overall benefit of biological therapy in unselected patient groups of CD patients regarding clinical, endoscopic and severe endoscopic POR (OR: 0.449, 0.272–0.741, p = 0.002; OR: 0.132, 0.055–0.317, p < 0.001, and OR: 0.263, 0.085–0.817, p = 0.021, respectively). In the course of direct comparison, there was no significant difference in POR rates between the 2 anti-TNF agents. Patients previously treated with biologicals were less likely to maintain remission after surgery (OR: 0.509, 0.303–0.853, p = 0.010).

**Conclusion:** Compared to the conventional therapies, biological agents are more effective in preventing clinical and endoscopic POR both in unselected and high-risk patients. In addition, biologicals should be considered for surgery in patients with preoperative anti-TNF therapy to maintain remission.

**Disclosure:** Nothing to disclose.

**P0375 EFFICACY AND SAFETY OF GRANULOCYTE ADSORPTION APERHERESIS IN ELDERLY PATIENTS WITH ULCERATIVE COLITIS**
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**Introduction:** The number of elderly patients with ulcerative colitis (UC) has been increasing. Elderly UC patients differ from younger patients with respect to the course of their disease, response to treatment, risk of adverse effects, and influence of UC on the quality of life. At our hospital, granulocyte adsorption apheresis (GAA) is often used to treat elderly UC patients.

**Methods:** The study included 80 patients evaluated. We divided them into an elderly group (aged ≥75 years) and a younger group (< 65 years old), and then we compared the groups’ (1) clinical characteristics, (2) the efficacy and adverse effects of CAP, and (3) the complications of PSL therapy.

**Results:** The remission rate was 78.8% in the elderly group and 87.5% in the younger group, and CAP demonstrated efficacy in both groups. There were significant differences between the 2 groups with respect to the age at the onset.
of UC, the estimated glomerular filtration rate on admission, underlying diseases, and concomitant therapies all correlated (all p < 0.05). Adverse events of CAP included headache (n = 2 in both groups), complications of blood reinforcement (n = 1 in the younger group), heparin allergy (n = 1 in the younger group), hypotension (n = 1 in the elderly group), and failure of blood removal (n = 2 in the elderly group). There were significant differences between the 2 groups with respect to the complications of PSL therapy (all p < 0.05).

Conclusion: Although the elderly group had longer durations of UC, a higher prevalence of underlying diseases, and a higher frequency of adverse events due to PSL therapy, CAP was effective in both groups. No serious adverse effects that required the discontinuation of CAP occurred in either group. Thus, CAP was safe and effective in both younger and elderly UC patients. CAP should be considered as a useful treatment option for UC, especially in patients with adverse events due to PSL therapy and elderly patients with underlying diseases.

Disclosure: Nothing to disclose.

P0376 DOES ANY CONNECTION EXIST BETWEEN BLOOD THIOPURINE LEVEL AND ANTI TNF DRUG LEVEL OR BODY COMPOSITION PARAMETERS - A CROSS-SECTIONAL STUDY IN A HUNGARIAN IBDD CENTRE

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Introduction: Thiopurines are the most commonly used immunosuppressive therapies in mild-to-moderate IBD. Therapeutic concentration of 6-TG is between 235–450 pmol/l × 10³ red blood cell count (RBC). The effect of body composition on 6-TG level was never studied. Furthermore, clinical data suggested a synergistic effect between thiopurine and anti-tumour necrosis factor (anti-TNF) therapy in IBD.

Aims and Methods: This is a cross-sectional study involving 96 IBD patients. Consecutive IBD patients on maintenance AZA (n = 32) and on IFX/AZA or ADA/AZA combinations (n = 32) and activity indices-based pair-matched controls on IFX or ADA monotherapy (n = 32) were prospectively enrolled. 6-TG level was measured with high performance liquid chromatography, IFX and ADA levels were assessed by ELISA method. Body composition analysis was performed with bioelectrical impedance analysis.

Results: Therapeutic concentration of 6-TG was found in 50 patients (78%), they received AZA for a mean 5.9 years. 14 patients (21.8%) had lower blood 6-TG level, they received AZA for an average of 7.5 years. The level of AZA metabolite 6-TG correlated with body weight-based AZA doses (p = 0.017) however it did not correlate with body surface area-based AZA doses (p = 0.081). With statistical analysis correlation was found with some of the investigated body composition parameters: total body water (r = 0.325, p = 0.011), intra-, extracellular water (r = 0.325 and r = 0.334, p = 0.008 and p = 0.008, respectively), scetellar muscle mass (r = 0.326, p = 0.001). However no correlation was found with body fat mass (r = -0.091, p = 0.487). 32 patients received concomitant biological therapy (14 ADA, 18 IFX). Difference was found in ADA trough levels between those on combined IFX/AZA therapy and those on ADA monotherapy (5.22 ± 5.17 mg/ml vs. 18.04 ±14.84 mg/ml, p = 0.006). In contrast, no difference was found in IFX trough levels between those on combined IFX/AZA therapy and those on IFX monotherapy (8.95 ± 10.08 mcg/ml vs. 12.13 ± 12.61 mcg/ml, p = 0.374).

Conclusion: Our study revealed that 6-TG level besides body weight-based AZA doses correlated with total body water, intra- extracellular water and scetellar muscle mass. We found a significant difference in ADA trough levels between the ADA/AZA combination group and the ADA monotherapy group. Preliminary results of our study suggest that favourable outcomes of combinations therapy may related to a synergistic effect between AZA metabolites and IFX or ADA trough levels. However the small number of the patients requires further investigations.

Disclosure: Nothing to disclose.

P0377 STRUCTURING CROHN'S DISEASE - CAN WE PREDICT NEED FOR SURGERY AT FIRST HOSPITALIZATIONS?

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Introduction: Patients with stricturing Crohn’s disease (CD) are frequently hospitalized and a significant percentage requires surgery in the course of the disease.

Aims and Methods: We aimed to assess if there are any predictors of surgical management by the time of the first admission to hospital with obstructed bowel syndrome.

Retrospective unicentric study. Patients over 18 years old, with structuring ileal or ileocolic involvement, with at least 1 hospitalization and a minimum follow-up of 1 year were included. Excluded patients with penetrating disease, those who had their first hospitalization before anti-TNF agents became available in our center and those without appropriate records. Several clinical, analytical and radiological variables were assessed. Statistical analysis was performed using SPSS v23.0.

Results: 43 patients of which 53.5% underwent surgery to treat structuring disease. Patients had a mean age of 43.3 ±10.8 years, 53.5% were females and the median follow up time was 11.0 ±7.0 years.

Comparing patients with and without need for surgery, no significant differences were found between groups regarding age at diagnosis, presence of perianal disease, family history and smoking habits, however females were more frequently admitted to surgery (73.9% vs 30.0%, p = 0.004) as well as patients with inflammatory behavior at diagnosis. Patients with inflammatory behavior at diagnosis (65.6% vs 18.2%, p = 0.006).

At the first hospitalization, patients with need for surgery were less frequently under anti-TNF (0.0% vs 20.0%, p = 0.039), presented with longer-standing obstruction (3.0 ±15 days vs 1.0 ±15 days, p = 0.010), higher leukocytes count (12.0 ±5.3 x10³/µL vs 9.2 ±2.6 x10³/µL, p = 0.037) and admission computed tomography (CT) more frequently showed proximal small bowel dilatation (86.4% vs 40.0%, p = 0.002) and longer extent of small bowel involved (8.0 ±12.0 cm vs 5.0 ±7.0 cm, p = 0.016). Also, patients that were diagnosed by the time of the first hospitalization were more frequently submitted to surgery than those who already had a CD diagnosis (60.9% vs 39.1%, p = 0.043).

Conclusion: Females, patients with structuring behavior from diagnosis and those diagnosed in the first hospitalization were more frequently submitted to surgery. Small bowel dilatation and extent of small bowel involved in admission CT, leukocyte count and duration of obstructed bowel symptoms at the first admission were also predictors of need for surgery. Anti-TNF therapy in the first admission seems to reduce need for surgery in this group of patients.

Disclosure: Nothing to declare.

P0378 THE ROLE OF STOMA FOR COLONIC AND PERIANAL CROHN'S DISEASE IN THE BIOLOGICAL ERA

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Introduction: In the biological era, surgical treatment continues to play an active role in some patients with colocoleral or perianal Crohn’s disease (CD).

Aims and Methods: Epidemiological analysis, surgical indication and clinical evolution of patients with CD with colorectal and/or perianal disease undergoing surgical treatment.

Retrospective study of patients with colonic and/or perianal CD who underwent colectomy, total proctocolectomy, or diverting ileostomy /colostomy between 2000-2016 in a tertiary hospital. Demographic and clinical data were collected.

Results: 20 patients were included, 70.0% were women, mean age was 44.5 years. The disease was located in the ileum and colon in 7, solely in the colon in 11 patients and in the ileum (L1p) in 2. 13 patients had perianal disease and 18 rectal involvement. The behaviour of CD according to the Vienna classification was non-stricturing non-penetrating in 12 patients, stricturing in 5 and in penetrating 3. Prior to surgery, 15 patients were treated with combination therapy, 2 with anti-TNF (previously withdrawal of azathioprine due to adverse events). 6 patients had no medical treatment due to inaugural disease at the time of surgery. The mean duration of disease before colectomy was 9.1 years. Surgical indications were: refractoriness to medical treatment in 8 patients with luminal disease and 8 with perianal fistulizing disease, perforation in 3 and Hoggins lymphoma of the rectum in 1. 9 patients required more than 1 surgical intervention, including 4 urgent surgeries. The surgeries performed were proctocolectomy in 10 patients, total colectomy with ileostomy in 3, proctectomy with colectomy in 2, segmental colectomy with colostomy in 1 and ostomy in 4 (3 colostomy and 1 ileostomy). The mean follow-up time was 5.4 years. Postoperative evolution: high-output ileostomy in 1 patient; pelvic floor dysynergia in the patient with ileo-anal pouch; 5 patients with relapse of CD in the ileum; 2 with proctitis (1 underwent
proctectomy later); I with perianal disease and I due to adenocarcinoma in follow-up. After 1st follow-up, 9 patients were with combination therapy, 3 with biological therapy and 2 with methotrexate.

Conclusion: In this study, 95% remained with stoma. More than half of the patients maintain/restart biological treatment.

Disclosure: Nothing to disclose.

P0379 ENTERIC RESECTION IN CROHN’S DISEASE - IS THERE A RELATIONSHIP BETWEEN THE TIMING OF IMMUNOSUPPRESSION ONSET AND THE EXTENSION OF THE RESECTED SMALL BOWEL?

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Introduction: Intestinal function is closely related to its length. An individualized approach regarding the need for resection of each affected segment of the bowel should be applied to the patient with Crohn’s disease (CD) requiring surgery. Several studies have been evaluating the relationship between the date of onset of anti-tumor necrosis factor (anti-TNF) agents or immunomodulators and the need of surgical procedures in CD. However, it is still unclear if the timing of the immunosuppression onset has impact in the length of the resected small bowel.

Aims and Methods: We propose to evaluate the relationship between the early treatment of CD patients with anti-TNF agents or immunomodulators with the extension of the resected small bowel. We perform a retrospective data analysis of a sample of cases with CD submitted to surgery. For each case, the date of diagnosis, immunomodulators or anti-TNF onset, and surgery was recorded. The extension of the resected small bowel was based on the anatopathological report.

Results: A total of 314 cases diagnosed between 1975 and 2017 (172 men (50.7%), mean age at diagnosis 28.9 ± 12.8 years) were evaluated. Multiple surgeries were performed in 20% (n = 63) of the cases. The most frequently performed surgery was the right ileocolic resection (77.3%, n = 222 patients).

The median time between diagnosis and the first surgery was 31 months (IQR 5–83 months). On average, the patients underwent resection of 23.6 ± 18.4 cm of the small bowel. Prior to the first surgery, 46.7% (n = 148) of the patients were treated with an immunomodulator (median time of therapy 16 months, IQR 3–42 months) and 21.8% (n = 69) were treated with an anti-TNF agent (median time of therapy 38 months, IQR 7–100 months). Neither immunomodulatory therapy (mean 23.2 ± 16.5 cm vs. 24.3 ± 20.4 cm, p = 0.67) nor anti-TNF therapy (mean 23.7 ± 19.5 cm vs. 24 cm, p = 0.61) was associated with lower extension of resected small bowel. No correlation was found between the time elapsed since diagnosis and introduction of the immunomodulator (r = 0.07, p = 0.43) or anti-TNF agent (r = 0.06, p = 0.53) and the extension of resected small bowel. Also, there was no correlation between the time elapsed between the introduction of immunomodulator (r = 0.06, p = 0.47) or anti-TNF agent (r = 0.08, p = 0.53) and time to surgery with the extension of resected small bowel.

Conclusion: In this group of patients, we found that the timing of introduction of immunomodulator or anti-TNF therapy did not influence the extent of the resected bowel.

Disclosure: Nothing to disclose.

P0380 HIGHER BMI BUT NOT SYSTEMIC IMMUNE SUPPRESSION INCREASES THE RISK OF SHORT-TERM POSTOPERATIVE COMPLICATIONS IN CROHN’S DISEASE PATIENTS

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Introduction: Several studies have focused at the risk factors of postoperative complications in Crohn’s disease (CD) patients with no conclusive results. Thus far, it is unclear whether immune suppression should be adjusted in a CD patient awaiting surgery for CD complications.

Aims and Methods: The aim of this study was to determine the risk factors associated with the postoperative complications in CD patients operated for luminal disease complications.

All consecutive CD patients operated on in 1 tertiary center between January 2015 and September 2017 were included. Complications within 30 days following surgery were categorized according to Clavien-Dindo classification. Patients’ demographics, nutritional status, disease localization and behavior, type of medical therapy, previous surgical interventions, type of surgical approach and duration of surgical intervention were noted. The association of postoperative complications with these factors was analyzed.

Results: In total, 91 procedures were performed in 86 CD patients (47.3% males; mean age 38 years, range 17–71; 56 pts (61.5%) with ileo-colonic disease, 11 pts (12.1%) with small bowel and 21 pts (23.1%) large bowel localization; 62 (68.1%) with stricturing disease). Based on body mass index, 23 (25.3%) patients were underweight, 42 (46.2%) had normal weight and 21 (23.1%) were overweight. Minority of patients had stenosis (16 pts (17.6%); 36 pts (39.6%) were using azathioprine; 33 (36.3%) anti-TNF; 7 (7.7%) vedolizumab and 1 patient was using trial medication.

The procedure was elective in 60.4% and one-third had repetitive surgery. Median duration of the procedure was 150 minutes (range 30–335) and median hospital stay was 6 days (range 3–32). 51 pts (56%) had simple resection, 24 (26.4%) had multiple resections, in 16 cases an ostomy was created. Laparoscopic approach was used in 44 cases (48.4%; 8 pts had single port laparoscopic procedure). 46 pts (50.5%) had laparotomy. There were 10 complications (11%) out of which 5 (5.5%) major complications (Clavien-Dindo IIIb and above). There was a significant difference in BMI between patients with major complications compared with patients without complications in all the groups with major complications vs. group without complications (p = 0.035). None of the other factors were associated with unfavorable postoperative outcomes.

Conclusion: Overweight represents a risk factor for postoperative complications in CD patients operated for luminal disease complications. Immune suppressive therapy, including systemic corticosteroids and anti-TNF biologics does not seem to confer an increased risk for surgical complications.

Disclosure: Nothing to disclose.

P0381 USING PATIENTS’ PREFERENCE IN RANDOMIZED CONTROLLED TRIALS

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Introduction: Randomized controlled trials (RCT) are the gold standard of assessment of efficacy in clinical medicine. However, many eligible trial participants have a preference for 1 of the intervention of the RCT, and therefore may decline randomization. Consequently, this could limit the extrapolation of the results to the clinical population (i.e. reduce external validity by randomization bias).

Recently, a preference for one randomization arm was encountered. Intervention may experience resentful demoralization, which may lead to worse outcomes (i.e. reduce internal validity by preference bias). Especially studies with a substation difference in interventions (e.g. surgery vs. medication), and studies with a subjective primary outcome (e.g. quality of life), are prone for randomization and preference bias.

The aim of this study was to determine whether preferences affect external and internal validity in trials.

Aims and Methods: A systematic review with meta-analyses was performed. 2 reviewers independently searched in MEDLINE, EMBASE, PsychINFO, and the Cochrane library for RCTs with a preference-arm published between 2005 and 2018. The trials that reported on allocation of patients to random or preference cohorts using the same inclusion criteria and protocol were included. We extracted data on study design, measurement of preference, recruitment, attrition, cross-over, and primary outcome at baseline and end of follow-up.

Results: In total 117 out of 3734 identified articles met screening criteria and 35 were eligible (to compare baseline and primary outcome difference between the placebo and preference cohort, 32 and 20 articles were included, resp.) Acceptance of randomization in all 35 trials varied from 1% to 81% and was lower than 50% in 23 of 35 studies. Higher education level, female, older age, race, and prior experience with 1 treatment arm were baseline characteristics of participants declining randomization. The primary outcome of the trials between randomized and preference groups was comparable, the difference in effect of the experimental intervention was 0.093 (95% CI –0.364–0.178), p = 0.502. After comparing only the 7 trials that adjusted for baseline difference the effect was even smaller, 0.026 (95%CI –0.211–0.263), p = 0.832.

Conclusion: Treatment preference led to a substantial proportion of a specific patient group refusing randomization, while it did not affect the primary outcome. Therefore, patients preference trials could increase external validity without compromising the internal validity compared to randomized controlled trials.

Disclosure: Nothing to disclose.

P0382 EARLY CLOSURE OF ILEAL POUCH-ANAL ANASTOMOTIC LEAKAGE PRESERVES POUCH FUNCTION; A PROSPECTIVE COHORT STUDY

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Introduction: In case of ileal pouch-anal anastomotic (IPAA) leakage, Endosponge®-assisted early surgical closure prevents chronic presacral abscesses compared to conventional treatment (defunctioning ileostomy and passive drainage). It was hypothesised that early closure would also improve long-term pouch function. The aim of this study was to compare pouch function and failure after early closure to conventional management of anastomotic leakage and to control IPAA patients without anastomotic leakage.

Disclosure: Nothing to disclose.
Aims and Methods: In this prospective cohort study, all consecutive patients who underwent colectomy for UC between 2002 and 2017, were sent a validated stool PCR questionnaire. Early surgical closure was defined as ≥3 days of hospitalization induced by acute diarrhea. The prevalence of children with autism spectrum disorders (ASD) is increasing worldwide (1). The cause of ASD is poorly understood and involves interactions of different genetic and environmental factors where gut microbiota could have a significant impact. The aims of the study were to evaluate fecal microbiota transplantation (FMT) effectiveness in children with ASD in treating autism spectrum disorders and gastrointestinal (GI) symptoms.

Aims and Methods: We performed FMT in 5 boys (5–8 yrs, every month, 3 times for each patient) with ASD and mild GI symptoms. The donor was the same 7 yrs. old healthy, unrelated girl. Her feces were infused into the cecum during colonoscopy. The patient’s gut before FMT was prepared with polyethylene glycol 4000 (Fortrans). Symptoms were checked every week after FMT with patient global impression score (PGI-R; the symptoms were rated on a scale of 1–7, where 1 = much worse, 7 = much better compared to baseline) (2) for ASD and gastrointestinal symptom rating scale (GSRS; 1 represents absence of troublesome symptoms and 7 represents very troublesome symptoms) (3).

Results: We filled GSRS and PGI-R scores by asking parents about their child’s health during phone call or when the patient came to the hospital for FMT. The total GSRS and PGI-R scores improved in all (1–5) patients after FMT (Table 1). The best improvement was seen after 2 wk. post FMT, less before second and third FMT. The FMT treatments were generally well-tolerated, without adverse effects.

Conclusion: FMT has positive effect on GI and autism spectrum disorders symptoms.

Disclosure: Nothing to disclose.

**References**

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<table>
<thead>
<tr>
<th>Patient</th>
<th>Before FMT</th>
<th>After 2 wks</th>
<th>After 1 mo</th>
<th>After 2 mo</th>
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</thead>
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<tr>
<td>1</td>
<td>GSRS:35</td>
<td>PGI-R:53</td>
<td>GSRS:22</td>
<td>PGI-R:49</td>
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<tr>
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<td>PGI-R:56</td>
<td>GSRS:21</td>
<td>PGI-R:53</td>
</tr>
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<td>GSRS:33</td>
<td>PGI-R:55</td>
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</tr>
<tr>
<td>5</td>
<td>GSRS:37</td>
<td>PGI-R:56</td>
<td>GSRS:27</td>
<td>PGI-R:54</td>
</tr>
</tbody>
</table>

Conclusion: Colitis mimicking ulcerative colitis is 1 of irAEs induced nivolumab. Our diagnostic criteria, which include apoptosis of colonic epithelial cells, may be appropriate in consideration of mucosal damages and subsequent clinical course.

Disclosure: Nothing to disclose.
Results: Overall, 29 (30%) of 96 samples were positive for pathogen at stool PCR. The most frequently detected virus was norovirus (28.2%) and adenovirus was detected in 1 sample, respectively. The positive rate for bacteria was 48.3% (28/58). C. perfringens was the most frequently detected, followed by campylobacter spp., Caldificle toxin B. The rate of antibiotics change, anti-diarrhoeal agent or probiotics change, additional endoscopy and image study (CT) were significantly higher in stool PCR positive group (p = 0.007, p < 0.01, p = 0.018 and p = 0.027, respectively).

There were no significant differences between groups in terms of antibiotics use and hospitalization. However, hospital of day decreased significantly in stool PCR positive group (p = 0.032).

On multivariate analysis, stool PCR positive was associated with increased rates of history of diabetes mellitus type 2, fluid therapy and anti-diarrheal agent use (HR, 3.857; 95% CI 2.381–9.238; p = 0.001) / HR 2.949; 95% CI 1.184–7.303; p = 0.020 / HR 2.945; 95% CI 1.522–5.699; p = 0.001).

Conclusion: With stool PCR positive, antibiotics changes and drug modification were associated shortening of hospitalization period, espacially in patients with diabetes.

Disclosure: Nothing to disclose

References

P0387 FECAL MICROBIOTA TRANSPLANTATION IN CLOSTRIDIUM DIFFICILE INFECTION: REAL-LIFE EXPERIENCE FROM AN ACADEMIC ITALIAN HOSPITAL

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Introduction: Gut microbiota helps us to regulate homeostasis functions. Its key indices. Physicians should be made aware of the increased VRE risk, and should consider VRE surveillance in those under long-term gastric acid suppression therapy.

Disclosure: Nothing to disclose

References

P0389 FECAL MICROBIOTRAL TRANSPLANTATION FOR CLOSTRIDIUM DIFFICILE INFECTION- A NATIONAL ISRAELI EXPERIENCE

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Introduction: Fecal microbial transplantation (FMT) has been established as an effective and safe therapy for recurrent Clostridium difficile infection (CDI), with cure rates of 85–95% [1]. In Israel, FMT for the treatment of recurrent CDI, has been performed for the past 3 years. It is widely accepted that at which FMT is performed in ambulatory as well as in hospitalized patients using multiple methods including colonoscopy, gastroscopy, and capsules [2–3].

Aims and Methods: We evaluated and described the efficacy and safety of FMT for CDI patients in a national retrospective cohort of the 5 medical centers performing FMT in Israel. All patients who received FMT for recurrent (recurrence within 8 weeks of the previous treatment), refractory (ongoing diarrhea despite antimicrobial treatment) or severe CDI (WBC > 15,000 c/μL ± CR > 1.5 times the premorbid level) from 2013 through 2017 were included.

Stool donors were screened according to the Israeli Ministry of Health guidelines. Fecal filtrates were locally prepared and stored frozen in −80°C. Clinical and laboratory data of patients were collected from patients’ medical files in which indications for FMT, risk factors and outcomes at 1 week, 2 and 6 months post FMT are routinely recorded.

Results: A total of 111 FMTs for CDI were performed: 45% via the lower GI route (LGI) through a colonoscopy, 22% via gastroscopy or feeding tube (upper GI - UGI), and 33% via oral capsules. A summary of patients’ characteristics, risk factors for CDI, indications and outcomes is depicted in Table 1.

Recurrent CDI was the leading indication for FMT in 74% of the patients while refractory and severe CDI were treated in 21% and 18% patients, respectively.

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Overall success rate was 87.4% (97 patients), with no significant difference between administration routes. Patients who achieved cure, were younger (age 63±22 compared with 73±12, p < 0.05), were less often defined as severe CDI, and were more likely to be treated as outpatients. Patients who were younger than 60 years old (n = 35), were mostly outpatients, compared to the elderly group, (86% vs. 63%, respectively, p < 0.05) and underwent FMT at a much later time from first disease episode (mean time from 1st CDI episode 27% vs. 102±112 days, p < 0.001). 11 patients died during the follow-up, none was attributed to the FMT procedure. No FMT related infections were recorded.

Disclosure: Nothing to disclose.

References

P0390 THE IMPACT OF CLOSTRIDIUM DIFFICILE INFECTION ON HOSPITALIZATION IN VENETO REGION

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Introduction: Clostridium difficile infection (CDI) has emerged as a major health-care-associated infection, because of the changing molecular epidemiology of the C. difficile, and the ageing of the population, without neglecting frequent exposure to broad-spectrum antibiotics and other predisposing medications, the prevalence of comorbidities, and the risk of hospitalization. In the last decade, analyses of hospitalization records and data on multiple causes of death demonstrated an important and constant increase in CDI rates. Aims and Methods: To evaluate the impact of CDI on hospitalization in Veneto Region (North-East Italy, approximately 4,900,000 inhabitants), a retrospective analysis was carried out from a population-based archives represented by hospital discharge records (HDR) according to the ICD9-CM. All discharges from 1 January 2007 to 31 December 2016 of Veneto population with a code for CDI (008.45) as principal or secondary diagnosis were extracted from the regional anonymous archive of discharge records. The Standardized Hospitalisation Rate (SHR) and in-hospital Mortality Rate (SMR) were calculated per 5-year age group. Results: 7,557 discharges with CDI were tracked in the study period and 88% of these hospitalizations involved subjects aged over 65 years, with CDI diagnosis as the primary in over 1-third of cases and an overall lenght of stay (LOS) of 25.6±22.7 days. Hospitalization distribution by gender showed a prevalence of females (63.7%) characterized by a higher mean age (80.2±14.6 vs. 75.6±16.4 yrs; p < 0.001). The SHR was 15.25 and SMR 1.72 both increased steeply and constantly in the analyzed period, and from the comparison of first and last year of the period emerged a rise of SHR (Chi square for trend: 141.702; p < 0.001) from 10.6 to 24.5 and also of SMR (Chi square for trend: 45.381; p < 0.001) from 0.6 to 3.7 per 100,000 inhabitants. The rate of CDI diagnoses per 10,000 annual admissions increased steeply with age, and reached a peak of 222.4 every 100,000 discharges among the very elderly (≥ 85 years). In the frame of over 65 years patients the age class distribution showed a higher risk in 75–84 (OR: 1.62; CI95%: 1.35–1.92; p < 0.001) and an almost double in >85 years (OR: 2.1; CI95%: 1.56–2.74; p < 0.001) respect to 65–74 age class. Conclusion: In the observation period SHR for CDI was almost doubled and SMR even increased 6-fold in 2016 respect to 2007. What emerged confirms the literature’s data about the time course of CDI infections, with an increase in their frequency, as well as in their severity and in the additional days of hospitalization. These dramatic scenario imposing the adoption of adequate containment measures to deal with a new epidemic phenomenon, mainly through policies to optimize antibiotic therapy both in the intra- and extra-hospital environment.

Disclosure: Nothing to disclose.

P0392 DECREASE OF BLOODSTREAM INFECTION RATES IN PATIENTS WITH CLOSTRIDIUM DIFFICILE INFECTION TREATED WITH FAEAL MICROBIOTA TRANSPLANTATION

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Introduction: Clostridium difficile infection, especially in its severe clinical picture, is a risk factor for bloodstream infections (BSI). A considerable body of evidence shows that fecal microbiota transplantation (FMT) is more effective than standard antibiotic regimens (metronidazole or vancomycin) in treating recurrent CDI, although its efficacy in reducing CDI-related BSI has not yet been demonstrated.

Aims and Methods: The aim of this study is to assess the rate of BSI in a cohort of patients with CDI treated with FMT or with standard antibiotic therapy. This is a single-centre, retrospective cohort study of patients with CDI treated with FMT either with standard antibiotic regimens (metronidazole or vancomycin) or fidaxomicin. The date of first fecal inoculation and the starting date of antibiotic treatment were considered as time 0 for the analysis.

Results: At November 2017, 282 subjects (F = 91, M = 171, mean age 74 years) were analysed for this study. Of them, 101 patients (36%) were treated with FMT from healthy donor and 181 (64%) received antibiotic therapy for CDI. No differences were found on demographic and clinical characteristics of the 2 study groups.

47 patients developed a BSI after FMT or standard antibiotic therapy. Compared to those who received antibiotic treatment for CDI, patients in the FMT group had a significantly lower risk of overall BSI (21.3% versus 8.9%; p = 0.008), fungal BSI (6.6% versus 1%; p = 0.036), polymicrobial BSI (6.1% versus 1%; p = 0.016). Subjects in the FMT group experienced also a significantly shorter length of hospitalization compared to those in the antibiotic group (13.4 days versus 29.8 days on average; p < 0.001) and a reduced death risk at 60 days (7.7% versus 1%; p = 0.015). Adverse events were similar between the 2 groups.

Conclusion: In our cohort, subjects with recurrent CDI treated with FMT experienced a significantly lower incidence of bloodstream infections, a shorter length...
of hospitalization and a reduced 60-day risk of death compared to those who received antibiotics. We can argue that a rapid restoration of healthy microbiota in people with CDI treated with FMT could explain the present results. Should these preliminary results be confirmed by prospective, randomized trials, the reduction of BSI in patients with recurrent CDI may be considered an additional relevant benefit of FMT.

Disclosure: Nothing to disclose

Aims and Methods: We aimed to study the profile and predictors of difficult to treat (DTT-TB) inclusive of MDR-TB patients of all the confirmed cases of abdominal TB. Clinical, laboratory and radiological data of abdominal TB (n = 83) were analysed from 2012-2017. Disease rates of previous years (2000-11) were compared. DTT-TB was defined as 1 of the following: 1) prolonged (>9months) WHO category-1 antibacterial therapy (ATT), 2) MDR-TB (failed WHO category-2± category-1 ATT or proven on GeneXpert) requiring second line therapy. DTT-TB was compared with standard ATT (WHO category 1 or 2 responsive of ≤9months duration of therapy) cases.

Results: Of all abdominal TB, MDR-TB was diagnosed in 3 of 38 (8%); 2000-11 and 13 of 83 (16%; 2012-17). An additional 7 of 83 children (2012-17) had prolonged category-1 ATT finally constituting 20 (24%) as DTT-TB. Table 1 shows the comparison of DTT-TB and standard therapy. Overall confirmation of diagnosis (n = 83) was 56 (67%) by microbiology or histology (caseating granuloma), the rest by discriminatory radiological ± laboratory features. Younger age, higher microbiological yield, presence of extra-abdominal, thoracic, and abdominal lymph node involvement and paucity of luminal involvement were significant in DTT-TB than standard therapy. In the DTT-TB group, prolonged ATT (n = 7) was administered for 17.7±5.1 months and MDR-TB (n = 13) for 18±6.9 months. At the end of 18 months, 3 of 13 (23%) MDR-TB were non-responsive to various second line agents and were labeled extended drug resistant TB.

Conclusion: An alarming rise of overall abdominal TB, MDR-TB and extended drug resistant TB is currently encountered in developing countries. MDR-TB is multibacillary and presents as disseminated disease affecting younger age groups.

Table 1: Comparison of difficult to treat TB versus standard therapy TB

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Difficult to treat TB (n = 20)</th>
<th>Standard therapy TB (n = 63)</th>
<th>p value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>9 (45)</td>
<td>32 (51)</td>
<td>0.6</td>
<td>0.7 (0.3-2.2)</td>
</tr>
<tr>
<td>Luminal involvement, n (%)</td>
<td>16 (80)</td>
<td>34 (54)</td>
<td>0.03</td>
<td>3.6 (1.1-12.1)</td>
</tr>
<tr>
<td>Extra-abdominal involvement, n (%)</td>
<td>14 (70)</td>
<td>18 (29)</td>
<td>0.001</td>
<td>5.8 (1.9-17.6)</td>
</tr>
<tr>
<td>Extra-abdominal involvement, n (%)</td>
<td>14 (70)</td>
<td>18 (29)</td>
<td>0.001</td>
<td>5.8 (1.9-17.6)</td>
</tr>
</tbody>
</table>

ATT: anti-tubercular therapy. Microbiological confirmation includes Ziehl-Neelsen stain for acid-fast bacilli, rapid solid medium culture, real-time polymerase chain reaction for M.tuberculosis and GeneXpert molecular technique.
**P0395 IMMUNOHISTOCHEMISTRY APPLICATION AS ONE STEP FOR DIAGNOSIS OF HUMAN INTESTINAL SPIROCHETOSIS**
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Introduction: Diagnosing human intestinal spirochetosis (HIS), a colorectal infectious disease caused by *B. aalborgi*, is difficult. The disease is classified as a phase-1 intestinal infection. In most cases, patients have no symptoms or present with non-specific gastrointestinal symptoms. The disease is confirmed by biopsy and detection of *B. aalborgi* using PCR in stool or sigmoidoscopic specimens in the pathology department at a single hospital.

Results: Among the 140 individuals examined (M:F=86:54; 20–94 yrs; median 64 yrs) during the period, 10 HIS-HE cases (7.1%; M:5; 5:34–75 yrs; median 57 yrs) were diagnosed, while HE pathology found eight HIS-HE cases (so-called ‘colon’ cases: thick and distinct; 5.7%) and 2 possible cases. All 8 HIS-HE cases matched HIS-HE cases. However, the 2 possible HIS-HE cases were denied by IHC, while another 2 of the HIS-HE cases were overlooked by HE. In the HIS-HE cases confirmed by HIS-IHC at the time, 4 HIS-HE cases have received endoscopy as follow-up for polys, 1 for ulcerative collitis, 2 for fecal occult blood, and 1 for watery diarrhea.

Conclusion: The hallmark of HIS can be observed histologically, and an initial IHC application might find more HIS cases in routine practice.

Disclosure: Nothing to disclose.

**P0396 LOW INTESTINAL BLEEDING: WHAT AND WHEN SHOULD WE BE LOOKING AT COLONOSCOPY?**
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4State Institute for Further Training of Physicians, Novoskuznetsk, Russian Federation
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Introduction: The recommended strategy of the use of colonoscopy after preparation by oral lavage at patients with low-intestinal bleeding identifies the source of bleeding in 23%–40%. The frequency of these sources are significantly different. Identifying the source of bleeding involves the wrong tactics and volume of treatment. What is more important at low intestinal bleeding: total colonoscopy or search for the true source of the bleeding?

Aims and Methods: Compare the structure identified during the colonoscopy sources of bleeding in patients presenting at patients previously oral lavage versus patients who performed urgent colonoscopy without bowel preparation.

A randomized cohort study. Included 252 patients admitted from the signs of intestinal hemorrhage in 2006–2015. 118 men, women 134. The average age of the patients was 60.1±15.7 years. In Hosp No 29 colonoscopy was performed at admission without prior preparation of the colon, the patient in Hosp No 1 performed lavage or enema preparation prior to colonoscopy within 24–48 hours of hospital stay.

Results: Significant differences in the structure of intestinal bleeding sources (p=2.3–4.500000, p=0.03390) are revealed. In patients without bowel preparation the most frequently detected were bleeding diverticula and cancers -17%, ulcerative colitis -10%, intestinal bleeding -16%, upper bleeding -16%. In preliminary bowel preparation the most likely cases of bleeding detected were cancers -7%, ulcerative colitis -15%, angiodysplasia -13%. The number of endoscopic findings in bowel preparation was 1.5 times higher against emergency colonoscopy without bowel preparation. The number and structure of the observed changes were significantly different between both groups, and depending on the sex of patients (p=2.3–112.4894, p<0.0000). There were no complications in both groups. Another aspect of the question consists of the need to use hemostasis methods. In our observations at active bleedings we used hemostasis methods in only 3 patients (1.2%). It not in favor of an early colonoscopy without preliminary preparation of a colon. These data differ from other authors who use a hemostasis in 25% or 40%. Apparently, tactical decisions in favor of using a colonoscopy without bowel preparation should be based on experience of clinical and regional features of nosological focal bleeding in patients with presumptive diverticular hemorrhage.

Conclusion: Performing a colonoscopy at an altitude of bleeding without colon preparation is safe, but significantly alters the structure of the true sources (causes) of bleeding. Colonoscopy after preliminary bowel preparation has significantly higher diagnostic capabilities, which complicates the identification of the true source of bleeding. The choice in favor of a colonoscopy without intestinal preparation should be individual.

Disclosure: Nothing to disclose.

**References**

**Disclosure:**
No financial disclosures.

**P0397 DO CLINICAL CHARACTERISTICS AND OUTCOME IN NONAGENARIANS WITH ACUTE LOWER GASTROINTESTINAL BLEEDING DIFFER FROM YOUNGER PATIENTS?**
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Introduction: The number of nonagenarians hospitalized for various reasons including acute lower gastrointestinal bleeding (ALGIB) is increasing worldwide.

Aims and Methods: Our aim was to evaluate whether clinical characteristics and outcomes in nonagenarians with ALGIB differ from younger patients.

Data from all nonagenarians with ALGIB hospitalized in our hospital over a 76-year period were compared with those <90 years old. Hemodynamic resuscitation, management of antithrombotic agents, early colonoscopy following bowel cleansing, capsule enteroscopy and endoscopic hemostasis when needed were the main steps in the management of patients with ALGIB. In cases of hemodynamic instability, emergent CTA was performed with embolization when appropriate.

Results: Data of 32 nonagenarians (91.8±2.1, 90–99) were compared with that of 496 patients <90years (68.8±14.1, 17–89). Nonagenarians were more commonly female (24/32 vs 232/496, p=0.003) with higher serum creatinine levels (1.4±0.8 vs 1.0 ±0.7, p=0.046) and higher rate of coexisting diseases (32/32 vs 430/496, p=0.023), mainly cardiovascular (23/32 vs 241/496, p=0.017). Proper bowel preparation (25/32 vs 438/496) and endoscopic examination (29/32 vs 417/496) did not differ. The cause of bleeding was not different (mainly diverticula, ischemic colitis and neoplasia in 8, 9 and 4/32 nonagenarians respectively). No significant difference was observed between the 2 groups regarding transfusions (1.1±1.8 vs 0.9±1.9, p=0.524), hospitalization days (5.0±4.2 vs 4.3±3.2, p=0.150), recurrence of bleeding (1.3±36/496, p=0.72), urgent surgical hemostasis (0.3±6/496, p=0.69) and mortality (2.3±411/496, p=0.19).

Conclusion: Despite the age and higher prevalence of concomitant diseases, nonagenarians had a worse bleeding outcome.

Disclosure: Nothing to disclose.

**P0398 MANAGEMENT OF ANTITHROMBOTIC AGENTS IN PATIENTS WITH PRESUMPTIVE DIVERTICULAR HEMORRHAGE**
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Introduction: It has been reported 5–15% of definite diverticular hemorrhage patients experience re-bleeding within 30 days regardless of status of re-initiation of antithrombotic agents. About 65% of diverticular hemorrhage patients are diagnosed as presumptive hemorrhage.

Aims and Methods: This study aimed to elucidate risk factors predicting re-bleeding in patients with presumptive diverticular hemorrhage. A total of 231 patients with presumptive diverticular hemorrhage from January 2004 to September 2017 were included retrospectively. The primary outcome was post-endoscopy re-bleeding among patients with presumptive diverticular hemorrhage. Age, sex, past medical history, laboratory results, colonoscopy procedure length, and site of bleeding were assessed as well as use of antithrombotic agents. Rebleeding was considered in patients with and without re-bleeding. In addition, among patients with presumptive diverticular hemorrhage using antithrombotic agents, we examined relationship between re-bleeding and when they restart their agents.

Result: Among the 231 patients receiving antithrombotic agents. Duration from colonoscopy to re-bleeding in patients taking antithrombotic agents and those not taking was 1.70 and 1.92 days, respectively (p=0.23). In addition, 17 of the 23 re-bleeding patients under antithrombotic agents had their antithrombotic agents re-initiated after the index
re-bleeding, with none of them experiencing another re-bleeding during the follow-up.

Conclusion: Use of antiatherosclerotic agents was not associated with re-bleeding in patients with presumptive diverticular hemorrhage after colonoscopy, potentially indicating the safety of reinitiating antiatherosclerotic agents.

### Table: Risk of re-bleeding in patients with presumptive diverticular hemorrhage.

<table>
<thead>
<tr>
<th>Location</th>
<th>p-value</th>
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<tr>
<td>- Cecum</td>
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</tr>
<tr>
<td>- Ascending colon</td>
<td>0.31</td>
</tr>
<tr>
<td>- Transverse colon</td>
<td>0.45</td>
</tr>
<tr>
<td>- Descending colon</td>
<td>0.57</td>
</tr>
<tr>
<td>- Sigmoid colon</td>
<td>0.29</td>
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Disclosure: Nothing to disclose.

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**P0399** **CUMULATIVE LEVELS OF FEACAL HEMOGLOBIN IN CONSECUTIVE ROUNDS OF FIT NEGATIVE PARTICIPANTS FOR IMPROVING COLORECTAL CANCER SCREENING MANAGEMENT**

**Aims and Methods:** Our hypothesis is that the cumulative concentration of fHb in consecutive rounds might be useful to detect those individuals with high risk of neoplasia undergoing to colonoscopy. However excretion of haemoglobin to faeces (fHb) is intermittent and can be due to difference causes other than neoplasia. Moreover, it has been shown that FIT pre analytics have sources of bias and the concentration of fHb is related with age and gender. For instance, an individual may present a positive result followed by a negative result or vice versa only in a few days.

**Results:** A multivariate logistic regression identified gender (men: odds ratio [OR], 1.70; 95% confidence interval [CI], 1.39–2.12) and mean fHb concentration of the first 2 rounds (ρ < 4 μg/g; g–4 μg/g; > 4 μg/g) as independent predictive factors for CRC. Combining these factors, different risk categories have been established. A 6.59-fold (95% CI, 3.80–11.42) higher risk of CRC was found between the 2 extremes categories (see table). The positive predictive value for CRC ranged from 8.8% to 39.8%. Interestingly, negative predictive values for CRC, ranged from 93.1% to 98.5%.

**Conclusion:** Cumulative fHb concentration together with gender in FIT negative participants could be a useful tool to assess the presence or absence of CRC in subsequent screening rounds and can help in the design of strategies and the management of the programmes to enhance their efficiency.

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**Disclosure:** Nothing to disclose.
increase did not reach statistical significance (35.64% vs 28.5%, p = 0.09).

Location of CRC in the 3 different groups is depicted in the table. Synchronous polyps were more commonly found in the right colon during G3 compared to G2 and G1 (G3 = 40.76% vs G2 = 17.12% vs G1 = 23.14%, p < 0.0001). Statistical significance remained even when analyzed separately for sex (females-right colon polyps G3 = 35.94% vs G2 = 2.7% vs G1 = 8.7%, p < 0.0001 and males right colon polyps G3 = 42.86% vs G2 = 24.32% vs G1 = 32%, p = 0.019).

Conclusion: Right colon CRCs as well as synchronous right colon polyps are significantly more frequently diagnosed in a single endoscopic center during the last 15 years. This may be due to better colon preparation, use of high definition endoscopes or increased awareness of right colon cancers by gastroenterologists.

Disclosure: Nothing to disclose

P0402 AGE AT MENARCHE AND RISK OF COLORECTAL ADENOMA

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Introduction: Limited data are available regarding the association between age at menarche and the risk of colorectal adenoma. Therefore, we aimed to evaluate the relationship between reproductive factors including age at menarche and the risk of colorectal adenoma.

Aims and Methods: A cross-sectional study was performed on asymptomatic female subjects who underwent colonoscopy between 2010 and 2014 as part of a comprehensive health screening program in Korea. The association between reproductive factors including age at menarche and the presence of adenomas was assessed using multivariate logistic regression analysis.

Results: Among 32,620 asymptomatic female subjects, the proportion of patients with menarche at 10–11, 12–13, 14–15, 16–17, and 18–19 years of age was 4.1%, 31.7%, 45.4%, 14.9%, and 4.0%, respectively. Age at menarche was not significantly associated with the risk of any adenoma (adjusted odds ratio [AOR], 0.99; 95% confidence interval [CI], 0.97 to 1.02; p = 0.500) and advanced adenoma (AOR, 0.98; 95% CI, 0.91 to 1.04; p = 0.468) after adjusting for confounding factors. Age at menarche was not significantly associated with the risk of adenoma even among the similar age group. In addition, parity, use of female hormones, and menopause were not associated with the risk of adenoma.

Conclusion: Age at menarche, parity, use of female hormones, and menopause were not significantly associated with the risk of colorectal adenoma. Our findings indicate that reproductive factors including age at menarche do not affect the development of colorectal adenoma.

<table>
<thead>
<tr>
<th>Any Adenoma</th>
<th>Advanced Adenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants’ age groups</td>
<td>adjusted odds ratio (95% CI)</td>
</tr>
<tr>
<td>30–34 (years)</td>
<td>1.01 (0.93–1.99)</td>
</tr>
<tr>
<td>35–39</td>
<td>0.94 (0.88–1.00)</td>
</tr>
<tr>
<td>40–44</td>
<td>0.97 (0.92–1.04)</td>
</tr>
<tr>
<td>45–49</td>
<td>1.06 (0.99–1.14)</td>
</tr>
<tr>
<td>50–54</td>
<td>1.10 (0.95–1.09)</td>
</tr>
<tr>
<td>≥55</td>
<td>1.03 (0.98–1.08)</td>
</tr>
</tbody>
</table>

[Risk of colorectal adenoma according to the age at menarche among similar age groups]

Disclosure: Nothing to disclose

P0403 METABOLIC FACTORS, LIFESTYLE HABITS AND AGING ARE ASSOCIATED WITH DEVELOPMENT OF COLORECTAL NEOPLASIA IN JAPAN

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Introduction: For the past decades, the incidence and mortality rate of colorectal cancer (CRC) has been increased in Japan and CRC is the third leading cause of cancer death in Japan. This may reflect economic development and concomitant shifts from traditional lifestyle towards a westernized lifestyle. The association of metabolic syndrome (MetS) and CRC has been reported in several studies, however, individual factors contributing to CRC occurrence have been obscure, especially in Japan.

Aims and Methods: In the present study, we investigated the risk factors such as metabolic and lifestyle factors for the occurrence of colorectal neoplasia (CRN; adenomatous polyp ≥ 5 mm in size and cancer) and advanced neoplasia (AN; advanced adenoma and cancer, ref.) by using comprehensive health checkup data. We conducted a retrospective analysis in clinical practice at a single center. Among 10138 subjects who took comprehensive health checkup at our hospital between in August 2012 and December 2016, 2769 subjects who also underwent screening colonoscopy were enrolled. A diagnosis of MetS was made by Metabolic Syndrome Diagnostic Criteria Exploratory Committee in Japan. Demographic characteristics, anthropometric measurements, visceral fat area (VFA) measured at the umbilical level by CT, hematological metabolic parameters, degree of liver fat evaluated by ultrasoundography, and current smoking and drinking habits were assessed. Association between variables and CRN or AN was evaluated by univariate analysis using t-test, X2 test, Mann-Whitney test, and then by multivariate analysis using multiple logistic regression model. A p value < 0.05 was considered statistically significant.

Results: Of 2769 subjects analyzed, 327 subjects had CRN (11.8%) and 99 had AN (3.3%). 676 subjects were diagnosed as MetS (24.4%) and presence of MetS was significantly associated with CRN and AN (p = 0.000, 0.004). Univariate analysis identified significant association of CRN with sex, age, body mass index (BMI), VFA, systolic and diastolic blood pressure (SBP/DBP), low-density lipoprotein (LDL)-cholesterol, triglycerides (TG), fasting plasma glucose (FBG), hemoglobin A1c (HbA1c), fatty liver, smoking habits, drinking habits and ≥ 10 kg weight gain compared with the body weight at the age of 20. Logistic regression analysis revealed that age, BMI, SBP, LDL TG, current smoking and drinking habits were independent factors associated with CRN (Table). Moreover, age, LDL TG and current smoking were recognized as independent factors associated with AN.

Conclusion: The present study demonstrated that metabolic factors, especially dyslipidemia, age, and current smoking were risk factors for development of colorectal neoplasia in Japan.

Disclosure: Nothing to disclose

Reference


P0404 COMPARISON OF COLORECTAL POLYS WITH SIZE BETWEEN 6 AND 20 MILLIMETERS IN YOUNGER AND OLDER INDIVIDUALS

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Introduction: According to the recommendation by the U.S. Multi-Society Task Force on Colorectal Cancer, colonoscopy screening for colorectal neoplasm should be performed for individuals for 50 years old and over. Over the last decades, the incidence and mortality of colorectal cancers (CRCs) in individuals who are 50 or more years old have been decreasing. In contrast, the incidence of CRCs in individuals less than 50 years old has been increasing. Several studies demonstrated that CRCs in older individuals have a different biology compared to younger individuals. However, the data on the characteristics of colon polyp in individuals aged <50 years is limited.

Aims and Methods: The aim of this study was to investigate the characteristics of colorectal neoplasm in individuals aged <50 years and to compared them to those of individuals ≥50 years old. From Jan 1, 2015, to Jan 31, 2017, patients
who underwent snare polypectomy with polyp’s size between 6 and 20 millimeters (mm) were enrolled in a tertiary medical center of northern Taiwan. The demography of patients and the polyp characteristics, including pathological findings, size, morphology and location, were recorded. Descriptive statistics and frequency distributions were calculated. The data were analyzed by using either the Mann-Whitney U test for continuous variables or chi-square test for categorical variables. Statistical significance was defined as p < 0.05.

Results: A total of 1925 polyps in 1424 patients were included in this study. There were 323 polyps in 264 patients < 50 years old (younger group) and 1602 polyps in 1160 patients ≥ 50 years old (older group). In the younger group, 193 patients were male (69.3 %), with a median age of 44 years old (range: 19-49 years old). The median size of polyps was 10 mm (range: 6-20 mm) in the younger group. Most polyps in the younger group were in the distal colon (65.2 %) and pedunculated shape (83.6 %). Furthermore, the ratio of the prevalence of the distal colon polyp and pedunculated polyp was significantly higher in the younger group (62.8 % vs. 55.2 %, p = 0.011; 16.4 % vs 12.3 %, p = 0.045) respectively. In the polyp pathological findings, there were 57 (17.1 %) polyps with high-grade dysplasia, 20 (6.2 %) sessile serrated adenomas, 158 (48.9 %) tubular adenoma, 52 (16.1 %) tubulovillous adenoma, 6 (1.9 %) villous adenoma and 2 (0.6 %) high-grade dysplasia in the younger group. In the high-risk polyp subgroup, the prevalence of sessile serrated adenoma and ≥ 10 mm serrated adenoma was significantly higher in the younger group compared to the older group (6.2 % vs 2.7 %, p = 0.002; 3.4 % vs. 1.4 %, p = 0.042) respectively. The prevalence of polyps with high-grade dysplasia was significantly higher in the older group (3.8 % vs 0.6 %, p = 0.014). There was no significant difference between both groups in terms of polyps with size ≥ 10 mm and polyps with villous component.

Conclusion: In the polyps with size between 6 and 20 mm, the prevalence of left sided polyps and pedunculated polyp is significantly higher in patients < 50 years old. In the high-risk polyp subgroup, the prevalence of sessile serrated adenoma is higher in younger group.

Disclosure: Nothing to disclose.

Aims and Methods: This study aimed to uncover the relevant driver genes maintaining EGFR-positive colorectal cancer cells, and to discover the efficiently therapeutic agents. EGFR-positive HCT116- and HT29-derived cancer stem-like cells (CSCs) were induced in vitro as studying models in this study. RNAseq technique following by pathway analyzation was used to identify the differentially expressed maintaining CSCs. Moreover, a panel containing 172 therapeutic agents targeting to the documental pathways of stem cells were applied to search for the efficient therapeutics against CSCs.

Results: RNAseq revealed that 654 genes were significantly up-regulated and 840 genes were down-regulated in the HCT116CSCs. Among the genes, notably, platelet-derived growth factor A (PDGFA) and signal transducer and activator of transcription 3 (STAT3) were relevant to Pathway in Cancer analyzed by using Pathway Analysis. Furthermore, the therapeutic screening indicated that the agents targeting to STAT3 and Wnt signaling pathways were efficient to reduce the cell viabilities of HCT116 and HT29 cells. Consequently, we figured out that inhibition of STAT3 by its specific inhibitors such as homoharringtonine and knockdow technique significantly reduced the formation and survival of the HT29-derived tumorspheres, whereas STAT3 phosphorylation was majorly regulated by EGFR to induce PDGFA and Wnt signaling cascade.

Conclusion: This study demonstrated the potential genes involving in the tumor sphere formation and survival in the selective EGFR-positive colorectal cancers. The data suggested that EGFR-STAT3 signaling pathway promoted and maintained the colorectal cancer stemness as a putative therapeutic target, where STAT3 may be through inducing PDGFA to activate Wnt signaling pathway.

Disclosure: Nothing to disclose.

P0405 SHORTER LIFE EXPECTANCY OF INTERVAL COLORECTAL CANCER AND LEAD TIME BIAS

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Introduction: The outcome of interval colorectal cancer (ICRC) varied in previous studies without accounting for lead time bias.

Aims and Methods: This nationwide cohort analysis estimates expected years of life lost (EYLL) to adjust for lead time bias and comparison between patients with ICRC and detectable colorectal cancer (DCRC). Patients with colorectal cancer (CRC) registered in Taiwan Cancer Registry during 2002 to 2009 were enrolled, including 22,169 CRC confirmed within 6 months after colonoscopy grouped as ICRC (DCRC) and 1,653 CRC diagnosed during 6–60 months after a negative colonoscopy grouped as ICRC. All patients were followed up until the end of 2011. We simulated age- and sex-matched references from life tables in Taiwan National Vital Statistics using Monte Carlo method. Life-time survival of the cancer patients was obtained from extrapolation of logit transform of the survival ratio between cancer cohorts and age- and sex-matched references. The LE (life expectancy) and EYLL were calculated after adjustment for age at diagnosis and/or lead time bias. There is a linear trend for increasing proportion of ICRC from distal to proximal colon, which seems to corroborate with different cancer recurrence patterns along culture time.

Results: Comparing with DCRC, ICRC were predominately older age, more on proximal sites, and more endoscopic polypometry procedures (p < 0.001). Patients with ICRC had consistently shorter LEs than those of DCRC after stratification of CRC patients into stages. There is no such trend if the comparison is performed through EYLL, or adjustment for age at diagnosis and/or lead time bias. There is a linear trend for increasing proportion of ICRC from distal to proximal colon, which seems to corroborate with different cancer recurrence patterns along culture time.

Conclusion: The evidence corroborates the hypothesis that the worse long-term outcome or shorter LE of ICRC largely results from lead time bias.

Disclosure: Nothing to disclose.

P0406 ACTIVATION OF STAT3 MEDIATES SURVIVAL OF CANCER STEM CELLS VIA PDGFA SIGNALING

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Introduction: Cancer stem cells are capable of cell division and survival against cancer therapies, leading to tumor progression and recurrence. The inhibitory agents against cancer stem cells may be efficient for eradicating tumors.

Aims and Methods: In this prospective study we cultured patient-derived tissue microfragments in stirred-tank culture systems (PDEs) - we studied culture viability (metabolic and morphologic evaluations), phenotype [gland and/or villi formation, mucin production, presence of tumor infiltrating lymphocytes (TILs), p53 staining, mismatch repair protein expression, microsatellite instability] and KRAS (exon 2) and BRAFV600E mutational status in in vitro cultures; we correlated culture viability and structure to the primary tumors.

Results: 11 CRCs were collected. All tumors were successfully cultured as PDEs for 28 to 122 days. Culture duration was determined by the frequency of sampling along culture time to assure a minimum PDE concentration. PDEs (N≥7/11) viable were used to determine drug efficacy, there are no available long-term validated models to test chemotherapy in patient-derived cultures, namely in the different carcinogenesis pathways.

Aims and Methods: We aim to develop an efficient methodology for culture of CRC samples originated from different carcinogenesis pathways.

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Introduction: Colorectal cancer (CRC) is the second most common cancer in developed countries. More than a quarter of these patients eventually receive chemotherapy. Several pathways leading to CRC are currently recognized, which may impact on therapy success. Although both short-term culture of tumor sections and xenotransplantation have been used to determine drug efficacy, there are no available long-term validated models to test chemotherapy in patient-derived cultures, namely in the different carcinogenesis pathways.

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Conclusion: In this prospective study we cultured patient-derived tissue microfragments in stirred-tank culture systems (PDES) - we studied culture viability (metabolic and morphologic evaluations), phenotype [gland and/or villi formation, mucin production, presence of tumor infiltrating lymphocytes (TILs), p53 staining, mismatch repair protein expression, microsatellite instability] and KRAS (exon 2) and BRAFV600E mutational status in in vitro cultures; we correlated culture viability and structure to the primary tumors.

Results: 11 CRCs were collected. All tumors were successfully cultured as PDES for 28 to 122 days. Culture duration was determined by the frequency of sampling along culture time to assure a minimum PDE concentration. PDES (N = 11/11) retained their origins’ architecture. There was always viable tumor for at least 28 days (~ 46 days, range 28-87 days) and for most cases (N = 7/11) viable stroma was retained for as long as the neoplastic cells. Capillaries were not preserved. PDES (N = 10/11) considerably lost tumor architectural, stroma cellularity and inflammatory cells, specifically TILs, at the first histological evaluation (days 7-11), but less significantly thereafter. After the first week of culture, PDE tumor cells progressively acquired a senescent phenotype. PDES (N = 10/11) replicate the original tumors’ immunohistochemical and genetic key features. One PDE showed a KRAS mutation undetected in the primary tumor, from day 0; p53 staining was also consistently different in the PDE.

Conclusion: PDE dynamic culture is an efficient method to culture human CRC. Overall the key pathological features of the primary tumors are retained over time, which supports the potential use in drug predictive assays. Divergent results may be due to intratumoral heterogeneity and optimization in tumor collection may be required to improve PDE representation of the primary tumor.

Disclosure: Isadora Rosa reports personal fees and/or non-financial support from MSD, Abbvie, Ferring, Dr Falk Pharma, Pharmakern, Hospira, Janssen and Takeda, outside the submitted work.
Lymphovascular invasion was present in 4/5 (80%) and perineural invasion in 3/5 (60%).

**Results:**

The detection of both EFEMP1 and CDH13, using real-time PCR, was associated with increased risk of CRC in both genders. The combined detection of both markers was highly correlated with the presence of CRC, with a positive predictive value of 95%.

**Conclusion:** The detection of EFEMP1 and CDH13 in the early stages of CRC could be a useful tool for the early detection of CRC, especially in women.

**Disclosure:** Nothing to disclose.

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**P0408 HDAC SELECTIVE INHIBITOR, ACY1215, INHIBIT COLON CANCER CELL LINE HCT116**

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**Introduction:**

Colorectal cancer is one of the most common cancers leading cause of death around the world, and 5-FU is the most common used chemotherapeutic drugs for colorectal cancer. However, resistance do occur. HDACs is a unique member of HDACs, and is involved in regulating diverse key biological processes including cell motility, cell division, protein trafficking, and apoptosis, thus playing important role in carcinogenesis. HDAC inhibitors have emerged as promising agents for the treatment of various forms of cancer, and ACY1215, the first oral HDAC6 inhibitor, has shown promising results for treatment of multiple myeloma in phase I and II clinical trials, however little is known about its role in colorectal cancer.

**Aims and Methods:**

We aimed to explore the effect of Rocinolast (ACY1215), a specific HDAC6 inhibitor, on the cell growth, migration and apoptosis of HCT116 cells, as well as its influence on the chemotherapeutic effect of 5-Fluorouracil (5-FU) on colon cancer.

**Results:**

When treating HCT116 cells with different concentration of ACY1215, and explore its effect on cell viability, proliferation, cell migration and apoptosis, and explore the potential mechanism of ACY1215 via detecting some cell signal related protein by western blot. And then explore the influence of ACY1215 treatment on the chemotherapeutic effect of 5-FU.

**Results:**

After treating HCT116 cells with ACY1215, the cell viability, colony formation, wound closure and migrated cell numbers were significantly reduced with the increasing concentration of ACY1215. When the proportion of apoptosis cells were significantly increased with the increased concentration of ACY1215 (p < 0.05), as well as the expression of apoptosis-related protein (PARP and Cleaved-Caspase 3). After treating HCT116 cells with ACY1215, the expression of p-ERK and ERK were decreased, while no obvious changes were noticed regarding the expression of MEK and ERK. Treating HCT116 cells with ACY1215 and/or 5-FU, we found that the cell viability, colony formation, wound closure and migrated cell numbers were significantly reduced when compared with control group, or correspond drug, or correspond drug with combined drugs (p < 0.05). The same tendency was noticed in regarding to the expression of apoptosis related protein (PARP and Cleaved-Caspase 3).

**Conclusion:** HDAC specific inhibitor, ACY1215, could inhibit the cell growth, proliferation and migration, and promote apoptosis of HCT116 colon cancer cells. ACY1215 exhibits its tumor suppression role via inhibition of the MEK/ERK signal pathway. ACY1215 may enhance the chemotherapeutic effect of 5-FU on colon cancer cells.

**Disclosure:** Nothing to disclose.

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**P0409 PEDIATRIC COLORECTAL CANCER - A HETEROGENEOUS ENTITY**

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**Introduction:**

Colorectal cancer (CRC) is extremely rare in pediatric patients. A poor outcome has been reported in parallel with unfavorable prognostic factors.

**Aims and Methods:**

We aimed to characterize at clinical, pathological and molecular level a group of pediatric CRC patients (< 18 years) - and evaluate overall and disease-free survival.

**Results:**

Included pediatric CRC patients diagnosed from January 2002 to January 2016. Clinical data, tumor features, and survival were evaluated.

Microsatellite instability (MSI) status, loss of heterozygosity for the microsatellite Bethesda microsatellite markers and expression of the DNA mismatch repair (MMR) proteins were analyzed. Germline mutation analysis was performed. All tumors were MMR-proficient.

**Conclusion:**

Pediatric CRC is a rare entity, with distinct histological and molecular presentations, resembling features from adult CRC. This study demonstrates the importance of comprehensive genetic analysis in pediatric CRC.

**Disclosure:** Nothing to disclose.

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**P0410 CANCER-ASSOCIATED FIBROBLASTS PROMOTES COLORECTAL CANCER THROUGH SECRECION OF TNFSF4 AND IGF2**

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**Introduction:**

As an essential part in stromal cells, cancer-associated fibroblast (CAF) plays an important role in the tumor microenvironment and exerts promoting effect in colorectal neoplastic progression. However, the detailed molecular mechanisms remain largely unknown.

**Aims and Methods:**

In this study, we proposed to reveal the oncogenic role of CAF in colorectal cancer (CRC) progression. The primary culture was employed for isolation of CAF and adjacent normal fibroblast (NF). The CRC cells were treated with conditional medium (CM) from NF and CAF for the assessment of cell proliferation rate and invasion ability. RNA-Seq analysis was applied to identify the differentially expressed genes in 3 paired NF and CAF samples. The candidate genes were validated by qRT-PCR in 18 paired primary samples and 7 top genes, TNFSF4 and IGF2, were selected for functional studies.

**Results:**

In primary culture, CAF-produced CM exhibited oncogenic function through promoting CRC cell proliferation and invasion. TNFSF4 and IGF2 were screened out showing the highest expression in CAFs compared with NFs with 14 and 12-time upregulation respectively. qRT-PCR confirmed the abundance of TNFSF4 (p < 0.0001) and IGF2 (p = 0.0056) in CAF.

**Conclusion:**

Immunohistochemistry staining on the tissue microarray demonstrated that TNFSF4 was predominantly expressed in fibroblasts but IGF2 was located both in the cancer cells and fibroblasts. Their receptors, OX40 and IGFFR were expressed in immune cells and cancer cells respectively. In the functional studies, both rhIGF2 and IGF2 CM promotes CRC cell proliferation and invasion in vitro.

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**Disclosure:** All authors have declared no conflicts of interest.
Results: CCS groups included CCS1: CDX (+) and MSI-L/MSS (14 cases), CCS2: MSI-H (5 cases), and CCS3: CDX (+) and MSI-L/MSS (5 cases). Invasive cancer was significantly higher in CCS3 than CCS1 (CCS1:CCS3, 5/14 vs. 5/5, p = 0.0048). K67 LI and epithelial serration were higher in CCS3 than in CCS1 (CCS1:CCS3, 63.4±4.0 vs. 83.0±5.8, 3.14±5/5, p = 0.0048, 0.031). CCS2 showed the highest mutation number, whereas KRAS and/or BRAF mutation number were higher in CCS3 than CCS1 (2.14 vs. 4.5, p = 0.038).

Conclusion: Early-stage SACs can be classified into 3 molecularly distinct subtypes with different clinicopathological and genetic characteristics.

Disclosure: Nothing to disclose

Reference

P0412 MB2D AND EZH2 REGULATE SFRP1 EXPRESSION WITHOUT AFFECTING ITS HYPERMETHYLATION IN COLORECTAL CANCER CELL LINE

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Introduction: The Secreted frizzled related proteins 1 (SFRP1) as extracellular inhibitors of Wnt signaling is downregulated by high frequency of promoter hypermethylation in the early stage of colorectal tumorigenesis. PCG proteins and MBD proteins important for gene epigenetic regulation have the ability to regulate gene expression. We aim to figure out the role of the specified PCG and MBD proteins in the regulation of SFRP1 gene expression.

Aims and Methods: The methylation status and mRNA expression of SFRP1 in CRC cell lines and human embryo intestinal mucosa cell CCC-HHE-2 are analyzed by Methylation-specific PCR (MSP) and real-time qPCR. The combination of MSP with qPCR proteins with SFRP1 gene is studied. The related genes are screened by chromatin immunoprecipitation (ChIP). We knock down related genes by RNA interference to clear its role in the regulation of SFRP1 gene expression and the effect on proliferation of colorectal tumor cells.

Results: The promoter of SFRP1 was unmethylated in control CRC cell lines and partly methylated in normal cell line CCC-HHE-2. The mRNA expression level of SFRP1 was down-regulated significantly in CRC cell lines compared to normal cell line (p < 0.05), but none of BMI1, EZH2 and MB2D proteins bound to SFRP1 in HCT116 (p > 0.05). The expression of SFRP1 is reactivated by MB2D siRNA (p < 0.05), but not by EZH2 siRNA in SW480 (p > 0.05). However, knockdown of the MB2D and EZH2 together can restore SFRP1 gene expression more effectively and inhibit the proliferation of SW480. All of those inhibitions cannot be provided by MBD2 and EZH2 together can restore SFRP1 gene expression more efficiently and inhibit the proliferation of SW480. All of those inhibitions cannot be increased by knockdown of SFRP1 promoter methylation.

Conclusion: MB2D and EZH2 regulate SFRP1 expression without affecting its hypermethylation in colorectal cancer cells.

Disclosure: Nothing to disclose

P0413 IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS IN THE TUMOR MICROENVIRONMENT OF COLORECTAL CANCER

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Introduction: Cancer microenvironment, including tumor endothelial cells (TECs) and cancer associated fibroblasts (CAF s), plays an important role in the pathogenesis of cancer and is considered as a potential therapeutic target.

Aims and Methods: We aimed to understand the molecular mechanism of microenvironment of colorectal cancer (CRC) and to identify novel therapeutic targets. The gene expression of normal cells in primary CRC and performed multivariate outcome analysis. Stromal cells and epithelial cells from surgically resected primary CRC (n = 14) and corresponding normal colonic tissues (n = 14) by using CD146 and EpCAM as markers. RNA sequencing (RNA-seq) was performed in 3 pairs of normal and tumor stromal cells. Expression of the gene was validated by quantitative RT-PCR (qRT-PCR) and immunohistochemistry. To analyze the gene function, human umbilical vein endothelial cells (HUVECs) and cultured CAFs were transfected with specific siRNAs after which cell viability assays and gene expression microarray were performed.

Results: RNA-seq analysis identified a series of 18 genes upregulated in tumor stromal cells isolated from primary CRC tissues. Through validating the results by qRT-PCR and immunohistochemistry, we identified AEBP1, as a novel candidate of gene. AEBP1 is expressed in TECs and CAFs in CRC tissues, and that the expression was higher in the invasive front. The Cancer Genome Atlas (TCGA) datasets revealed that higher expression of AEBP1 is associated with worse overall survival of CRC patients. Expression of AEBP1 was also upregulated in HUVECs treated with TNM obtained from CRC cell lines. Knockdown of AEBP1 in HUVECs suppressed in vitro tube formation. Knockdown of AEBP1 in HUVECs and CAFs suppressed cell proliferation and induced G1 cell cycle arrest. Microarray analysis revealed that knockdown of AEBP1 in HUVECs significantly affected the expression signature of angiogenesis-related genes including POSTN and SFRP1. To confirm our findings in vivo, we co-transplanted CRC cells with HUVECs into nude mice. We found that knockdown of AEBP1 in HUVECs resulted in reduced micro vessel formations in the xenograft tissues. Moreover, we found that injection of siRNAs targeting mouse AEBP1 suppressed in vitro tumor growth.

Conclusion: Our results suggest that AEBP1 may play an important role in the microenvironment in CRC, and that it could be a potential therapeutic target.

Disclosure: Nothing to disclose

P0414 SYSTEMATIC REVIEW AND META-ANALYSIS: DIAGNOSTIC ACCURACY OF QUANTITATIVE FECAL IMMUNOCHEMICAL TESTS FOR COLORECTAL CANCER DETECTION IN SYMPTOMATIC PATIENTS

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Introduction: The quantitative fecal immunochromostatic test (FIT) is a non-invasive biomarker for the early detection of colorectal cancer (CRC). Recently, the National Institute for Health and Care Excellence (NICE) has recommended the adoption of FIT in primary care to guide referral for suspected colorectal cancer in people without rectal bleeding who have unexplained symptoms but do not meet the suspected cancer pathway referral (1).

Aims and Methods: Our goal is to assess the diagnostic accuracy of FIT for CRC detection in symptomatic patients. 2 searches independently reviewed online databases including MEDLINE, Embase expanding the search to bibliography and authors of relevant studies. All studies evaluating the diagnostic accuracy of quantitative FIT for CRC in symptomatic patients until May 2017 were included. Studies were classified by FIT threshold, brand, percentage of symptoms and CRC prevalence. Quality of studies was evaluated, and global sensitivity and specificity were estimated in addition to the ROC curve (sROC) taking the area under the curve (AUC) as a global precision estimator in those subgroups formed by at least three studies, using a random effect model. Heterogeneity was determined by means of the Q statistic of Cochran. Threshold effect was examined by calculating Spearman’s rank correlation.

Results: 13 studies were included in our review accumulating a sample of 12,584 patients (52% women). Data from 7 cohorts were obtained for patients scheduled consecutively to undergo elective colonoscopy due to several indications, with their CRC prevalence ranging from 0.4 to 7.1%. The remaining 6 were carried out on purely symptomatic patients with CRC prevalence ranging from 2.3 to 16.8%.

The pooled sensitivity for CRC detection of OC-Sensor® at the 0, 10 and 20 μg/g cut-off was 98% (95% confidence interval CI 96–99%), 91% (95% CI 88–93%) and 90% (95% CI 87–93%), respectively. Conversely, pooled specificity at the same thresholds was 36% (95% CI, 34–37%), 80% (95% CI 79–81) and 83% (95% CI 81–84%), respectively. At the threshold with the best discriminatory ability (20 μg/g of feces) the AUC was 0.93 (95% CI, 0.91–0.96). The number of available studies performed with the OC-Sensor® allowed for the conduct of a subgroup analysis based on the prevalence of CRC and the percentage of symptoms at the 10 μg/g cut-off. Pooled sensitivities were higher in the studies reporting a CRC prevalence ≥3% (92%, 95% CI; 89–94%) and in those performed only on a symptomatic population (94%, 95% CI, 91–97%); Conversely, the test’s specificity in those subgroups was 70% (5% CI, 68–71%) and 66% (95% CI, 64–67%), respectively.

3 studies using OC-Sensor® with the same threshold identified 79% (95% CI; 76–81%) of patients with significative colonic lesions (SCL), with a 70% (95% CI; 68–72%) specificity, respectively.

Only 3 studies evaluated HM-Jack® at different thresholds. The AUC was 0.88 (95% CI, 0.77–0.98). There was substantial heterogeneity between studies specifically in the pooled specificity estimates.

Conclusion: The diagnostic accuracy of FIT is highly sensitive for CRC detection in symptomatic patients. However, its global accuracy may depend on the prevalence of another SCL. Caution is recommended when using it to rule out CRC in this setting.

Disclosure: The work described in this abstract has been previously presented as an oral presentation at a Spanish scientific meeting (Asociación Española de Gastroenterología) in Madrid in March 2018.

Reference
P0415 ACCURACY OF QUANTITATIVE FECAL IMMUNOCHEMICAL TEST TO DETECT COLORECTAL CANCER. REAL-LIFE DATA IN 22,819 PATIENTS FROM THE GENERAL PRACTICE SETTING IN SPAIN

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Introduction: The quantitative immunochromical fecal occult blood test (FIT) has proved its worth on both CRC screening and in the timely assessment of patients with symptoms of lower bowel disease (1). However, its use in routine clinical practice remains unknown, as does its accuracy to detect CRC in this setting.

Aims and Methods: Our purpose was to describe the use of FIT in 2 Spanish regions and estimate its accuracy in real practice, in order to consider whether or not it is comparable to theoretical values.

Retrospective observational study with long-term follow-up. We included all subjects from the metropolitan area of San Sebastian (SS) and the province of Ourense (Ou) who had been performed a FIT determination (OC-Sensor®) requested at their primary care center between January 2009 and May 2015. CRC diagnosis was determined in the following 2 years using discharge information obtained from the national surveillance system for hospital data. Conjoint Minimo Basico de Datos (CMBD), provided by the Ministry of Health. Global accuracy for detecting CRC was assessed by means of the receiver operating characteristics (ROC) curve and its area under the curve (AUC). Sensitivity and specificity were calculated using 10 and 20 g/g feces as thresholds. Subgroup analysis were conducted using 10 μg/g cut-off to assess differences between center, age, sex and test indication (CRC screening / symptom evaluation).

Results: During the studied period, at least 1 FIT determination was requested to 22,819 patients (54.1% women). 5,265 people were from SS and 17,554 from Ou with significant differences with regard to age (SS=60.4±16.3, Ou=64.9±16.1; p<0.0001) and CRC diagnosis was determined in the following 2 years using discharge information obtained from the national surveillance system for hospital data. Conjoint Minimo Basico de Datos (CMBD), provided by the Ministry of Health. Global accuracy for detecting CRC was assessed by means of the receiver operating characteristics (ROC) curve and its area under the curve (AUC). Sensitivity and specificity were calculated using 10 and 20 g/g feces as thresholds. Subgroup analysis were conducted using 10 μg/g cut-off to assess differences between center, age, sex and test indication (CRC screening / symptom evaluation).

With regard to subgroup analysis, no differences were found in sensitivity between regions (SS 85.0%, CI 95% 84.5–85.6; Ou 84.5% CI 95% 83.8–85.3; p=0.72), age (< 50y 85.0%, CI 95% 84.0–86.0, ≥50y 85.5% CI 95% 84.9–86.2; p=0.21), sex (men 90.5%, CI 95% 89.0–91.9, women 89.5% CI 95% 88.5–89.3, p=0.57) or CRC diagnosis (SS 10%, Ou 2% <p=0.001) or CRC diagnosis (SS 10%, Ou 2% <p=0.001). The reason for requesting the test was available for SS subjects (53.9% symptom evaluation). Subgroup analysis were conducted using 10 μg/g cut-off to assess differences between center, age, sex and test indication (CRC screening / symptom evaluation).

Conclusion: The AUC of FIT to detect CRC was 0.85 (CI 95% 0.84-0.87). Sensitivity and specificity at the 10 and 20 g/g cut-offs were 91% (CI 95% 87.6–93.5) vs 88% (CI 95% 84.3–90.9) and 77.8% (CI 95% 77.2–78.4) vs 85.2% (CI 95% 84.7–85.8) respectively.

Drs. Jonathan Manning was an investigator in the MORA study and has received honoraria from Norgine Ltd or investigator advisory board; Cesare Hassan was an investigator in the DAYB study and received honoraria from Norgine Ltd or investigator advisory board; Jonathan Manning was an investigator in the MORA study and has received honoraria from Norgine Ltd. For disclosure, please refer to the conflict of interest section.

Acknowledgements: This work was partially supported by the Alexander S. Eckle Foundation. The authors declare no conflicts of interest.

P0416 HIGH-QUALITY CLEANSING IMPROVES LESION DETECTION DURING COLONOSCOPY COMPARED TO ADEQUATE CLEANSING: POST HOC ANALYSIS OF 1170 CENTRAL-READER ASSESSED PATIENTS IN THREE RANDOMISED PHASE 3 TRIALS

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Introduction: Effective colonoscopy requires successful bowel preparation. ‘Adequate’ preparation allows detection of lesions >5 mm and has been defined as a Boston Bowel Preparation Scale (BBPS) score of ≥2 per segment. This post hoc analysis determined the relationship between BBPS scores and adenoma and polyp detection in patients who had identified scores in each of the 3 colon segments, using pooled data from 3 identically designed Phase 3, multicentre, randomised trials.

Aims and Methods: Analyzed patients had: treatment-blinded central reader assessed BBPS scores where the BBPS score was identical in each segment, and recorded polyp and adenoma counts. Patients were stratified to assess the relationship between low-quality cleansing (BBPS of 1–1,1–2 or ≥2–2) or high-quality cleansing (BBPS of 3–3,3–4, and ADR and PDR. A logistic regression (LR) model was fitted to assess whether ≥1 polyps and, separately, ≥1 adenomas, were detected including the BBPS score group and study as fixed effects.

Results: 1170 patients were analysed (Table 1). For low, adequate and high-quality cleansing, the PDRs were: 40.7%, 41.7%, 54.8%, and the ADRs were: 27.8%, 26.0% and 42.8%. The odds ratio (OR) for detection were significantly higher with high-quality versus adequate cleansing (PDR OR: 1.60, 95% confidence interval [CI] 1.14–2.24, p<0.0067; ADR OR: 1.97, 95% CI 1.39–2.80, p<0.0001). LR analysis revealed a significant correlation between BBPS score and PDR (p=0.0239) and ADR (p=0.0006).

Conclusion: In patients who had uniform low, adequate or high-quality cleansing in each respective colon segment, there was a strong correlation between higher cleansing scores and increased PDR and ADR.

Abstract No: P0416

<table>
<thead>
<tr>
<th>Overall colon lesion detection rates</th>
<th>High-Quality</th>
<th>Adequate</th>
<th>Low-Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDR, n (%)</td>
<td>(N=166)</td>
<td>(N=54)</td>
<td>(N=54)</td>
</tr>
<tr>
<td>91 (54.8)</td>
<td>396 (41.7)</td>
<td>22 (40.7)</td>
<td></td>
</tr>
<tr>
<td>ADR, n (%)</td>
<td>(N=166)</td>
<td>(N=54)</td>
<td>(N=54)</td>
</tr>
<tr>
<td>71 (42.8)</td>
<td>247 (26.0)</td>
<td>15 (27.8)</td>
<td></td>
</tr>
<tr>
<td>LR Analysis of Association between Uniform BBPS Score Group and PDR, Pue.</td>
<td>0.0239</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LR Analysis of Association between Uniform BBPS Score Group and ADR, P-value</td>
<td>0.0006</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Aims and Methods: Patients aged 18-85 years were included if they had fully reported HCS scores, adenoma and polyp counts, and also identical segmental HCS scores (range 0-4) in all 5 HCS colon segments. A logistic regression analysis was performed using the Cox proportional hazard (CH) (Cox) and p-value (p) for the resulting trend in lesion detection, when segmental HCS scores increased incrementally from 0 to 4.

Results: 469 patients were included in this analysis (Table 1). When uniform segmental HCS scores were increased from 0, 1, 2, 3, and 4, the resulting ADRs increased continuously (0%, 10.0%, 25.6%, 32.4% and 53.8%) as did the PDRs (0%, 30%, 43.5%, 51.4%, and 61.5%). The corresponding OR (CI) and [P] were, for ADR 1.61 (1.182-2.199) [0.0026], and for PDR 1.38 (1.021-1.863) [0.0361].

Conclusion: ADR and PDR increased continuously with improved colon cleansing quality. There was a strong association between uniform segmental HCS scores and both ADR and PDR.

Disclosure: Jonathan Manning was an investigator in the MORA study and has received honoraria from Norgine Ltd. for investigator advisory board attendance and clinical conference attendance as a presenting author; Cesare Hassan was an investigator in the DAVB study and received honoraria from Norgine Ltd. for investigator advisory board attendance; Juha Halonen and Bharat Amlani are employees of Norgine Ltd; Michael Epstein was an investigator in the NOCT study and has acted as a safety advisor for Aspire Bariatrics, a consultant for Efizio Pharma and IM HealthScience, as a speaker for Daichi Sankyo and Pfizer.

Table 1. Uniform segmental HCS scores vs lesion detection rates

<table>
<thead>
<tr>
<th>Segment</th>
<th>ADR, n (%)</th>
<th>PDR, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>97 (25.6)</td>
<td>164 (43.3)</td>
</tr>
<tr>
<td>3</td>
<td>12 (32.4)</td>
<td>19 (51.4)</td>
</tr>
<tr>
<td>4</td>
<td>21 (53.8)</td>
<td>24 (61.5)</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

N = 4

Logistic regression analysis of the trend for uniform HCS scores vs ADR: Odds ratio (95% CI) [P-value]

ADR, p = 0.0026

PDR, p = 0.0361

Logistic regression analysis of the trend for uniform HCS scores vs PDR: Odds ratio (95% CI) [P-value]

ADR, p = 0.0026

PDR, p = 0.0361

**P0418 RAID-CRC: A NOVEL NON-INVASIVE TOOL FOR COLORECTAL CANCER SCREENING BASED ON BACTERIAL SIGNATURES CAPABLE OF REDUCING THE FAECAL IMMUNOCHEMICAL TEST FALSE-POSITIVE RESULTS**

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Introduction: Colorectal cancer (CRC) is the third main cause of cancer mortality. Around 75% of CRC are sporadic and they usually develop without symptoms. Therefore, some countries are implementing CRC national screening policies in order to detect lesions at an early stage by using non-invasive tools. One of the most common tools is the faecal immunochemical test (FIT). Despite affordability, FIT shows a low sensitivity for precancerous lesions (29%) and a low positive predictive value (8%), which produces a high rate of false positive results. Hence, CRC-screening organizations are demanding new, non-invasive tools, capable of decreasing false positive rates, thus reducing the number of unnecessary colonoscopies. The aim of this study was to develop a new, non-invasive CRC screening tool based on bacterial faecal markers, which in combination with FIT (thereby named RAID-CRC), could reduce the false-positive rate.

Aims and Methods: We performed the FIT analysis (OC-Sensor® Kit) and the bacterial markers analysis (CR1-CRC10) in stool samples from individuals with normal colonoscopy (167), non-advanced adenomas (88), advanced adenomas (30) and CRC (48). All participants showed CRC-associated symptoms. The RAID-CRC algorithm was designed using machine learning technology.

Results: Performance of FIT for advanced neoplasia (i.e. advanced adenoma and CRC) was determined by using the cut-off value established in Catalonia (OC-Sensor®, 20 μg Haemoglobin of faeces) for a population-based screening approach. Sensitivity and specificity values of 83% and 80%, respectively, and positive and negative predictive values of 56% and 94%, respectively, were obtained. When RAID-CRC was used, the corresponding values were 80% and 90% for sensitivity and specificity, respectively, and 70% and 94% for positive and negative predictive values, respectively, resulting in a 50% reduction of the false-positive rate.

Conclusion: RAID-CRC is a promising tool for CRC screening because of its non-invasiveness, its low cost and its capacity for lowering the number of false-positive results associated with the use of FIT. Therefore, RAID-CRC use would lead to a reduction up to 30% of unnecessary colonoscopies and their derived costs. However, since our study was based on a small sample of individuals, this new approach warrants to be validated in a screening scenario.

Disclosure: Prof. Garcia-Gil, Dr. Aldeguer, Dr. Serra-Pagés, Dr. Serrano, Dr. Ramio-Pujol, Mr. Amoedo, Ms. Oliver are employees from GoodGut, company who has received private and public funding. The rest of the authors have nothing to disclose.

**P0419 CLINICAL AND PATHOLOGICAL OVERLAP AMONG THE HAMARTOMATOUS POLYPOSIS SYNDROMES CAN RESULT IN ERRONEOUS DIAGNOSIS**

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Introduction: Hamartomatous polyposis syndromes (HPS) are a group of rare autosomal-dominant syndromes, associated with hamartomatous polyps and gastrointestinal (GI) tract malignancies, including: Juvenile polyposis (JPS), Peutz-Jeghers syndrome (PJS) and Cowden disease (CD). There is a known clinical and histological overlap between syndromes. Appropriate diagnosis dictates cancer prevention surveillance for the proband and family carriers. Yet, more than 50% of clinically diagnosed cases have no genetic diagnosis.

Aims and Methods: We aimed to describe phenotype, genotype, histology and outcomes of individuals/families with HPS, study overlap between syndromes and erroneous diagnosis according to genetic findings.

Retrospective cohort-study of consecutive HPS patients. Demographic, clinicopathological and genetic data were obtained from computerized-medical-records.

Results: 52 individuals from 34 families were included. Phenotypic, oncologic and genetic findings of the 3 syndromes are described in Table 1. Clinical manifestations included mainly rectal bleeding (49% JPS, 23% PJS, 25% CD) and bowel obstruction (46.15% JPS, 11.4% JPS). Pathological report varied widely, with 75% of JPS, 61% of PJS and 50% of CD having a polyp diagnosis different from the syndrome hallmark, with some patients having up to 6 different types of polyps. Overall 22/52 (42.3%) of patients had a histological diagnosis of adenoma during follow up (48.5% of JPS, 38.4% of PJS and 25% of CD). 4 patients had an initial incorrect diagnosis, with subsequent review of pathology and genetic testing unveiling the correct syndrome. Gastrointestinal cancer history was positive in 65%, 40% and 50% of JPS, PJS and CD families, respectively. 5 patients developed cancers (2 gastrointestinal, 1 thyroid, 1 breast and 1 with both breast cancer and liposarcoma of the chest). 18 (34.6%) patients tested positive for mutations in either STK11, PTEN, SMAD4 or BMPR1A. 2 additional patients were found to harbour novel gene mutations in AKT1 and TM7SF3. Sanger sequencing had a positive detection rate of 45.4% while next generation sequencing (NGS) had a 100% detection rate.

Conclusion: HPS present various phenotypes with apparent redundancy in histological diagnosis, requiring pathology review. Cancer rates are low at this cohort, potentially due to the young mean age. The NGS era should shed light on further candidate-genes and genetic alterations in order to better understand cancer related mechanisms and prevent malignancy.

Disclosure: Nothing to disclose.

**P0420 ERCC6L PROMOTES CELL GROWTH AND INVASION IN HUMAN COLORECTAL CANCER**

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Introduction: Excisome repair genes (ERCC6L, 66), a newly discovered DNA helicase, has been discovered highly expressed in diverse human cancers. However, the precise role of ERCC6L in colorectal cancer (CRC) remains unclear.

Aims and Methods: This study aimed to explore the potential role of ERCC6L in the development and progression of CRC. Real-time quantitative polymerase chain reaction (qRT-PCR) and western blot were used to detect the expression of ERCC6L in 30 colorectal cancer patients. 9 pairs of CRC tissues were examined.
by immunohistochemistry. The function of ERCC6L in cell proliferation, cycle, apoptosis, invasion and colony-forming ability was examined in CRC cell lines. Results: ERCC6L was highly expressed in CRC tissues and CRC cell lines. The expression of ERCC6L was related to tumor size, but not to other clinical features such as age, gender, differentiation and clinical stage. We found that silencing of ERCC6L by small interfering RNA (siRNA) remarkably inhibited the proliferation rate and colony-forming ability of CRC cell lines. Flow cytometry analysis showed that knockdown of ERCC6L in CRC cells blocked the cell cycle progression and more cells were delayed in G0/G1 phase without affecting apoptosis. Moreover, knockdown of ERCC6L remarkably decreased the invasion number of CRC cells compared with the cells treated with negative control. Conclusion: Our results suggest that ERCC6L can stimulate cancer cell proliferation by promoting cell cycle progression, and it may be a potential target for cancer therapy.

Disclosure: Nothing to disclose

P0421 TARGETED UPLC-MS METABOLOMIC ANALYSIS OF HUMAN FAECE REVEALS NOVEL LOW-INVASIVE CANDIDATE MARKERS FOR COLORECTAL CANCER

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Introduction: A simple, low invasive test with high sensitivity for both colorectal cancer and advanced precancerous lesions might increase uptake and adherence rates, which could improve clinical outcomes. Thanks to the technological advances, these days metabolomics technology offers a powerful tool for biomarker discovery.

Aims and Methods: In this study we have performed a targeted ultra-performance liquid chromatography/time-of-flight mass spectrometry (UPLC-(TOF) MS)-based metabolomics approach to identify faecal biomarkers for the detection of patients with advanced neoplasia. A cohort of 80 patients with advanced neoplasia (40 advanced adenomas and 40 cancers) and 49 healthy subjects were enrolled in the study. We evaluated the faecal levels of 105 metabolites including glycerolipids, glycerophospholipids, sterol lipids and sphingolipids.

Results: We found a panel of 18 metabolites that were significantly altered in patients with advanced neoplasia compared to healthy controls. Combinations of seven of these metabolites including ChoE(18:1), ChoE(18:2), ChoE(20:4), PE(16:0/18:1), SM(42:3) and TG(54:1) discriminated advanced neoplasia with a predictive model that provide an area under the curve (AUC) value of 0.821. Furthermore, the levels of the cholesteryl esters correlated positively with the faecal haemoglobin concentration and its inclusion in the metabolomics signature improved the predictive model to an AUC of 0.885.

Conclusion: Our results suggest that ERCC6L can stimulate cancer cell proliferation by promoting cell cycle progression, and it may be a potential target for cancer therapy.

Disclosure: Nothing to disclose

P0423 PEDIUNCULATED MORPHOLOGY IS AN INDEPENDENT RISK FACTOR FOR A FAVORABLE ONCOLOGIC OUTCOME IN PATIENTS WITH T1 COLORECTAL CANCER


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4University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, Netherlands
5UvU University Medical Center Amsterdam, Critical Care Medicine, Amsterdam, Netherlands
6University Medical Center Utrecht, Pathology, Utrecht, Netherlands
7Gelderse Vallei Hospital, Gastroenterology and Hepatology, Ede, Netherlands
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11Isala Clinics, Gastroenterology and Hepatology, Zwolle, Netherlands
12Rijnstate Hospital, Gastroenterology and Hepatology, Arnhem, Netherlands
13Diakonessenhuis Hospital, Gastroenterology and Hepatology, Utrecht, Netherlands
14Groene Hart Hospital, Gastroenterology and Hepatology, Gouda, Netherlands
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Pedunculated morphology is independently associated with a better prognosis (OR 0.60; 95% CI 0.38–0.98, p = 0.007). The association between morphology and the primary composite endpoint adverse oncologic outcome adjusted for clinical variables, histological variables and treatment approach were defined as lymph node metastasis, distant metastasis, local recurrence or residual tissue. Secondary end-points were metastasis, recurrence and incomplete resection.

Results: In total, 1,656 patients with T1 CRC with a median follow-up time of 42.5 months (IQR 18.5–77.5) were included. Adverse oncologic outcomes were observed in 9.3% (67/723) of pedunculated T1 CRCs vs 16.6% (155/933) of non-pedunculated T1 CRCs. Pedunculated morphology was independently associated with a decreased risk for adverse oncologic outcomes (adjusted OR 0.61; 95% CI 0.43–0.86; p = 0.005). Metastasis, incomplete resection and recurrence were observed in 8.5%, 6.5% and 5.4% of patients, respectively. Pedunculated morphology was also independently associated with a reduced risk for metastasis (adjusted OR 0.41; 0.25–0.69; p = 0.003), incomplete resection (adjusted OR 0.60; 95% CI 0.38–0.98; p = 0.03) and recurrence (adjusted HR 0.51; 95% CI 0.32–0.84; p = 0.007).

Conclusion: Pedunculated morphology is independently associated with a better oncologic outcome with no additional treatment. Incorporating morphology in future risk assessment is therefore likely to refine risk prediction in T1 CRC, thereby improving patient selection for surgery.

Disclosure: Nothing to disclose

P0424 LONG-TERM ONCOLOGIC OUTCOMES OF SELF-EXPANDING METALLIC STENTS AS A BRIDGE TO SURGERY IN MALIGNANT LEFT-SIDED COLON OBSTRUCTION COMPARED WITH EMERGENCY SURGERY
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Introduction: Self-expandable metallic stents (SEMS) are used as a bridge to surgery in malignant left-sided large bowel obstruction (MLO). However, the oncologic outcome after endoscopic stenting remains to be assessed.

Aims and Methods: The aim of this study is to compare the oncologic outcomes of SEMS with those of emergency surgery for MLO. A database of MLO between January 2001 and December 2012 were reviewed. They were divided into those who underwent bridge-to-surgery with SEMS and those who undergone emergency surgery. The 2 groups were compared in terms of disease-free survival (DFS) and overall survival (OS).

Results: 93 patients underwent SEMS and 41 patients underwent ES. Clinicopathological features did not differ significantly between the SEMS and ES groups. (28 (30.0%) patients with sufficient recurrence in SEMS group and 14 (31.4%) patients suffered recurrence in ES group. There were no differences in 5-year DFS (67.6% vs. 64.6%; p = 0.761) and OS rates (71.0% vs. 64.9%; p = 0.554) between the 2 groups.

Conclusion: The SEMS as a bridge to surgery is equivalent to emergency surgery for MLO with regards to oncologic safety.

Disclosure: Nothing to disclose

P0425 HIGH PRETREATMENT PLASMA D-DIMER LEVELS ARE ASSOCIATED WITH POOR SURVIVAL AFTER CURATIVE RESECTION IN PATIENTS WITH COLON CANCER
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Introduction: Coagulation pathways are activated in patients with malignancies. Precancerous versus non-pedunculated CRC have not been performed and current risk stratification for adverse events such as lymph node metastasis is based on histology only.

Aims and Methods: We aimed to compare adverse oncologic outcomes of pedunculated versus non-pedunculated T1 CRCs. Patients diagnosed with T1 CRC between 2000 and 2014 in 14 Dutch hospitals were included. We evaluated the association between morphology and the primary endpoint adverse oncologic outcome adjusted for clinical variables, histological variables and treatment approach. Adverse oncologic outcomes were defined as lymph node metastasis, distant metastasis, local recurrence or residual tissue. Secondary end-points were metastasis, recurrence and incomplete resection.

Results: In total, 1,656 patients with T1 CRC with a median follow-up time of 42.5 months (IQR 18.5–77.5) were included. Adverse oncologic outcomes were observed in 9.3% (67/723) of pedunculated T1 CRCs vs 16.6% (155/933) of non-pedunculated T1 CRCs. Pedunculated morphology was independently associated with a decreased risk for adverse oncologic outcomes (adjusted OR 0.61; 95% CI 0.43–0.86; p = 0.005). Metastasis, incomplete resection and recurrence were observed in 8.5%, 6.5% and 5.4% of patients, respectively. Pedunculated morphology was also independently associated with a reduced risk for metastasis (adjusted OR 0.41; 0.25–0.69; p = 0.003), incomplete resection (adjusted OR 0.60; 95% CI 0.38–0.98; p = 0.03) and recurrence (adjusted HR 0.51; 95% CI 0.32–0.84; p = 0.007).

Conclusion: Pedunculated morphology is independently associated with a better oncologic outcome with no additional treatment. Incorporating morphology in future risk assessment is therefore likely to refine risk prediction in T1 CRC, thereby improving patient selection for surgery.

Disclosure: Nothing to disclose

P0426 ARE ADDITIONAL TREATMENTS REALLY NEEDED AFTER ENDOSCOPIC RESECTION FOR RECTAL SMALL NEUROENDOCRINE TUMORS?
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Introduction: Little is known about the long-term outcomes of endoscopically resected rectal neuroendocrine tumors (NETs).

Aims and Methods: The present study aimed to investigate treatment strategies and long-term outcomes of endoscopic resection of small rectal NETs and long-term outcomes of endoscopically resected rectal NETs. We analyzed medical records of patients who underwent ER for rectal NETS from January 2005 to December 2016. The clinicopathological characteristics of these lesions were analyzed and long-term outcomes were evaluated.

Results: A total of 322 patients were studied. The complete and curative resection rate were 76.4% and 55.9%, respectively. Rectal NETs initially resected as polyps and treated with conventional EMR were observed more frequently in the curative resection group (p = 0.041 and p = 0.012, respectively). After ER, only 44 of the 142 patients (31.0%) who did not meet the criteria for curative resection received additional salvage treatment. In multivariate analysis, lesions diagnosed via biopsies (OR, 0.096; p = 0.002) or suspected as NETs initially (OR, 0.04; p = 0.001) were less likely to undergo additional treatment. Positive lymphovascular invasion (OR 61.71; p < 0.001), positive OR 75.993; p < 0.001, or indefinite OR 13.203; p = 0.001) resection margins were more likely to undergo additional treatment. Although lymph node metastasis was found in 6 patients, none experienced local or metastatic tumor recurrence during the median follow-up of 40.49 months.

Conclusion: Long-term outcomes after ER for rectal NETS were excellent. The prognosis showed favorable outcomes regardless of whether patients receive additional salvage treatment.

Disclosure: Nothing to disclose

P0427 IMPACT OF PRIMARY TUMOR LOCATION AS A PREDICTIVE FACTOR IN CYTOTOXIC ANTI-CANCER AGENT FOR COLORECTAL CANCER (CRC) BASED ON COLLAGEN GEL DROPLET-EMBEDDED DRUG SENSITIVITY TEST (CD-DST)
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Introduction: We have reported the usefulness of CD-DST for the individualization of first-line treatment in CRC (UEGW: 2014; P1538, 2015; P1681, 2016; P0929, 2017; P0466).

In recent years, primary tumor location in CRC as a predictive factor has attracted attention. Several reports have recently addressed the predictive impact of primary tumor location in CRC. A better outcome for left-sided colorectal cancer (CRC) compared with right-sided CRC has been reported. However, in those reports, the chemotherapy regimens always included molecularly-targeted agents. To the best of our knowledge, the impact of primary tumor location as a predictive factor in cytotoxic anti-cancer agent alone (FOLOX/FOLFIRI without molecularly-targeted agents) remains to be explained.

Aims and Methods: The purpose of this study was to clarify the impact of primary tumor location as a predictive factor in cytotoxic anti-cancer agent using CD-DST. Between Mar. 2008 and Apr. 2017, we obtained tumor specimens from 133 CRC patients (CC; n=87, Rectal Cancer; n=46) without preoperative chemother- apy. Written informed consent for measurement of individual chemosensitivity was obtained from all patients. Approval for the present study was obtained from the Tobu Chikuji Hospital Institutional Review Board (No: 02.03.29. #1).
CD-DST was performed and the growth inhibition rate (IR) was determined by incubation with 5-FU and l-OHP. The IR values under each condition and the relationship between the tumor side and the IR values were evaluated using linear regression analysis and t-test, respectively. Cancers present normal or distal of the splenic flexure were classified as right-side or left-side, respectively.

Results: There was a strong correlation between the IRs (%) of the FOLFOX and FOLFIRI regimens for right-sided vs left-sided tumors. In the FOLFOX regimen, the IRs (%) of right-sided and left-sided tumors were 57.4 ± 2.5 and 58.5 ± 1.8, respectively (p = 0.72). In the FOLFIRI regimen, the IRs (%) of right-sided and left-sided tumors were 67.0 ± 2.3 and 65.8 ± 1.9, respectively (p = 0.9).

Moreover, in 87 CT patients, there was also no significant difference in the IRs (%) of the FOLFOX and FOLFIRI regimens for right-sided vs left-sided tumors. In the FOLFIRI regimen, the IRs (%) of right-sided and left-sided tumors were 67.0 ± 2.3 and 69.1 ± 2.4, respectively (p = 0.53).

Of the 133 patients, 42 patients received palliative chemotherapy after surgery. From the 42 patients, the same results were also obtained.

Conclusion: In this study, there was no impact of primary tumor location in cytotoxic anti-cancer agent regimens for CRC. In contrast, as previously reported, a better outcome for left-sided CC compared with right-sided CC depended on one’s tumor biology, especially when using molecular-targeted agent regimens.

As such, our findings underscore the fact that molecularly-targeted agents rather than cytotoxic anti-cancer agents may result in a better outcome for left-sided tumors.

Disclosure: Nothing to disclose

References:
P0431  RAID-LS: A NON-INVASIVE TOOL BASED ON A FAEAL BACTERIAL SIGNATURE FOR LYNCH SYNDROME SURVEILLANCE

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Introduction: Lynch syndrome carriers’ surveillance is performed through endoscopic examinations and with intervals of no more than 2 years. Colonoscopy allows direct visualization of the entire colon but requires bowel preparation, sedation, there is risk of intestinal perforation, it is time consuming and it has high associated costs. These are some of the reasons for which there is low surveillance acceptance among patients.

Aims and Methods: The aims of this work were to compare a specific faecal bacterial signature of sporadic colorectal cancer patients (CRC) and inflammatory bowel disease patients (IBD) with Lynch carriers and develop a non-invasive tool, hereby named RAID-LS, based on these bacterial signatures, which enabled the detection of neoplasia in Lynch population.

A cohort consisting of 66 Lynch syndrome carriers who underwent a surveillance colonoscopy were recruited. A second cohort consisting of control individuals was recruited through the regional CRC screening program or for presenting CRC compatible symptomatology. We performed the analysis of 9 CRC-specific bacterial markers (CRC1, 2, 3, 4, 5, 6, 7, 9, 10) and 4 associated to IBD (IBD1, 2, 3, 4) in stool samples. The RAID-LS was eventually defined using 3 of the analysed biomarkers.

Results: Comparison between those Lynch syndrome carriers who had had CRC and those with no CRC personal background did not show significant differences in the abundance of any of the analysed bacterial markers.

When Lynch with a normal colonoscopy (NC) were compared to control subjects with NC, non-advanced adenomas and advanced adenomas, significant differences were found in the abundance of 4 (CRC1, p = 0.014; CRC3, p < 0.001; CRC6, p < 0.001; CRC7, p = 0.03), 7 (CRC2, p = 0.043; CRC3, p < 0.001; CRC5, p < 0.001; CRC6, p < 0.001; IBD2, p = 0.013; IBD4, p = 0.003) and 9 bacterial markers (CRC2, p = 0.010; CRC3, p < 0.001; CRC5, p < 0.001; CRC6, p < 0.001; CRC7, p < 0.001; IBD2, p = 0.013; IBD2, p = 0.046; IBD3, p = 0.003; IBD4, p = 0.005), respectively. Interestingly, only CRC3 showed significant differences when NC Lynch were compared to control subjects with CRC (p = 0.034).

We designed the RAID-LS algorithm combining CRC1, CRC3 and IBD2 bacterial markers. This combination allowed the detection of neoplastic lesions in Lynch syndrome carriers with sensitivity, specificity, true and negative predictive values of 100%, 72%, 42% and 100%, respectively (AUC = 0.859, 95% CI (0.754-0.964)). These results led to a false-positive rate of only a 23%, reducing by 60% the number of colonoscopies.

Conclusion: Healthy Lynch syndrome carriers show a similar microbiota to that of patients with tumour lesions, suggesting that there is an inflammatory basal gut environment in Lynch similar to that of CRC. RAID-LS efficiently detects pre-neoplastic lesions in Lynch carriers. The use of this tool would suppose a breakthrough for Lynch carriers, who will significantly improve their quality of life by expanding the intervals between colonoscopic surveillance.

Disclosure: Prof. García-Gil, Dr. Aldeguer, Dr. Serra-Pagés, Dr. Serrano, Dr. Ramíó-Pujol, Mr. Amoedo, Ms. Oliver are employees from GoodGut, company who has received private and public funding. The rest of the authors have nothing to disclose.

P0432 COMPARISON OF THREE LYMPH NODE STAGING SCHEMES FOR PREDICTING SURVIVAL IN PATIENTS WITH COLORECTAL CANCER: A LARGE POPULATION DATABASE AND CHINESE MULTICENTER VALIDATION

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Introduction: Several node staging schemes have been proposed for colorectal cancer (CRC) and multiple studies have been conducted to whether number-based scheme (pN), ratio-based scheme (rN) or log odds of positive lymph nodes scheme (LODDS) was associated with CRC survival. However, to the best of our knowledge, there was no study investigate which kind of node staging schemes predicted CRC survival to the best using predicting capacity and the optimal system remains controversial.

Aims and Methods: This study aims to compare 3 node staging schemes in predicting survival outcome in patients with colorectal cancer. Patients with CRC were identified from the Surveillance, Epidemiology, and End Results (SEER) database, and a Chinese multicenter cohort was used for independent validation. The prognostic performance of 3 node staging schemes predicting CRC cause-specific survival (CSS) was compared, involving pN, rN and LODDS. Prediction performance were assessed for overall survival using R2, discriminatory capacity using Harrell’s C statistic, time-dependent receiver operating characteristic (tdROC) at 1, 3, 5, 7, 10 year survival and clinical utility using decision curve analysis (DCA) at 1, 3, 5, 7, 10 year survival. Sensitivity analyses were performed when competing risk was considered or when overall survival (OS) was used. R2 and Harrell’s C statistic was assessed for each multivariate model after including sex, race, age, tumor location, T stage, M stage, grade, histology and size.

Comparison in predicting OS was also performed in Chinese multicenter cohort using R2, Harrell’s C statistic and tdROC.

Results: There were 240,886 patients in the SEER database and 1316 in the Chinese multicenter cohort. LODDS scheme performed better in overall performance R2 (LODDS vs. rN vs. pN: 19.4% vs. 17.6% vs. 9.4%), predictive accuracy (LODDS vs. Harrell’s C statistic (LODDS vs. rN vs. pN: 0.727 vs. 0.719 vs. 0.712) and ROC (LODDS vs. rN vs. pN: 1year: 74.4 vs. 76.1 vs. 77.3; 3year: 75.5 vs. 76.5 vs. 77.4; 1year: 74.9 vs. 75.6 vs. 76.4; 3year: 74.4 vs. 74.9 vs. 75.2; 1year: 73.6 vs. 73.9 vs. 73.9) than either pN or rN, for patients with colorectal cancer in SEER database. DCA also showed LODDS scheme had higher net benefit than either pN or rN (LODDS vs. rN vs. pN: 1year: 0.019 vs. 0.019 vs. 0.007; 3year: 0.116 vs. 0.118 vs. 0.052; 5year: 0.171 vs. 0.139 vs. 0.139; 7year: 0.200 vs. 0.184 vs. 0.184; 1year: 0.226 vs. 0.219 vs. 0.219) when threshold probability was set at 20%. Similar results could be attained in the sensitivity analysis, multivariate cox model and independent Chinese multicenter cohort.

Conclusion: LODDS performed better than rN, and pN in predicting CRC survival.

Disclosure: Nothing to disclose.

Abstract No: P0432: Overall prognostic performance of node staging schemes for colorectal cancer using different analytic strategy

Analysis R2 Harrell’s C index ROC at 1 year ROC at 3 year ROC at 5 year ROC at 7 year ROC at 10 year

Multivariate model
pN 0.214 0.754 (0.753-0.755) 80.7 80.5 79.5 78.4 77.4
rN 0.239 0.768 (0.767-0.769) 81.8 81.9 80.9 79.7 78.5
LODDS 0.252 0.775 (0.774-0.776) 82.1 82.7 81.7 80.5 79.2

Chinese multicenter cohort
pN 0.118 0.638 (0.616-0.661) 69.0 68.3 67.3 65.4 64 NA
rN 0.138 0.646 (0.624-0.668) 71.9 68.7 67.4 66.2 66 NA
LODDS 0.143 0.656 (0.630-0.682) 73.4 70.3 69.1 69.0 69.0 NA
A total of 237 patients with pT1 rectal cancer were enrolled. Median follow-up period was 57 months (range, 12–180 months). Group A, B, and C were 29, 169, and 39 cases. RR in group A, B, and C was 20.7% (6 cases), 4.0% (1 case), and 0.0% (0 case), respectively. In Group A, 3 cases developed local recurrence and the other 3 cases developed distant metastasis. In Group B, 2 cases developed local recurrence and the other 6 cases developed distant metastasis. RR in group A was significantly higher than group B and C (p = 0.001), 5-year DFS in group B (95.3%) and group C (96.3%) were significantly better comparing group A (70.8%) (A vs B, A vs C, p < 0.05). 5-year OS in group B (97.2%) and group C (96.2%) was also better comparing with group A (88.7%), however the difference was not significant among 3 groups. And, there were no significant differences between group B and C. DFS, OS, and DFS. Ionic Conclusion: Long-term outcomes of adj CRT after local resection for patients with high-risk pT1 rectal cancer were similar to those of surgical resection. Adj CRT may be a treatment option if patients with high risk pT1 rectal cancer reject additional surgery. Disclosure: Nothing to disclose

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P0435 SCAR-BIOPSIES AFTER MALIGNANT COLORECTAL POLYECTOMY OF UNCERTAIN RADICALITY
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Introduction: We previously reported the risk for local recurrence was significantly lower with rectal cancer patients with cancer when treated with only endoscopic resection (ER) for pT1 colorectal cancer having high risk of lymph node metastasis. Especially, patients with high-risk pT1 rectal cancer should be recommended additional surgery after ER to prevent recurrence. However, the role of additional surgery with high-risk pT1 rectal cancer was impossible to be established due to additional surgery because of high invasiveness including permanent stomata. Recently, we have experimentally performed adjuvant chemoradiotherapy (adj CRT) for only patients who had rejected additional surgery after local resection including ER or transanal local excision for pT1 rectal cancer in the rectum.

Aims and Methods: Our aim is to clarify long-term outcomes of local resection followed by adj CRT for patients with high-risk pT1 rectal cancer. We retrospectively collected all data on patients with high-risk pT1 rectal cancer treated from January 2000 to December 2016 in our hospital. Patients were classified into 3 groups: patients undergoing only local resection (group A), patients undergoing initial or additional surgical resection with lymph node dissection (group B), and patients undergoing local resection after local resection for pT1 rectal cancer (group C). Adj CRT consisted of continuous infusion of 5-fluorouracil or oral administration of capecitabine, and concurrent radiation of 45 Gy in total. We assessed to compare the recurrence rate (RR), 5-year disease-free survival (DFS), and 5-year overall survival (OS) between each groups.

Results: A total of 237 patients with pT1 rectal cancer were enrolled. Median follow-up period was 57 months (range, 12–180 months). Group A, B, and C were 29, 169, and 39 cases. RR in group A, B, and C was 20.7% (6 cases), 4.0% (1 case), and 0.0% (0 case), respectively. In Group A, 3 cases developed local recurrence and the other 3 cases developed distant metastasis. In Group B, 2 cases developed local recurrence and the other 6 cases developed distant metastasis. RR in group A was significantly higher than group B and C (p = 0.001). 5-year DFS in group B (95.3%) and group C (96.3%) were significantly better comparing group A (70.8%) (A vs B, A vs C, p < 0.05). 5-year OS in group B (97.2%) and group C (96.2%) was also better comparing with group A (88.7%), however the difference was not significant among 3 groups. And, there were no significant differences between group B and C. DFS, OS, and DFS. Ionic Conclusion: Long-term outcomes of adj CRT after local resection for patients with high-risk pT1 rectal cancer were similar to those of surgical resection. Adj CRT may be a treatment option if patients with high risk pT1 rectal cancer reject additional surgery. Disclosure: Nothing to disclose

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P0436 ALCOHOL CONSUMPTION IS ASSOCIATED WITH THE RISK OF DEVELOPING COLORECTAL NEOPLASIA: PROPENSITY MATCHING ANALYSIS
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Introduction: Despite the well-known association between alcohol consumption and colorectal neoplasms, the cumulative effect of alcohol consumption at the time of surveillance colonoscopy has not been investigated. Alcohol consumption after polypectomy is not included in the risk factors for the determination of the time interval of surveillance colonoscopy.

Aims and Methods: This study aimed to determine if alcohol consumption is associated with the development of CRN at the time of surveillance colonoscopy taking consideration of index colonoscopy findings and data on alcohol consumption. We prospectively identified 1,448 patients who underwent index and subsequent surveillance colonoscopy during the study period. The association between significant alcohol consumption (>30g/day, females >20g/day) and development of new CRN was examined. Moreover, significant alcohol consumption was a risk factor for CRN occurrence at the time of surveillance colonoscopy with marginal significance in male (aHR: 2.64, 95% CI: 0.93–7.52, p = 0.07). There was no association between significant alcohol consumption and overall CRN occurrence at the time of surveillance colonoscopy (aHR: 2.01, 95% CI: 1.14–3.52, p = 0.02). Furthermore, there is no association between significant alcohol consumption and development of advanced CRN on surveillance colonoscopy (aHR: 2.01, 95% CI: 1.14–3.52, p = 0.02). However, it was assumed that the risk of overall CRN occurrence, especially in patients in the normal or low-risk categories at index colonoscopy, was associated with significant alcohol consumption. Significant alcohol consumption was associated with the overall CRN occurrence at the time of surveillance colonoscopy in the normal (aHR: 1.90, 95% CI: 1.16–3.13, p = 0.01) and low-risk groups (aHR: 2.13, 95% CI: 0.98–4.62, p = 0.06). Moreover, significant alcohol consumption was a risk factor for CRN occurrence at the time of surveillance colonoscopy, suggesting that it is too low to safely exclude residual cancer. These biopsies should not be used to determine the value of this 1mm cut-off to predict local recurrence of cancer.

Disclosure: Nothing to disclose
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P0437 LONG-TERM OUTCOMES AFTER ENDOSCOPIC VERSUS SURGICAL TREATMENT OF T1 COLRECTAL CARCINOMA

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Introduction: The gold standard for treatment of T1 carcinoma used to be an oncological surgical resection including resection of draining lymph nodes. The number of endoscopic resections of T1 carcinoma will continue to increase in line with the increased detection. Increasing evidence showed that endoscopic resection is adequate for T1 carcinoma with a low risk for LMN. Long-term outcomes of patients with T1 colorectal cancer (CRC) treated by endoscopic resection (ER) or surgical resection have not been well established in Korea.

Aims and Methods: The aim of this study was to evaluate the long-term outcomes among patients with T1 CRC. This retrospective study included 386 patients with T1 CRC with initial endoscopy (n = 188) or surgery (n = 198) between 2000 and 2010 at the St. Mary's Hospital. Patients who did not meet the criteria including those with disease recurrence were excluded. The outcomes were compared in the Japanese Society for Cancer of the Colon and Rectum guidelines (negative resection margin, no lymphovascular invasion, submucosal invasion depth < 1000 μm, well/moderately differentiated adenocarcinoma, grade 3 tumor budding) were defined as 'low risk', and were subdivided into 4 groups: ER with low risk (Group A: 71 patients), ER with high risk (Group B: 117 patients), surgery with low risk (Group A: 65 patients), surgery with high risk (Group B: 133 patients).

Results: During follow-up period, local recurrence or distant metastasis was developed in 8 (1.8%) patients (Group A: 0, Group B: 4, Group C: 0, Group D: 4). 5-year recurrence free survival rate was significantly lower in Group B (Group A: 100%, Group B: 85.0%, Group C: 98.5%, Group D: 95.6%, p = 0.02). However, there was no statistically significant difference in the 5-year overall survival rate among treatment methods (Group A: 100%, Group B: 94.2, Group C: 98.5%, Group D: 98.1%, p = 0.23). Among patients (n = 285) who underwent surgery, lymph node metastasis (LNM) was observed in 33 (11.6%) patients. In the multivariate analysis, lymphatic invasion and depth of submucosal invasion were independent risk factors of LNM.

Conclusion: Endoscopic resection of T1 CRC in patients with low risk is safe. ER for T1 CRC did not worsen the clinical outcomes of patients who required additional surgical resection.

Disclosure: Nothing to disclose

P0438 QUALITY OF LIFE AND WORRY ABOUT CANCER RECURRANCE IN T1 COLRECTAL CANCER PATIENTS TREATED WITH ENDOSCOPIC OR SURGICAL TUMOUR RESECTION

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Introduction: To optimise therapeutic decision-making in T1 colorectal cancer (T1 CRC) patients, it is important to elicit the patient’s perspective next to considering medical outcomes. Because empirical data on patient-reported impact of different treatment options are lacking, we evaluated patients’ quality of life, perceived time to recovery and worry about cancer recurrence after endoscopic or surgical treatment for T1 CRC.

Aims and Methods: In this cross-sectional study, we selected patients with histologically confirmed T1 CRC, who had participated in the Dutch Bowel Cancer Audit (ABK). These patients received endoscopic or surgical treatment between January 2014 and July 2017. Quality of life was measured using the EORTC QLQ-C30 and the EQ-SD-5L questionnaire. We used the Cancer Worry Scale to evaluate patients’ worry about cancer recurrence. A question on perceived time to recovery after treatment was also included in the set of questionnaires sent to the patient.

Results: Of all 119 eligible patients, 92.4% responded to the questionnaire (endoscopy group: 55/62, surgery group: 55/57). Compared to the surgery group, perceived time to recovery was on average 3 months faster in endoscopically treated patients after adjustment for confounders (p = 0.001). The 2 treatment groups did not show any significant difference in global quality of life, functioning domains as well as symptom severity. Moreover, patients in the endoscopy group did not report significantly more worries about cancer recurrence than those in the surgery group.

Conclusion: From the patient’s perspective, endoscopic treatment provides a quicker recovery than surgery, without provoking more cancer recurrence worries or any deterioration in quality of life. These results contributed to the shared therapeutic decision-making process of clinicians and T1 CRC patients.

Disclosure: Nothing to disclose

P0439 THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY IN FUNCTIONAL ANORECTAL DISORDERS: RESULTS FROM A LARGE OBSERVATIONAL COHORT STUDY

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Introduction: The aim of the study was to describe the results of 3-dimensional high-resolution anorectal manometry (3DHRAM) in a large cohort of patients with functional anorectal disorders.

Aims and Methods: In this single-centre retrospective study, all consecutive patients referred for investigation of faecal incontinence (FI) or dyssynergic defecation (DD) underwent 3DHRAM. The parameters analysed were usual manometric data, repartition of dyssynergic patterns, and the prevalence of a new ‘muscular subtype classification’ underlying dyssynergia, of anal sphincter defects and of pelvic floor disorders.

Results: Final analyses were performed in 1477 patients of mean age 54 ± 16 years, 825 were suffering from DD and 652 from FI. Among the patients, 86% met dyssynergia diagnostic criteria. Dyssynergic pattern II was the most frequently observed (56%) in women and in men suffering from FI, as well as in women with DD. Type I was the most frequently observed in men with DD (49%). Regarding the muscle type subgroups, combined puborectalis muscle involvement with external anal sphincter profile was the most frequently observed pattern. The global prevalence of rectal intussusception and of excessive peri-anal relaxation were 13% and 21%, respectively. The type III dyssynergic pattern was more frequently associated with pelvic floor disorders than other types (p < 0.001).

Conclusion: This large cohort study provides reference values of 3DHRAM in patients with functional anorectal disorders. Further studies will be necessary to assess the prevalence of pelvic floor disorders in healthy volunteers and to develop new scores and classifications including all of these new parameters.

Disclosure: VB, MB and CA have conflicts of interests. They previously have worked for Given Imaging as experts in order to teach 3DHRAM to other practitioners.

P0440 THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY CAN PREDICT RESPONSE TO BIOFEEDBACK THERAPY IN DEFECATION DISORDERS

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Introduction: Biofeedback therapy (BT) is a simple and effective technique for managing outlet constipation and faecal incontinence. Several clinical factors are known to predict BT response, but a 50% failure rate persists. Better selection of BT responsive patients is required. We aimed to determine whether the defecation disorder type per high-resolution manometry (HRM) was predictive of BT response.

Aims and Methods: We analyzed clinical, manometric and ultrasound endoscopic data from patients who underwent BT in our department between January 2015 and December 2016. Patients were classified into 4 groups per the following defecation disorder classification criteria: rectal pressure > 40 mmHg and anal paradoxical contraction (type I); rectal pressure < 40 mmHg and anal paradoxical contraction (type II); rectal pressure > 40 mmHg and incomplete anal relaxation (type III); and rectal pressure < 40 mmHg and incomplete anal relaxation (type IV). An experienced single operator conducted 10 weekly 20-minute sessions. Efficacy was evaluated with the visual analog scale.

Results: Of 92 patients, 47 (50.5%) responded to BT. Type IV and type II defecation disorders were predictive of success (p = 0.03) OR = 5.93 [1.02; 24.92] and failure (p = 0.05) OR = 0.41 [0.17; 0.99], respectively. The KESS score severity before BT (p = 0.03) OR = 0.9 [0.81; 0.99] was also predictive of failure.

Conclusion: The manometry types identified according to the defecation disorder classification criteria were predictive of BT response. Our data confirm the role of 3-dimensional HRM in the therapeutic management of anorectal functional disorders.

Disclosure: VB, MB and CA have conflicts of interests. They previously have worked for Medtronic as experts in order to teach 3DHRAM to other practitioners.
P0441 WHOLE AND REGIONAL ASSESSMENT OF CONTRACTILE TEMPERATURE AND PH PROFILE IN PATIENTS WITH FUNCTIONAL CONSTIPATION, IRRRITABLE BOWEL SYNDROME WITH CONSTIPATION AND HEALTHY VOLUNTEERS USING WIRELESS MOTILITY CAPSULE

Introduction: Constipation is a very common disorder with a wide spectrum, from functional constipation (FC) to irritable bowel syndrome with constipation (IBS-C). There are similarities and differences between FC and IBS-C including changes in gut microbiota compared to healthy volunteers (HV). The wireless motility capsule (WMC) incorporates measurements of pressure, temperature and pH along the gastrointestinal (GI) tract. Whole and regional transit times, pressure pattern and pH have been described in several populations.

Methods: This is a prospective study conducted at 2 GI Motility Labs, in the INCNMSZ and IMUBU-V. We included patients fulfilling Rome III criteria for FC and IBS-C. HV were asymptomatic, no major comorbidities, no previous GI surgery. After a 12-hour fast, WMC was administered without having consumed antibiotics in the previous month, no bowel preparation and no fiber supplement administered for 7 days before WMC. Subjects were instructed to wear a receiver and a diary until WMC was expelled or for up to 120 hrs. Whole and regional transit time, pressure pattern and pH profile were evaluated. For detailed analysis, small bowel (SB) and colon were divided into quartiles. The data were analyzed using specialized software (GIMS data viewer, Buffalo, NY). The variables are summarized with medians, frequencies and percentages. Non-parametric tests were used for comparisons.

Results: 52 subjects were included, 17 HV, median age 39 yo (25–54, 25th–75th), IBS-C 27 (21–34), FC 23 (21–27). 8 IBS-C, median age 29.5 yo (24–41.5), BMI 25.9 kg/m² (21.2–28.7) and 27 FC median age, 41 yo (31–56), BMI 26.8 kg/m² (23.5–32.9). There was no difference in age distribution (p = 0.35) or BMI (p = 0.52). No changes were shown in whole and regional transit times and pressure pattern between groups (p > 0.05) (Table). FC had a lower SB pH profile, 6.66 (6.42–6.88, p = 0.039) compared to HV 6.87 (6.7–7.03) and IBS-C 7.03 (6.97–7.10) (Figure). Similarly, at ileum (distal quartile in SB), pH was lower in FC 7.18 (7.08–7.42, p = 0.023) vs HV 7.44 (7.19–7.66) and IBS-C 7.54 (7.47–7.66). At cecum (1st quartile for SB); pH had lower in FC 5.72 (5.4–6.22) compared to IBS-C 6.31 (6.14–6.82; p = 0.024) but not different to HV.

Conclusion: FC presents a more acidic profile in the SB, ileum and cecum. This leads to the hypothesis that changes in pH may be due to differences in microbiota composition between study populations. It is necessary to evaluate these findings when comparing microbiota with intraluminal pH and symptom profile.

Disclosure: Nothing to disclose.

P0442 LONG-TERM LINK BETWEEN THE SEVERITY OF FAECAL INCONTINENCE AND THE EXTENT OF THE OBSTETRICAL ANAL SPHINCTER DISRUPTION

Introduction: Anal sphincter disruption, mainly from obstetrical origin, is frequent in patients suffering from fecal incontinence (FI). However, the link between the extent of the disruption and the severity of FI is not clear according to the time between the anal sphincter disruption and the apparition of FI. Our main objective was to assess, in the long term, the link between the anal sphincter disruption and the severity of FI.

Aims and Methods: In this retrospective study, all patients referred to our center for investigation of FI including an endo-anal ultrasonography (EUS) and a 3D manometric data, the voluntary contraction was lower in patients with EAS disruption in 8.4%, both IAS and EAS disruption in 60%. Considering manometric data, the voluntary contraction was lower in patients with EAS disruption. In the long term, this role is reduced due to the multifactorial nature of FI.

Disclosure: WV and CA have conflicts of interest. They previously have worked for Asta in astaxanthin experts in order to teach 3-dimensional high-resolution manometry to other practitioners.

P0443 POLYETHYLENE GLYCOL 3350 PLUS ELECTROLYTES FOR CHRONIC CONSTIPATION: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED MEDIUM-TERM STUDY WITH AN EXTENSIONAL 52 WEEKS OPEN-LABEL, LONG-TERM STUDY

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Introduction: Although polyethylene glycol 3350 plus electrolytes (PEG3350+E) is the most popular osmotic laxative in Europe, prospective long term (over 6 months) safety and efficacy clinical data has not been available to date. In Japan, the current standard cure of chronic constipation is magnesium oxide. PEG3350+E has not previously been used as treatment for chronic constipation.

Aims and Methods: We aimed to determine the efficacy and safety of PEG3350+E for the treatment of chronic constipation with an extensional long term study in Japan. We report a Phase 3 trial; a randomized, double-blind, placebo-controlled medium-term study (Confirmatory phase) with an extensional open-label, long-term (52 weeks) study (Extensional phase) in patients with chronic constipation who satisfied Rome III criteria for functional constipation. In the Confirmatory phase, 156 patients were randomized to receive PEG3350+E (80) or placebo (76) orally for 2 weeks. In the Extensional phase, 153 patients moved from the Confirmatory phase and received PEG3350+E orally. Starting dose was 13.7g/day dissolved in 125mL of water; dose titration was allowed in both phases within the range of 13.7–41.4g/day, according to the patient’s bowel condition. We monitored bowel function (including number of bowel movements, stool consistency) and adverse events. The primary end point of the Confirmatory phase was the increase from baseline (last week of run-in period: Week -1) in spontaneous bowel movements (SBM) per week during Week 2 of treatment. Secondary endpoints included frequency of complete spontaneous bowel movements (CSBMs), proportion of responders (defined as 3 or more SBM/CSBM per week with an increase from baseline of at least 1 SBM/CSBM per week), the median day to first SBM, stool consistency.

Results: In the Confirmatory phase, the difference from baseline in frequency of SBMs in Week 2 was significantly increased with PEG3350+E (4.3 ± 2.9 [Mean ± SD]) compared with placebo (1.6 ± 2.0, p < 0.001). Similarly, the frequency of CSBMs and proportion of responders were significantly improved with PEG3350+E compared to placebo.

In the Extensional phase, PEG3350+E showed sustained improvement in bowel function. The difference from baseline in frequency of SBMs in Week 1 and Week 2 were 2.98 ± 2.27 and 4.34 ± 2.89 respectively. Thus, it showed an increasing trend until Week 2 and remained stable at 3.89–4.82 times from Week 2 through Week 52. The frequency of SBMs from Week 1 to Week 52 was significantly increased compared with baseline. The SBM proportion of responders was 78.4% (95% CI: 71.26%–84.21%) in Week 1 and remained stable at 78.4%–94.0% from Week 1 to Week 52. In the Confirmatory phase, the incidence of adverse events (AEs) of placebo and PEG3350+E were 19.7% (15/76 patients) and 20.0% (16/80 patients) in the PEG3350+E group, respectively. The incidence of adverse drug reactions (ADRs) of placebo and PEG3350+E were 5.3% (4/76 patients) and 7.5% (6/80 patients) respectively.

In the whole phase 3 trial, the incidence of AEs was 78.8 % (123/156 patients) and the incidence of ADRs was 21.2 % (33/156 patients). The most common ADRs were gastrointestinal disorders (abdominal pain: 4.5%, diarrhea: 3.8%, nausea: 3.2% and abdominal distension: 2.6%). The incidence of AEs did not increase through the whole phase 3 trial.

Conclusion: PEG3350+E resolves constipation compared to placebo in the medium term, is well tolerated and improves bowel functions when administered for 52 weeks in Japanese patients with chronic constipation.

Disclosure: This study was supported by EA Pharma Co., Ltd. Atsushi Nakajima as the clinical trial advisor
**P0444** CHELOSTYRAMINE AS AN ADJUNCT TO PERCUTANEOUS TIBIAL NERVE STIMULATION FOR THE MANAGEMENT OF FECAL INCONTINENCE A Marić1, N Zarate Lopez1, A Raeburn2, V Passananti2, A Emmanuel1
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**Introduction:** Patients with fecal incontinence (FI) who are refractory to Loperamide and biofeedback may respond to neuremodulation. Previous data suggests a possible benefit of Cholestyramine, an anion exchange resin, binds to bile in the gastrointestinal tract, for FI management. We report a single center experience of Cholestyramine in the treatment of FI.

**Aims and Methods:** We report 44 patients with FI refractory to lifestyle modifications, Loperamide and biofeedback therapy. All patients had organic disorders excluded by serology and endoscopy, and also had intact anal sphincters on endoanal ultrasound. Group A received Cholestyramine (median dose 4.9g per day) along with Percutaneous tibial nerve stimulation (PTNS) for 12 weeks and Group B received PTNS alone. Bristol stool form scale (BSFS), weekly incontinence episodes, weekly stool frequency, median St Mark’s faecal incontinence score and days per week with abdominal pain were assessed at baseline and 12 weeks after therapy. SeHCAT studies were undertaken in some patients during PTNS.

**Results:** Data is shown in the Table with group A patients showing greater improvement in stool form, bowel frequency, episodes of incontinence and incontinence score compared to Group B. Only Group A patients had reduced abdominal pain. A responder analysis (>50% episodes reduction) was greater in Group A than B (73% vs 48%).

In total, 26 patients underwent SeHCAT testing, 13 in each group: in Group A 7/13 were of whom 6 responded to cholestyramine + PTNS, in Group B 5/13 were positive, none of whom responded to PTNS alone.

**Conclusion:** Cholestyramine is efficient adjunctive therapy to PTNS for FI management. A positive SeHCAT was seen in 46% of patients, and associated with an excellent response to Cholestyramine.

**Disclosure:** Nothing to disclose.

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**P0446** CHANGES IN PSYCHOLOGICAL PROCESSES THROUGHOUT ANORECTAL BIOFEEDBACK THERAPY: CORRELATIONS WITH DYSENTERGY DEFACTION AND FECAL INCONTINENCE OUTCOMES A Beath1, Y Mazor2, A Malcolm3, J Kellow2, C Sequeira3, G Prott3, M.P Jones1
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**Introduction:** Anorectal biofeedback (BF) therapy has established efficacy for both fecal incontinence and dysentergic defecation. The BF program involves education and advice on toileting behaviour and positioning, diarrheagusting, manometric-based biofeedback aimed at normalising anorectal physiology, sensory retraining and balloon expulsion retraining. In addition to pre-treatment clinical state [1], some psychological characteristics of patients have shown to predict BF efficacy [2]. Although psychological mechanisms must be involved in this learning process, there is little information on the psychological changes that occur through anorectal BF.

**Aims and Methods:** Our aims were to determine (1) what psychological traits change as a result of BF, and (2) whether changes in psychological traits correlate with changes in patient symptoms and quality of life, in order to better understand their role in treatment efficacy. 67 patients (M longstanding = 57, SD = 17, 93% female) presenting to the Neurogastroenterology Unit at the Royal North Shore Hospital (Sydney, Australia) with fecal incontinence (FI) (n = 39) or dysentergic defecation (n = 28) underwent a 6-visit instrumental anorectal BF program. Measures of executive function, cognitive flexibility, perceived stress, emotion regulation and self-efficacy were recorded prior to and at the end of the program. Patient reported outcomes were symptom severity (Fecal Incontinence Severity Index and Constipation Score) and quality of life (Fecal Incontinence QOL and Patient Assessment of Constipation QOL) for FI and dysentergic defecation patients as appropriate. Spearman’s correlations above 0.3 were considered clinically meaningful (and bolded in the Table).

**Results:** Patients’ perceived stress, executive function, cognitive flexibility, self-efficacy, and adaptive health-focused emotion regulation significantly improved throughout BF (all ΔZ≤2.13, all ps ≤ 0.05). Change in psychological traits correlated more strongly with changes in QoL, as opposed to symptom severity (see Table). Improvement in constipation QoL was moderately correlated with greater decrease in stress and executive function impairment; improvement in FI QoL correlated with greater reduction in self-blame and catastrophizing, and increases in cognitive flexibility and self-efficacy.

**Conclusion:** Psychological traits of emotion regulation, cognitive functioning and stress improve through BF and correlate with improvements in PRO. While we cannot conclude causal direction of the relationships, our results open the possibility of potential mechanisms in BF efficacy, with potentially different mechanisms for dysentergic defecation and FI.

Table. Spearman’s correlations between change in psychological traits with change in BF PROs. * p ≤0.10 ** p ≤0.05 *** p ≤0.01

<table>
<thead>
<tr>
<th>Psychological Trait</th>
<th>Change in Fecal Incontinence Constipation Severity Index</th>
<th>QOL</th>
<th>Change in Fecal Incontinence Constipation Severity Index</th>
<th>QOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SeHCAT</td>
<td>0.177</td>
<td>0.028</td>
<td>0.010</td>
<td>0.031</td>
</tr>
<tr>
<td>Cognitive flexibility</td>
<td>-0.297</td>
<td>0.177</td>
<td>0.031</td>
<td>0.031**</td>
</tr>
<tr>
<td>Emotion regulation: self-blame</td>
<td>0.049</td>
<td>-0.177</td>
<td>-0.031</td>
<td>0.031**</td>
</tr>
<tr>
<td>Emotion regulation: acceptance</td>
<td>0.206</td>
<td>0.252</td>
<td>-0.031</td>
<td>0.031**</td>
</tr>
<tr>
<td>Emotion regulation: positive refocus</td>
<td>-0.016</td>
<td>0.177</td>
<td>0.031</td>
<td>0.031**</td>
</tr>
<tr>
<td>Emotion regulation: catastrophizing</td>
<td>-0.069</td>
<td>-0.124</td>
<td>0.002</td>
<td>-0.031</td>
</tr>
<tr>
<td>Emotion regulation: putting into perspective</td>
<td>-0.007</td>
<td>-0.126</td>
<td>0.283</td>
<td>-0.031</td>
</tr>
</tbody>
</table>

**Disclosure:** This abstract was submitted for presentation at Digestive Diseases Week 2018.

**References**
P0447 VALIDATION OF THE "FAILURE TO PROVIDE ADEQUATE RELIEF" PROSTATE SCORING SYSTEM: A SPECIFIC CLINICAL SETTING
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Introduction: Treatment of chronic idiopathic constipation is empiric, based on step-wise approach. Long-term conservative management (lifestyle advice and laxatives) do not relieve symptoms, secondary approaches with prokinetic or secretagogues are used before considering hospital-based care (biofeedback, psychosocial support, transanal irrigation (TAI), surgery). Nevertheless, patients are often unsatisfied with care and fail to progress to adequate levels of therapy. The 3-point Failure to Provide Adequate Relief (F-PR) scale was developed to facilitate the recognition of when to move from each step to the next. The aim of this research was to validate F-PR in a tertiary clinical setting.

Results: A total of 403 consultations were accomplished, in 200 of which clinical assessment identified inadequate relief with current therapy (laxatives 81 patients, enemas 22 patients, prucalopride 42 patients, lubiprostone 12 patients, transanal irrigation 20 patients, biofeedback 97 patients, surgery 3 patients or combination 127 patients). Neither duration nor type of treatment was correlated with relief. A total of 403 consultations of the F-PR had >96% but poor sensitivity (15-67%). Cumulatively, none of the subjects with 4 or more of 5 positive responses on the F-PR had adequate relief with their current treatment.

Conclusion: We have shown that the F-PR has excellent specificity, suggesting it is a useful confirmatory test to confirm a clinical suspicion of inadequate relief. Good sensitivity is only seen when there are no positive F-PR replies implying the F-PR is only of screening value when there is high likelihood of treatment satisfaction. As such, the F-PR may have a role in confirming efficacy of treatments in future stepwise therapy for chronic constipation.

Disclosure: Nothing to disclose

P0448 RISK OF COLONIC DIVERTICULAR REBLEEDING ACCORDING TO ENDOSCOPIC APPEARANCE
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Introduction: Re-occurrence of bleeding (rebleeding) of colonic diverticula after endoscopic hemostasis is a clinical problem.

Aims and Methods: This study aimed to examine whether endoscopic visibility of colonic diverticula and bleeding affects the rebleeding after endoscopic hemostasis. We performed a retrospective review of endoscopic images and medical charts of patients with colonic diverticular bleeding who underwent endoscopic hemostasis. Endoscopic visibility was classified into 2 types according to visibility of the source of bleeding: source invisibility due to bleeding or attached hematin (type 1), or endoscopically visible responsive vessels (type 2). Rebleeding rates within 1 year after initial hemostasis were examined.

Results: Of 93 patients with successful endoscopic hemostasis, 38 (41%) showed type 1 visibility, while the remaining presented type 2. All patients received hemostasis with clipping, rebleeding developed in 20 patients (22%). Type 1 visibility was more likely to be observed in patients with rebleeding (65% vs. 34%, p = 0.06). Kaplan-Meier curve showed the cumulative incidence of rebleeding was significantly higher in patients with type 1 visibility than those with type 2 visibility (p = 0.0033, log-rank test)

Conclusion: Hemostasis by clipping for colonic diverticular bleeding without definite observation of the source of bleeding may not be sufficiently effective. Other hemostatic methods, including band ligation, should be considered when the source of bleeding is unclear.

Disclosure: Nothing to disclose

P0449 THE “DICA” ENDOSCOPIC CLASSIFICATION FOR DIVERTICULAR DISEASE OF THE Colon SHOWS A SIGNIFICANT INTEROBSERVER AGREEMENT AMONG COMMUNITY ENDOSCOPISTS
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Introduction: A validated endoscopic classification of Diverticular disease (DD) of the Colon, called DICA (Diverticular Inflammation and Complication Assessment), is currently available.

Aims and Methods: Our aim was to assess the agreement on this classification among an endoscopists community setting.

The DICA score for DD resulted in the sum of the scores for extent of diverticulosis, number of diverticula per district, presence and type of inflammation, and presence and type of complications: DICA 1 (upto 3 points); DICA 2 (4 from 7 points); DICA 3 (over 7 points). A total of 35 endoscopists,
subdivided between expert (31 raters, namely endoscopists using this classification) and non-expert (14 raters, not expert about DICA classification (24 raters)), independently scored a set of DD endoscopic videos using DICA classification.

The percentages of overall agreement on DICA score and a free-marginal multirater kappa (κ) coefficient were reported as statistical measures of inter-rater agreement.

Results: 1375 visualizations were performed. The overall agreement levels among the total group of raters were: DICA 1, 70.2%; DICA 2, 70.5%; DICA 3, 81.3%. The inter-rater agreement between the 55 evaluators varied as follows: DICA 1, free-marginal κ = 0.553; DICA 2, free-marginal κ = 0.558; DICA 3, free-marginal κ = 0.719. The overall agreement levels among the expert group of raters were: DICA 1, 78.8%; DICA 2, 80.2%; DICA 3, 88.5%. The inter-rater agreement between the 31 expert evaluators varied as follows: DICA 1, free-marginal κ = 0.682; DICA 2, free-marginal κ = 0.712; DICA 3, free-marginal κ = 0.828

Conclusion: DICA score is a simple, reproducible, and easy-to-use endoscopic scoring system for diverticular disease of the colon. The inter-rater agreement in this study was strong with a significant improvement in the expert subgroup of raters.

Disclosure: Nothing to disclose.

P0450 LONG-TERM EFFICACY OF RIFAXIMIN IN MANAGING SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON

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Introduction: Symptomatic Uncomplicated Diverticular Disease (SUDD) affects about 20% of patients having diverticular disease. However, there is no consensus about the best treatment in treating this disease and in preventing the disease’s complications. Rifaximin, a not absorbable antibiotic, is currently advised as effective treatment in controlling symptoms and in preventing complications, but no long-term data are available.

Aims and Methods: Our aim was to assess the outcome of a cohort of SUDD patients treated with rifaximin during a retrospective follow-up study. The study group (group A) included 346 SUDD patients with a median (range) age of 61(49–83) years, of whom 216 (62.4%) were females. Patients were treated with rifaximin 800 mg/day for 7 days/month. The control group (group B) included 470 patients SUDD taking spasmodics when needed, with a median (range) age of 59 (47–81) years, of whom 288 (61.5%) were females. Diagnosis of SUDD was performed by colonoscopy and by clinical accepted criteria. Follow-up was for a period of 12 months or whenever patients considered necessary. At each control visit, symptoms were assessed by the Global Symptomatic Score (GSS), assessing 4 main variables (left lower abdominal pain, bloating, diarrhea, constipation) graded as 0 = no symptom; 1 = mild, symptoms easily tolerated; 2 = moderate, symptoms sufficient to cause interference with usual daily activities; and 3 = severe, incapacitating symptoms with inability to perform normal activities).

Results: At baseline global symptomatic score (interquartile range) was 7 (5–8) in the study group and 6 (4–8) in the control group (p = 0.243). Either abdominal pain, or bloating or bowel alteration were significantly reduced in the study group with respect to the control group. The number of visit/patient/year were 2.4 patient/year in group A and 4.2 patients/year in group B (p = 0.02). Acute diverticulitis occurred in 9 patients (2.6%) in group A and in 21 patients (4.6%) in group B (p = 0.01). Surgery due to complication of the disease occurred in 4 patients (1.16%) in group A and 9 (1.91%) in group B (p = 0.06). Deaths due to disease were 0 in group A and 2 (0.42%) in group B (p = 0.03).

Conclusion: Rifaximin is effective in the symptomatic relief of symptomatic uncomplicated diverticular disease of the colon. In particular, symptomatic relief was due to a significant reduction in bloating and bowel alteration symptoms. Finally, rifaximin seems to be also effective in reducing the risk of disease’s complications.

Disclosure: Nothing to disclose.

P0451 DEMOGRAPHIC AND CLINICAL FACTORS ASSOCIATED WITH TREATMENT USE IN PATIENTS WITH DIVERTICULAR DISEASE: RESULTS FROM THE ITALIAN NATIONAL REGISTRY REMAD

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Introduction: Although diverticular disease is an extremely common condition, its effective treatment represents a difficult task in daily clinical practice. We have used the Italian national ‘Registro Malattia Diverticolare’ (REMAD) registry, an ongoing 5-year prospective, observational, multicenter cohort study in 1206 consecutive patients with diverticular disease, to assess the prevalence of treatment use in the different clinical entities of this disorder and the demographic and clinical factors associated.

Aims and Methods: At the entry in the REMAD registry, patients were categorized in subgroups according to different clinical entities (diverticulitis, symptomatic uncomplicated diverticular disease (S UDD), previous diverticular (PD)). Demographic, clinical and lifestyle factors and quality of life were registered (Carabotti et al., UEG Journal 2018 in press) as well as the use of 1 or more treatments for diverticular disease (including poorly absorbed antibiotics, like rifaximin, mesalazine, probiotics, prebiotics, fibers, and antisepsimeds) in the last year. Logistic regression analysis was used to assess the association between demographic and clinical factors with treatment assumption.

Results: Of the 1206 subjects included in the study have taken at least 1 treatment for diverticular disease in the last year. Of these subjects, 166 belong to diverticulosis group (a total of 702 subjects with diverticulosis, 23.6%), 165 to SUDD group (of a total of 295 subjects with SUDD, 55.9%), and 169 to PD group (of a total of 209 subjects with PD, 80.9%) (p = 0.0001 for all). In both groups, poorly absorbed antibiotics, particularly rifaximin, were the most common treatment, accounting for 87.3% in diverticulosis, 84.8% in SUDD and 75.7% in PD. In a multivariate analysis, the following factors resulted to be significantly associated with treatment use: female gender (OR = 1.6; 95% CI, 1.1–2.2), family history of colon diverticulosis (OR = 1.5; 95% CI, 1.1–2.1), gastrointestinal comorbidity (OR = 1.9; 95% CI, 1.4–2.5) and impairment of quality of life, particularly the physical component summary (PCS) score (OR = 1.6; 95% CI, 1.2–2.2). Interestingly, older age (OR = 2.04; 95% CI, 1.1–3.7) and gastrointestinal comorbidity (OR = 2.1; 95% CI, 1.4–3.2) were the most relevant factors associated with the use of treatments in diverticulosis, while first-degree family history for colon cancer (OR = 2.4; 95% CI, 1.0–5.7) and for diverticulosis (OR = 2.5; 95% CI, 1.1–4.9), the presence of gastrointestinal comorbidity (OR = 2.3; 95% CI, 1.3–4.3) and the impairment of PCS score (OR = 2.2; 95% CI, 1.2–4.2) were significantly associated with treatment use in SUDD.

Conclusion: Pharmacological approaches targeting enteric bacteria (with poorly absorbed antibiotics, like rifaximin) are the most commonly used treatments for diverticular disease, due to their ability of controlling symptoms and also preventing complications. In addition, this nationwide registry study identified different demographic and clinical factors associated with the use of pharmacological approaches in the distinct clinical entities of diverticular disease. The optimal regimen of therapy must be established in ad hoc studies. ClinicalTrial.gov Identifier: NCT03325829.

Disclosure: Nothing to disclose.

P0452 ACUTE COLON DIVERTICULITIS HOSPITALIZATION TRENDS IN VENETO REGION (NORTHEAST ITALY)

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Introduction: Diverticular disease (DD) of the colon represents a common clinical condition affecting with high rate the population in developed countries. Several epidemiological studies have clearly shown that in the last decades the rates of hospital admissions for Acute Colon Diverticulitis (ACD), the most important complication of DD, is progressively increased.

Aims and Methods: Describe the Hospitalization trend for ACD in Veneto region (North East Italy), including in-hospital mortality, and evaluate the impact of specialist admission hospital units as Gastroenterologic (GE) units.

Data were obtained from the Veneto Region anonymous Hospital Discharge data from 2000 to 2017, in which diverticulitis of colon [ICD-9-CM code 562.11 and 562.13 (diverticulitis with and without mention of haemorrhage) was the primary diagnosis.

Standardized Hospitalization Rate (SHR) per 5-year group (ref. pop. Veneto 2009) was calculated and expressed per 100,000 population.

To evaluate the impact of admission hospital units on the outcome of ACD management we analyzed in-hospital mortality, need for surgery (NFS) and lenght of stay (LOS).

Disclosure: Nothing to disclose.
significantly showed an important increase from 0.37 to 0.98 (p

Through the years the NFS rate was stable with an increase of mortality.

Women showed an higher prevalence of hospitalization compared to men (OR: 1.34; 95% CI: 1.27–1.32; p < 0.001).

Conclusion: It appear that ACD is an emerging health-care problem related to the rising of age.

Disclosure: Nothing to disclose

P0945 MAJOR GENETIC RISK VARIANTS IN DIVERTICULITIS AND DIVERTICULOSIS

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Introduction: Human papillomavirus-associated anal intraepithelial neoplasia (AIN) is a precursor of invasive anal carcinoma. High-resolution anoscopy (HRA) is recommended as a screening tool for AIN (1). However, the diagnostic accuracy of this method is unclear. In contrast, anal mapping biopsies (AMB) are not widely performed and are not included in the current guidelines.

Aims and Methods: We aimed to evaluate HRA as a screening tool for AIN in comparison to anal mapping biopsies as the gold standard.

Results: 29 patients (20 male, 9 female) with anal mapping were analysed during 2 years. Of the 20 male patients, 11 were HIV positive and 14 practiced men sex with men (MSM). All women were HIV negative. HRA identified 23 lesions suspicious for AIN. 22 lesions (96%) were histologically confirmed as AIN.

Conclusion: This study shows that, although most AIN are detected with HRA, they are considered prior to local therapy, at least in high-risk patients with positive results in the HRA study.

Disclosure: Grant by Olympus, comparative study HRA vs. endoscopy for AIN diagnostics

References

P0944 EVALUATION OF HIGH-RESOLUTION ANOSCOPY AS A SCREENING TOOL FOR ANAL INTRAEPITHELIAL NEOPLASIA (AIN): A COMPARISON TO THE GOLD STANDARD ANAL MAPPING BIOPSIES

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4Cantonal Hospital St. Gallen, Institute for Pathology, St. Gallen, Switzerland

Introduction: Human papillomavirus-associated anal intraepithelial neoplasia (AIN) is a precursor of invasive anal carcinoma. High-resolution anoscopy (HRA) is recommended as a screening tool for AIN (1). However, the diagnostic accuracy of this method is unclear. In contrast, anal mapping biopsies (AMB) are not widely performed and are not included in the current guidelines.

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Conclusion: This study shows that, although most AIN are detected with HRA, they are considered prior to local therapy, at least in high-risk patients with positive results in the HRA study.

Disclosure: Nothing to disclose

PO455  DIAGNOSIS OF HIRSCHSPRUNG’S DISEASE IN CHILDREN - PRELIMINARY APPLICATION OF A NOVEL ENDOSCOPIC TECHNIQUE FOR RETACAL BIOPSY

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Introduction: The diagnosis of Hirschprung’s disease (HD) relies on anorectal manometry, barium enema and rectal biopsy. The role of endoscopic biopsy is not well-known for the diagnosis of HD in children.

Aims and Methods: In this study, we evaluated the safety and adequacy of biopsies procured by endoscopic mucosal resection (EMR) for the diagnosis of HD. All the children with suspected HD underwent anorectal manometry and barium enema. Children with absence of recto-anal inhibitory reflex and / or radiological lesions procured by endoscopic mucosal resection (EMR) for the diagnosis of HD.

Aims and Methods: Prospective (2016–2018) randomized non-blinded sequential trial with four interventions (IH).

Comparative study on the efficacy and safety of 4 instrumental modalities for the screening of anal carcinoma in HIV infected patients. High-definition imaging with the BLI technology also allows for identification of vascular patterns, which might help to characterize dysplastic anal lesions and might therefore allow for more targeted diagnosis and treatment.

Disclosure: Nothing to disclose

PO456  HEMORROIDETQ STUDY: PROSPECTIVE EVALUATION OF FOUR NON-SURGICAL INTRAMURAL MODALITIES FOR THE TREATMENT OF PROLAPSED HEMORRHOIDAL DISEASE

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Introduction: Persistent symptomatic hemorrhoidal disease after general counsel- measures requires instrumental intervention. The benefit of the association of phlebotonics is uncertain.

Aims and Methods: Comparative study on the efficacy and safety of 4 instrumental non-surgical modalities for treatment of prolapsed internal hemorrhoids (IH).

Prospective (2016–2018) randomized non-blinded sequential trial with four interventions: Rubber band ligation (B) or Sclerotherapy with Foam Polidocanol (PLD) vs. Ligature + phlebotonics (B+P) vs. PLD + P. Inclusion of adult patients with IH (grade II-III) diagnosis with no previous instrumental treat- ment, after signed written consent. Demographic and clinical characterization. Assessment of outcomes: Safety (adverse events after intervention); efficacy (complete, partial or absent response) at week 4–8 (short-term) and weeks 12–24 and 44–52 (long-term). Intervention if indicated, at the same timepoints.

Statistics: One-way ANOVA, Welch and Levene test; chi-square.

Results: 68 patients were included (37 males, mean age 54 ±12.8 years) and distributed among the 4 treatment groups (19 vs.19 vs.17 vs.13), adjusted for age (p=0.92) and gender (p=0.86).

Short-term analysis - all patients were evaluated for this analysis. 3 cases of self- limited pain only, were documented. Efficacy was superior for B group [no case of lack of response and 12/19 cases of complete response (p=0.006)].

Long-term analysis - 46 patients were assessed (5 dropouts, 17 still incomplete follow-up). 100% and 43% of re-interventions were performed on the 2nd and 3rd timepoints without reported adverse events. In this long-term evaluation there is no difference between the treatment modality and the efficacy, time made the outcomes similar between treatment groups: The efficacy of each treatment is provided in 75% complete response and 25% partial response, with numerical superiority for the PLD + P group (87.5% and 12.5%, respectively).

Conclusion: Non-surgical instrumental IH therapy is safe and globally effective. B showed to have superior efficacy at week 4 to 8, after a single intervention. Efficacy over time and after re-interventions is similar for B and PLD. Combined PLD + P therapy seems to enhance sustained efficacy over time.

Disclosure: Nothing to disclose

PO457  HIGH-INTENSITY CONTRAST IMAGING ASSISTED HIGH-RESOLUTION ANOSCOPY FOR ANAL CARCINOMA SCREENING IN HIV-INFECTED PATIENTS

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Introduction: Human immunodeficiency virus (HIV) infection contributes to the occurrence of anal cancer in men who have sex with men (MSM), leading to a 30–100 fold higher anal carcinoma incidence in this patient group. Therefore convenient screening tools are mandatory to identify anal intraepithelial neoplasia (AIN) at early stages, which allow an early curative intervention.

Aims and Methods: In this pilot study we screened for anal carcinoma in HIV positive MSM, receiving stable antiretroviral therapy. Endoscopic high-intensity contrast imaging (HIC) and the most recently introduced Blue Light Imaging (BLI) with optical magnification were applied during high-resolution anoscopy. The HIC/BLI equipped endoscope was advanced into the anal region of interest via a pro-inserted standard rectoscope. Conventional imaging in combination with time-em, -enhancement, and swaps as well as directed biopsies served as refer- ence methods to identify AIN.

Results: Following preliminary inclusion of consecutive HIV patients, median (range) age 49.5 (37–61) years, CD4+ 363 (295–1076) cells/µl and HIV- RNA 10 (4–34) copies/ml, we were able to identify 1 patient with condyoma acuminata and low-grade AIN. HIC/BLI as well as aceto-enhancement both resulted in consistent findings and lead to the diagnosis of AIN. In addition more superficial HIC/BLI revealed superficial vascular patterns that was seen in the identified AIN and condyloma lesions. In contrast, anal swaps and cytology, showing inconclusive results (PAP Iib) in 20% (1/5) and normal cytology in 80% (4/5), were not able to identify AIN in these patients.

Conclusion: HIC/BLI enhanced anoscopy provides an additional time-sparring method for the screening of anal carcinoma in HIV infected patients. High-definition imaging with the BLI technology also allows for identification of vascular patterns, which might help to characterize dysplastic anal lesions and might therefore allow for more targeted diagnosis and treatment.

Disclosure: Nothing to disclose

PO458  A EUROPEAN MULTICENTRE POST-AUTHORISATION STUDY ON THE EFFICACY AND SAFETY OF A BOWEL CLEANSING PREPARATION: COMPLIANCE WITH INSTRUCTIONS OF USE, TOLERABILITY AND SAFETY IN REAL-LIFE SETTING

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In:vestigators assessed oral Trisulphate Solution (OTS) is a low-volume bowel cleansing solution administered as 2 x 500 ml saline sulphate solution followed by 2 x 1 l water or clear liquids (for hydration). The aim of this study was to: assess misuse (defined as non-compliance with hydration); describe the safety profile overall and in case of misuse; and identify any immediate/acute adverse events (AEs) in special populations (the elderly and patients at risk of electrolyte shifts).

Aims and Methods: This was a prospective, non-interventional, multicentre, European Post Authorisation Safety Study (PASS) in patients receiving OTS for colonoscopy. The PASS was conducted in patients at risk of electrolyte shifts. The European Post Authorisation Safety Study (PASS) in patients receiving OTS for colonoscopy. The PASS was conducted in patients at risk of electrolyte shifts. The study was conducted in: Germany, the Netherlands and Poland. 1206 patients took OTS and provided 1048/1196 patients (87.6%). 329 patients (27.3%) experienced 758 related treat- ments in compliance. Reported colon cleansing level was excellent-to-good in 96.8%. Subgroup analyses (age, gender, dosing regimen) revealed no differ- ences in compliance. No AEs suggestive of dehydration were reported in 1048/1196 patients (87.6%). 329 patients (27.3%) experienced 758 related treat- ments in compliance. Reported colon cleansing level was excellent-to-good in 96.8%. Subgroup analyses (age, gender, dosing regimen) revealed no differ- ences in compliance. No AEs suggestive of dehydration were
noted in non-compliant patients. No acute AEIs were observed in special popula-
tions. TEAEs did not differ in nature and intensity from the known safety profile overall and in special populations.

**Conclusion:** In this non-interventional study, treatment compliance to hydration guidelines was excellent or good in 94.5% of patients. The safety profile of OTS was good and similar to previous reports overall and in special populations.

<table>
<thead>
<tr>
<th>Compliance to hydration guidelines: registry population (N = 1177)</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>Compliant patients (volume taken ≥75%)</td>
<td>1112 (94.5)</td>
</tr>
<tr>
<td>Excellent (100%)</td>
<td>1022 (88.6)</td>
</tr>
<tr>
<td>Good (&lt;100 and ≥75%)</td>
<td>90 (7.6)</td>
</tr>
<tr>
<td>Compliant patients to hydration guidelines by subgroups n (%) [95% CI]</td>
<td></td>
</tr>
<tr>
<td>&lt;65 years (n = 720)</td>
<td>689 (95.7) [93.9; 97.1]</td>
</tr>
<tr>
<td>≥65 years (n = 457)</td>
<td>423 (92.6) [89.9; 94.8]</td>
</tr>
<tr>
<td>Male (n = 606)</td>
<td>576 (95.0) [93.0; 96.6]</td>
</tr>
<tr>
<td>Female (n = 571)</td>
<td>536 (93.9) [91.6; 95.7]</td>
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<tr>
<th>Related TEAEs: safety population (N = 1206)</th>
<th>n (%)</th>
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**P0459 OPTIMAL TIMING OF ADDING SIMETHICONE FOR BETTER BOWEL PREPARATION USING POLYETHYLENE GLYCOL PLUS ASCORBIC ACID: A DOUBLE-BLIND RANDOMIZED TRIAL

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**Aims and Methods:** The aim of this study was to determine the optimal timing to add simethicone for improving bowel preparation during colonoscopy using PEG-Asc. Antifoaming agent, simethicone was known to enhance colonic visualization during colonoscopy.

**Conclusions:** Bowel preparation with PEG-Asc plus simethicone eliminates air from the colon more effectively. Furthermore, adding simethicone at the optimal time could improve the quality of bowel preparation, especially enhancing diminutive PDR.

**Disclosure:** Nothing to disclose.

**P0460 PUBLIC ATTITUDES TO COLONOSCOPY: HOW MUCH BOWEL PREPARATION LIQUID MUST BE DRUNK BEFORE A COLONOSCOPY?

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**Introduction:** In European countries, public beliefs and attitudes to bowel preparation before colonoscopy are poorly understood. A survey was conducted to address the issue.

**Aims and Methods:** An online survey was conducted in 5 large European countries (UK, Germany, France, Spain, and Italy), among members of the general public who had not had a colonoscopy. A total of 10 questions asked: Before a colonoscopy can be undertaken, the colon must be cleaned by the patient drinking a bowel preparation solution. How much of the bowel preparation liquid do you think a patient needs to drink prior to the procedure? The survey targeted 500 people aged 18–70 years from each country, and aimed to balance respondent groups for region, gender, age, and occupation.

**Results:** Among 53,795 invited persons, 18,650 (35%) responded to the survey and 2,500 (5%) completed the survey who had never had a colonoscopy before across the 5 assessed EU countries. Among these, 13% respondents believed they had to drink maximally 1½-litre bowel preparation liquid. 16% believed they must drink between 1½ and 1 litre, while 38% thought they must drink 1 whole litre. Fewer, 22%, expected to drink 2 litres, and only 12% believed they must drink more than 2 litres. Taken together, nearly 9 out of 10 potential colonoscopy patients expected to drink maximally 2 litres of bowel preparation liquid to accomplish their colon cleansing. The national levels were comparable except for Germany, where only 8 out of 10 respondents expected to drink maximally 2 litres.

**Conclusion:** The vast majority of people in UK, Germany, France, Spain, and Italy expect to drink 2 litres or less of a bowel preparation liquid before a colonoscopy. Such widespread public beliefs could potentially collide with clinical practice where patients must often drink 3 litres or more to adequately prepare their bowel. The new availability in Europe of highly effective low-volume bowel preparations such as the 1 L polyethylene glycol NER1006 can help close this perceptual gap whilst ensuring reliable cleansing success at a reduced fluid volume intake.

**Disclosure:** Amlani B, employee of Norgine; Radaelli F, speaker and advisory board member for Norgine, Boehringer Ingelheim; Bhandari P, nothing to disclose.

**P0461 GENOMIC MEDICINE IN GASTROENTEROLOGY, PRESENT AND FUTURE: A NATIONWIDE SURVEY OF UK GASTROENTEROLOGY TRAINEES

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**Introduction:** Genomics and personalised medicine are increasingly relevant for patients with gastrointestinal conditions. In the United Kingdom, the higher training curricula of other specialities (e.g. cardiology and oncology) have been revised with the addition of modular training in genomics. We aim to capture the current state of genomics training in gastroenterology in the UK to review current understanding, clinical experience and long-term training needs of trainees, and to assess their preparedness for future consultant practice.

**Aims and Methods:** A web-based nationwide survey of all UK Gastroenterology specialty trainees was carried out in November and December 2017, supported by the British Society of Gastroenterology national training committee.

**Results:** 100 trainees (representing 15.2% of the 658 UK gastroenterology trainees) across 17 of 18 regions responded to this survey, representing a full range of gastroenterology registrar training levels. Only 9% and 16% of trainees believe that their local training programme adequately prepares them for future clinical practice utilising genomic medicine and personalised medicine respectively. Barriers identified (with percentage agreeing or strongly agreeing in parentheses) include the need for greater education of trainees (93%), inadequate clinical guidance to base interventions on the results of genomic testing (53%), concerns over misinterpretation by patients (43%) and overuse/misuse of testing by clinicians (34%).

When assessing current mainstream genetic and personalised tests, trainees felt prepared to perform HFE genotyping (98%), assess TPMT status (97%), and...
interpret HLA typing for suspected coeliac disease (85%). However, only a minority of these felt prepared to perform the following investigations: poly-
posis screening (34%), hereditary pancreatic cancer screening (30%), testing for Lynch Syndrome (33%), and KRAS testing for colorectal cancer (20%). For their future
clinical practice, 76% of trainees did not know what mainstreaming of genomics would entail, with only 6% of trainees having recruited patients for the UK
100,000 genomics project.

Most trainees would support having dedicated training days on genomic medi-
cine (83%), formal training provisions for the mainstreaming of genomic testing (64%), an update to both the UK gastroenterology specialist training cur-
as well as the specialty examinations (57%), and better-defined pathways for referral to local genomic services (91%).

Conclusion: Most British gastroenterology trainees feel ill-equipped to practise genomics and personalised medicine as consultants, at a time of progressive main-
streaming of genomic practice in our specialty. We propose that the UK gastro-
enterology specialty curriculum requires specific revision to prepare trainees for
genomics in their future clinical practice, and recommend that other European gastroenterology training programmes also assess their local genomic training
requirements.

Disclosure: Nothing to disclose

Reference

P0462 FEAR-OF-CANCER-RELATED PSYCHOLOGICAL BARRIERS TO COLONOSCOPY IN FECAL OCCULT BLOOD TEST (FOBT)-POSITIVE COLONOSCOPY REFUSERS
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Introduction: Up to 25% of fecal occult blood test (FOBT)-positive participants of colorectal cancer (CRC) screening programs fail to show up for colonoscopy. For
to many of them, the main obstacle is not lack of information, oppositional
personality or denial, but rather a fear of finding out that they have cancer. The
fear paralyzes their ability to start the work up. At the same time, they are
completely aware of and frightened of the potential consequences of not under-
going the test. This unresolved emotional stress leads to feelings of anxiety and
grip, and often results in coping by self-explanations as to why the need for the
test may not apply in their case, doing repeated FOBTs in the hope the results
will be normal, and procrastination - the practice of performing less urgent tasks
in preference to more urgent ones, to transfer attention away from it. Physicians
often mistake coping mechanisms as patient resistance. Motivational interview (MI)
is a psychological intervention technique designed to facilitate a patient’s awareness of the barriers, and aimed to challenge the
feeling of colorectal cancer (CRC) screening programs fail to show up for colonoscopy. MI is an efficient and
valuable tool, and in our cohort helped 38% of patients to overcome this barrier.

Disclosure: This work was supported by Israel Cancer Association research grant

References
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viewing: an evidence-based approach to counseling helps patients follow
in a community health center: a randomized, controlled trial. J Gen Intern

P0463 PREVENTING COLON CANCER VS. EARLY DIAGNOSIS, WHAT IS BEST? A META-ANALYSIS OF THE U.S. PREVENTIVE SERVICES TASK FORCE EVIDENCE REPORT ON SCREENING TESTS
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Introduction: As of 2009, 19 out of 27 EU countries had a program for colorectal cancer (CRC) screening, with at least 3 countries currently using flexible sigmoidoscopy (FS). FS is the only cancer screening test proven to reduce all-cause mortality in randomized controlled trials. We hypothesize that this unique all-
cause mortality reduction is attributable to colorectal cancer prevention rather
than early detection.

Aims and Methods: Exploration of the relationship between mortality reduction and CRC prevention in randomized controlled trials of CRC screening. Study
Design: Random effects meta-analysis with correlation of study outcomes using
Pearson correlation coefficient followed by linear regression for statistically

Abstract No: P0463

<table>
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<tr>
<th>Study/Subgroup</th>
<th>Screening</th>
<th>Usual Care</th>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>Total</td>
<td></td>
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<td>Total (95% CI)</td>
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<td>172252</td>
<td>29.3%</td>
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<tr>
<td>Heterogeneity:</td>
<td>Tau 2 = 0.0001; Chi2 = 0.22, df = 4 (p = 0.99); I2 = 0%</td>
<td>Test for overall effect: Z = -2.88 (p = 0.0040)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FOBT

Shaakat 2013 (Minnesota,30.0y) | 22076 | 31157 | 20.2% | [0.984, 1.009] |
| Schefoldfield 2012 (Nottingham,19.5y) | 40681 | 76056 | 22.4% | [1.001, 0.992, 1.011] |
| Lindholmen 2008 (Gotteborg,15.6y) | 10591 | 34144 | 13.1% | [1.016, 0.993, 1.039] |
| Kronborg 2004 (Fjens,17.0y) | 12205 | 30966 | 15.0% | [0.996, 0.077, 0.104] |
| Total (95% CI) | 85553 | 17232 | 70.7% | [1.001, 0.992, 1.010] |
| Heterogeneity: | Tauc 2 = 0.0001; Chi2 = 2.33, df = 4 (p = 0.51); I2 = 0% | Test for overall effect: Z = 0.22 (p = 0.83) |
significant correlations. Setting or Dataset: Randomized controlled trials specified in the U.S. Preventive Services Task Force 2016 Evidence Report for Colorectal Cancer Screening. Patients: 786,769 normal risk males and females age 45 to 80 years. Interventions: CRC screening with FS or fecal occult blood test (FOBT). Main and Secondary Outcome Measures: All-cause mortality, CRC incidence, mortality attributed to CRC, quantitative comparison of these outcomes for different tests, and correlations of these outcomes.

Results: FS reduces all-cause mortality (relative risk [RR], 0.975; 95% CI, 0.958–0.992) and reduces CRC incidence (RR, 0.79; 95% CI, 0.74–0.84) at 10.5–11.9 years of follow-up, with an all-cause mortality reduction which shows a strong linear correlation with CRC incidence reduction (R, 0.95; 95% CI 0.42–0.99). FOBT does not reduce all-cause mortality (RR, 1.001; 95% CI, 0.992–1.010) nor CRC incidence (RR, 0.96; 95% CI, 0.89–1.02) but does reduce mortality attributed to CRC (RR, 0.78–0.91) at 15.6–30.0 years. Conclusion: All-cause mortality reduction displays a dose-response relationship with CRC prevention and regression analysis indicates that CRC prevention is the sole mechanism of action affecting all-cause mortality in these trials. Early detection of CRC does not appear to reduce all-cause mortality. These findings should inform updated recommendations for effective CRC screening in populations. 

Disclosure: Nothing to disclose.
P0467 ABERRANT EXPRESSION OF SPP1 THROUGH DOWNREGULATION OF HELIOS IN GASTRIC CANCER

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Introduction: Helios remains a cancer-testable biomarker. The activation of Helios in gastric cancer is driven by the dysregulation of cytokine signaling. In this study, we aimed to elucidate the expression of Helios in gastric cancer cell lines and its regulatory mechanism between Helios signaling and miR-590-5p.

Aims and Methods: To elucidate the Helios function in gastric cancer cells, we used 1K2F2-targeting CRISPR-Cas9 system to knock-out Helios expression in AGS cell line. The CCK8-dependent proliferation assay, wound healing assay and invasion assay were performed. We further analyzed the gene expression between AGS and AGS-KO cells by next generation sequencing (NGS), and finally validated the gene expression in AGS and AGS-KO cells by qRT-PCR.

Results: K RK34 expression was significantly decreased, while the mobility and invasiveness were increased in Helios knockdown AGS cells compared to parental cells. The data of NGS indicated an increase of SPP1 expression upon depletion of Helios, and increased in Helios knockdown AGS cells compared to parental cells. The data of qRT-PCR further confirmed to be a direct target of miR-590-5p. Their expressions showed a negative correlation in primary GC samples (r = -0.278, p < 0.001, n = 367), miR-590-5p suppressed the tumorigenic properties of GC cells. Re-overexpression of Helios partly reversed the tumor-suppressive effect of miR-590-5p.

Conclusion: Helios is overexpressed and plays a tumorogenous role in gastric cancerogenesis. The activation of Helios in gastric cancer is partly due to the silence of a tumor-suppressive miRNA, miR-590-5p. These findings comprehensively deciphered the regulatory mechanism between Helios signaling and miR-590-5p, which might imply a constructive therapeutic intervention in GC.

Disclosure: Nothing to disclose

P0408 METHYLOMICS ANALYSIS IDENTIFIES SPG20 AS A SENSITIVE NON-INVASIVE BIOMARKER FOR EARLY DETECTION OF GASTRIC CANCER

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Introduction: Gastric cancer remains a cancer with high incidence and poor long-term survival in Taiwan, despite of the effort to eradicate H. pylori infection. Helios belongs to Ikaros family proteins, which perform as tumor suppressors because many studies reported that abnormal expressions of these proteins. Helios belongs to Ikaros family proteins, which perform as tumor suppressors. However, the clinical significance of aberrant epigenetic silencing of STAT3 targets in gastric cancer is not fully understood.

Aims and Methods: To identify STAT3 targets that are epigenetically silenced by STAT3 in gastric cancer, Illumina 850K methylation microarray was performed in AGS gastric cancer cells and cells depleted with STAT3. Bisulphite pyrosequencing or methylation-specific PCR (MSP) was also performed to examine promoter methylation of the identified targets in tissue or serum/plasma samples from patients with gastric cancer (n = 53), IM (n = 8), gastritis (n = 12) and a panel of gastric epithelial cells including cancer cell lines. We further explored a methylomic drug treatment by DNMT inhibitor together with qRT-PCR to use DNA methylation in the expression of the identified targets.

Results: Integrative methylation microarray and computational analysis identified STAT3 targets that showed epigenetic silencing in STAT3 depleted AGS cells. To confirm our results, bisulphite pyrosequencing confirmed that promoter region of SPG20 was hypermethylated in a panel of gastric cancer cell lines including AGS cells but not in GE2 immortalized gastric epithelia. These results were expected, SPG20 is highly downregulated in a panel of gastric cancer cell lines in which the expression can be restored by the treatment of DNMT inhibitor thus suggesting that SPG20 is epigenetically silenced by promoter methylation. To determine the clinical significance of SPG20 methylation in gastric cancer, we examined promoter methylation of SPG20 in 53 paired of gastric cancer patient samples, 8 samples of intestinal metaplasia (IM) and 12 samples of gastritis by bisulphite pyrosequencing. Interestingly, promoter methylation of SPG20 is significantly higher in cancer tissues than that of gastritis (p < 0.01 and p < 0.05). In addition, there is no association between SPG20 methylation and tumor grade, stage and patient’s survival suggesting that methylation of SPG20 may be an early event. To confirm this hypothesis, we performed methylation specific PCR (MSP) in cDNA isolated from serum samples of gastric cancer (n = 53), IM (n = 5) and gastritis (n = 9). Interestingly, SPG20 methylation showed a progressive increase in tumor progression (SPG20 methylation% in gastritis = 37.5%, IM = 66.7%, cancer = 91.7%, p < 0.05).

Conclusion: Taken together, SPG20, a potential STAT3 target, is frequently hypermethylated in gastric cancer. Methylation of SPG20 may be a novel non-invasive biomarker for early detection of gastric cancer.

Disclosure: Nothing to disclose

P0407 THE CYTOTOXIC EFFECT OF HYPERTERMIA IN ADDITION TO CISPLATIN IS ENHANCED BY PRIOR HO-1 SILENCING IN OVARIAN BUT NOT GASTRIC CANCER CELLS

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Introduction: Hyperthermic intraperattional chemotherapy (HIPEC) is a treatment method to cure intraperattionally spread gastric and ovarian cancer. Although a number of clinical trials report satisfactory results, data remains controversial. Heat shock proteins are known being responsible for cellular resistance to temperature. HO-1 is a heat shock protein, which is induced by hyperthermia.

Aims and Methods: To identify the therapeutic strategy for ovarian cancer, we performed in vitro cell survival assay with combination of HO-1 silencing by siRNA and hyperthermia. The results showed that HO-1 silencing in ovarian cancer cells (A2780, A2780/DOX) improved the response to hyperthermia. These results suggest that HO-1 silencing might enhance the therapeutic effect of HIPEC in ovarian cancer.

Conclusion: HO-1 silencing may enhance the therapeutic effect of HIPEC in ovarian cancer.

Disclosure: Nothing to disclose
Aims and Methods: The aim of our in vitro study was to clarify the response of gastric and ovarian cancer cells to hyperthermia and cisplatin, following the modulation of HO-1 expression. AGS (gastric adenocarcinoma), OVCAR-3 (ovarian adenocarcinoma) cells were treated with different temperature regimes (normothermia: 37°C; and hyperthermia: 43°C) either with cisplatin for one hour. Prior the treatment experimental groups of cells were HO-1 silenced by siRNA transfection. MTT was used to evaluate cells viability. Apoptosis was assessed by flow cytometry, using Annexin V-PE and 7AAD. Real-time cell analysis was used to evaluate the changes of viable cell rates in real time manner. HO-1 expression was detected by QRT PCR and Western blot.

Results: Cisplatin increased HO-1 expression by 3.73-fold in normothermia and 2.4-fold in hyperthermia for OVCAR-3 cells. Hyperthermia stimulated the increase of HO-1 expression significantly by 1.34-fold. HO-1 expression was not affected neither by temperature, nor by cisplatin in AGS cells. In OVCAR-3 protein level, HO-1 expression was increased similarly as for RNA - by cisplatin not affected neither by temperature, nor by cisplatin in AGS cells. In OVCAR-3 an analyzer was used to evaluate the changes of viable cell rates in real time.

Conclusion: Cisplatin and hyperthermia enhanced this effect by additional 20%. In AGS cells, HO-1 silencing reduced viability at 43°C resulted in drop of cells viability by 36% and HO-1 silencing enhanced this effect by additional 20%. In AGS cells, HO-1 silencing reduced the viability by 16% at 37°C. HO-1 silencing in normothermia increased apoptosis rates by 3.09-fold and 6.84-fold in OVCAR-3 and AGS cells respectively. Real time cell analysis showed that exposure to cisplatin gradually decreased cell index of OVCAR-3 and AGS (HO-1 silenced) cells in normothermia. Hyperthermia enhanced this effect in OVCAR-3 cells, while AGS cell index stayed similar.

Disclosure: Nothing to disclose.
P0474 EFFECT OF MYD88 DEFICIENCY ON INTESTINAL INFLAMMATION AND MICROBIOTA IN COLITIS MICE

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Introduction: MyD88 is a key signaling adaptor for TLRs and involved in intestinal microbiota-host interaction associated innate and adaptive immune. This study aims at investigating the effect of MyD88 on colonic inflammation and gut flora.

Methods and Aims: MyD88 knockout mice and their wild-type littermates were kept under the same environment except for treated with normal drinking water (WT) or 3% DSS (WT-DSS) or 3% DSS and WT-DSS (WT-DSS groups) for 7 days. Disease activity index (DAI) and histological score of colitis (HS) inflammatory cytokines were evaluated to determine the colonic inflammation severity. TGF-β1, EGF, COX-2 and tight-junction (T-J) protein mRNA was measured by qPCR to access epithelial restoration. NF-κB activation was evaluated by Western-blotting and measured by Grey-scale value. Proximal colonic mucosa was used to analyze gut mucosal flora using high-througput sequencing analysis targeting V4-V5 regions of the bacterial 16S rRNA gene. Statistical analysis was performed using one-way ANOVA analysis and the Post hoc LSD test or Tamhane's T2 test.

Results: Colonic NF-κB activation was significantly inhibited in MyD88-DSS group compared to WT-DSS group, suggesting the inhibitory effect of MyD88 deletion on NF-κB activation. However, deletion of MyD88 failed to improve DAI and HS in DSS-colitis mice as compared to WT-DSS group. Besides, the difference of colonic IL-1β, TNF α and IFN γ mRNA expression drastically decreased in MyD88 deficient mice with or without DSS challenge. TGF-β1, EGF, COX-2 and T-J protein mRNA was not significantly different among groups, suggesting relatively normal epithelial reconstruction ability in WT-DSS, MyD88 KO and MyD88-DSS groups as compared to WT group.

Colon mucosal morphology analysis showed that the alpha diversity was not significantly different among groups in terms of diversity index (Shannon and inverse Simpson) and bacterial culture abundance (Chao). At phylum level, the proportion of Proteobacteria dramatically elevated to 41.9% in MyD88 KO mice as compared to WT, WT-DSS and MyD88-DSS groups (7.0%, 16.1% and 22.3%, respectively), within which pathogenic bacteria such as Pseudomonadiales, Burkholderiales and Enterobacteriales were predominately increased at order level in MyD88 KO mice. The percentage of probiotics such as Lactobacillus decreased in MyD88 KO group (31.5%) and further dropped to 11.2% and 4.1% in WT-DSS or MyD88-DSS groups as compared to WT (35.5%).

Conclusion: Deficiency of MyD88 inhibited NF-κB activation but not colonic inflammation in mice with colitis possibly due to MyD88 deletion associated pathogenic-riched and probiotics-exhausted gut microbiota.

Disclosure: Nothing to disclose

P0475 PILOT STUDY ON THE EFFECTIVENESS OF THE COMBINATION OF HYALURONIC ACID, COINDRITIN SULFATE AND POLYOXAMER 407 IN SCAR HEALING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF THE ESOPHAGUS IN PORCINE DISEASE

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Introduction: Hyaluronic acid + chondroitin sulfate + poloxamer 407 (HA+CS) has shown efficacy in the repair of microscopically-damaged esophageal epithelium caused by gastrointestinal reflux (GER). However, there are no studies that show efficacy in the repair of macroscopic damage of the mucosa and/or submucosa.

Aims and Methods: Primary Objective: To assess the efficacy of HA+CS in healing scar due to deep submucosal injury after endoscopic submucosal dissection (ESD) of the esophagus in porcine models. Secondary Objective: To evaluate the efficacy of HA+CS in the prevention of esophageal stenosis secondary to ESD. This was a randomized, experimental, endoscopists- and pathologist-blinded pilot study. Dissection of 4% of the middle-dorsal esophagus was performed in 6 anesthetized pigs (female Landrace-Large Whites). In 3 pigs (C1, C4 and C5) 10 ml of HA+CS (1 sachet) was injected on the surface of the eschar, infiltrating it with a syringe on the submucosa of the eschar edges. This was followed by treatment with HA+CS sachet every 2 days + Omeprazole 20 mg/d (CS). The other 3 pigs received only the standard treatment, Omeprazole 20 mg/12h po, to avoid potential additional damage from GER. The pigs were kept on a liquid diet for the first 24 hours and then started on a regular diet. After 15 days, an endoscopic evaluation was conducted to assess the degree of stenosis and healing grade using the modified Manchester scale for the clinical evaluation of scars. Finally, histological analysis was conducted by 2 pathologists, following necropsy.

Results: The average weight at the beginning of the study for the HA+CS group was 44.63 kg and 44.13 kg respectively, and 36.48 kg vs 41.80 kg respectively at the end of the treatment. There were no differences in the mean size of eschars (9.9 mm in the HA+CS group vs 8.82 mm in control group) or in their location (15.66 mm from the gastrooesophageal junction in the HA+CS group vs 11.66 mm in the control group). All the eschars covered more than 50% of the circumference. Stenosis presented in 100% of the cases. In 2 (33.3%) cases, the endoscope could be passed through the stricture (C2 and C6). The score on the modified Manchester scale was 4.3 for the HA+CS group and 3.3 for the control group.

Complications: perforation with paraesophageal collection in C4. Histological analysis: Higher inflammatory infiltrate with predominance of neutrophils, lymphocytes, macrophages (acute inflammatory reaction) in the control pigs vs. the pigs treated with HA+CS, and there was no inflammatory infiltrate (lymphocytes) predominated. In the control group, neovascularization consisted of small to medium vessels and the reorganization of the connective tissue process was in its beginning phase, whereas in the HA+CS group the blood vessels were increased and the reorganization of the connective tissue was more advanced, as evidenced by the presence of fibroblasts well organized in parallel lines. 1 of the HA+CS-treated pigs showed re-epithelialization on 1 border (C1).

Conclusion: The histological results suggest that HA+CS promotes the repair of esophageal mucosa after ESD, although a clinically significant difference to control treatment was not shown, as all the pigs developed stenosis. More studies are required, with a larger sample size, to evaluate the efficacy of HA+CS in the repair of macroscopic damage of the mucosa.

Disclosure: This study has been funded by Norgine and has received collaboration from Pentax and SimMedical Canaries

P0476 PANCOLITIS INCREASES THE MORTALITY RISK OF CYTOMEGALOVIRUS COLITIS IN PATIENTS WITHOUT INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT STUDY

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Introduction: Cytomegalovirus (CMV) colitis typically presents in immunocompromised patients, such as IBD patients. Several studies have been conducted on the endoscopic findings of CMV colitis in IBD patients; however, those of CMV colitis in non-IBD patients and their relationship with in-hospital mortality are unclear.

Aims and Methods: We aimed to describe the endoscopic presentation in these patients and to determine the endoscopic predictor of in-hospital mortality. Patients with CMV colitis diagnosed using histology between April 2002 and December 2016 at the Linkou Chang Chung Memorial Hospital, Taiwan, were retrospectively enrolled. Patients diagnosed with IBD during follow-up were excluded. Patient data, including underlying diseases, endoscopic presentation, laboratory data, clinical course, complications and clinical outcomes were collected. The independent risk factors for in-hospital mortality were analysed with logistic regression. The difference of overall survival was compared with Kaplan-Meier survival curve and log rank test. All statistical calculations were performed using SPSS software, version 21 (IBM, Armonk, New York).

Results: 69 patients were enrolled, including 8 IBD patients. Within the 61 non-IBD patients, 31 were diagnosed by colonoscopy and others by sigmoidoscopy. Ulceration (77%) was the most common endoscopic finding, followed by a cobble stone appearance (19.7%), colitis with without erosions (9.8%), pseudomembrane (9.8%) and tumour/polyp-like lesions (8.2%). Among the patients who underwent full-length colonoscopy, 35.3% presented with right-sided colitis, 23.5% with left-sided colitis and 32.4% with pancolitis. Pancolitis was identified as a negative predictor of in-hospital mortality (odds ratio, 6.8; 95% confidence interval, 1.233-37.497; p = 0.028) and overall survival (log rank p = 0.018).

Conclusion: Colonoscopy is recommended for precise CMV colitis diagnosis and outcome prediction in non-IBD patients.

Disclosure: Nothing to disclose

P0477 CLOSTRIDIUM DIFFICILE ISOLATION AND CHARACTERISATION - RESULTS OF A PILOT STUDY

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Introduction: Clostridium difficile (CD) infection can lead to severe infectious colitis. Different bacterial toxins and diminished host immune response contribute to symptomatic disease. Inflammatory bowel diseases (IBD), ulcerative colitis, and Crohn’s disease are chronic diseases causing a prolonged inflammation of gastrointestinal tract. In these patients colonisation with CD is often confirmed but its role is inconclusive.

Aims and Methods: The aim of the study was to compare CD colonization and selected inflammatory parameters in patients with IBD and other diseases in
hospitalized patients. We obtained fecal samples from 161 randomly selected patients, hospitalized at Department of Gastroenterology during the period between 1/1/2015 - 1/5/2016. Total DNA was isolated from feces and CD was detected using the real time PCR amplification of specific 16S RNA gene and toxicogenic strains were confirmed by the amplification of tcdB gene. After collecting information, inflammatory parameters (neutrophil granulocytes, leukocytes, CRP, erythrocyte sedimentation, albumin, ferritin, and iron) and therapy (pre-and hospital antibiotics, corticosteroids, biological therapy) we divided isolates in 2 groups: IBD group and control group.

Results: The final analysis included 151 samples, (male 75, female 76), 48 (31.8%) were positive for CD, 11 of which (11/103, 10.7%) were tcdB+. Between the 2 groups, significant differences were confirmed only in the use of corticosteroids and biological therapy prior to hospitalization, p < 0.01. Regarding the use of antibiotics prior to hospitalization, differences between the 2 groups were not confirmed, p = 0.72. There were no significant differences observed in inflammatory parameters within IBD patients (CD positive compared to CD negative).

Conclusion: The results of our study suggest that IBD patients and patients from the control group were colonized with CD in comparable proportions. The majority of strains were nontoxicogenic, which will not cause CD infections, but could be regarded as a marker for disturbed gut microbiota.

Disclosure: Nothing to disclose

References


P0478 UNIVERSAL ANTIBIOTIC PROPHYLAXIS MAY BE UNNECESSARY IN ACUTE VARICEAL BLEEDING: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Randomized controlled trials conducted from the 1990s to early 2000s showed efficacy of antibiotic prophylaxis in acute variceal bleeding. Over the past decades, however, endoscopic and systemic therapy for variceal bleeding has improved remarkably, and the necessity of antibiotic prophylaxis could have decreased.

Aims and Methods: In this study, we aimed to evaluate the efficacy of antibiotic prophylaxis with our most recent data. We retrospectively studied clinical characteristics, treatment and outcomes of 150 patients (116 men, median age: 62 years) with acute variceal bleeding, who were admitted to our hospital between January 2012 and December 2016. Those who had obvious infection or aspiration pneumonia at admission were excluded. Patients were classified into 2 groups according to presence or absence of antibiotic prophylaxis. Rates of obvious bacterial infection, suspicious infection, in-hospital mortality, in-hospital rebleeding, and readmission within 30 days were compared between the 2 groups.

Multivariate analysis was also performed to evaluate the efficacy of antibiotic prophylaxis.

Results: The median Child-Pugh score was 8. Immediate endoscopy was performed in 148 patients, and active bleeding was observed in 80 patients. Endoscopic variceal ligation was performed in 111 patients. Hemostasis was achieved in 148 patients. 2 patients died of uncontrollable bleeding (1 with and 1 without endoscopy). 46 patients (30.7%) received antibiotic prophylaxis. The rates of obvious bacterial infection, suspicious infection, in-hospital mortality, in-hospital rebleeding, and readmission within 30 days were not different significantly between the 2 groups. In the multivariate analyses, antibiotic prophylaxis was not associated with any of these outcomes. Instead, high serum creatinine levels at admission (greater than 1 mg/dL) were significantly associated with bacterial infection (adjusted odds ratio 12.5, 95% CI 1.24–126), and higher Child-Pugh score (per point) was associated with mortality (adjusted odds ratio 3.57, 95% CI 1.25–10.2).

Conclusion: Universal antibiotic prophylaxis may be unnecessary in acute variceal bleeding. Impaired renal function at admission was a risk factor for bacterial infection and might be applied to a risk stratification approach for antibiotic prophylaxis.

Disclosure: Nothing to disclose

P0479 AIMS65 IS THE MOST ACCURATE RISK-SCORING SYSTEM FOR PREDICTING MORTALITY OF PATIENTS WITH DUODENAL ULCER BLEEDING

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Introduction: In spite of the advance of endoscopic hemostasis for upper gastrointestinal bleeding, treating duodenal ulcer bleeding is sometimes difficult and does not yield good prognosis.

Aims and Methods: In this study, we evaluated and compared various risk-scoring systems for upper gastrointestinal bleeding to predict outcomes of patients who underwent endoscopic treatment for duodenal ulcer bleeding. Bleeding from peptic ulcer was diagnosed in 1,147 patients (892 patients with gastric and 255 with duodenal ulcer) among 7,106 patients who underwent emergent esophagogastroduodenoscopy for upper gastrointestinal bleeding at our hospital from July 2007 to June 2017. We retrospectively reviewed electronic medical records of the 1,147 patients and compared their prognosis after endoscopic therapy between gastric and duodenal ulcer patients. In the 255 patients with duodenal ulcer, we evaluated the following risk-scoring system: Glasgow Blatchford, AIMS65, admission Rockall and full Rockall scores, to predict inhospital mortality by analyzing their area under the receiver operating characteristic curve (AUROC).

Results: The mortality rate of patients with duodenal ulcer bleeding was 6.7% (17/255), which were significantly higher than that of those with gastric ulcer bleeding (0.67%, 6/892) (p < 0.001). In the duodenal ulcer patients, risk scores were significantly higher in patients with in-hospital mortality than those without in the following systems, and AUROC of AIMS65 (0.83) was highest among them (Table). With more than 2 points of AIMS65 score as a cut-off value, sensitivity and specificity to predict in-hospital mortality of patients with duodenal ulcer bleeding were 0.882 and 0.597, respectively.

Conclusion: The conclusion of patients with duodenal ulcer bleeding was poorer than that of patients with gastric ulcer. The AIMS65 score may be useful to predict the outcome after endoscopic treatment for duodenal ulcer bleeding, especially in the situation at deciding the indication of endoscopic hemostasis because this scoring system can be calculated without endoscopic findings.

Disclosure: Nothing to disclose

P0480 EFFECTS OF ASPIRIN ON MORTALITY AND RE-BLEEDING IN PATIENTS WITH NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Aims and Methods: Our primary aim was to synthesize the evidence comparing mortality and re-bleeding rates in patients who resume aspirin compared to those who do not after NVUGIB. Our secondary aim was to determine whether being on aspirin upon presentation with NVUGIB is associated with worse outcomes compared to not being on it.

We conducted a systematic review of randomized controlled trials (RCTs) and observational studies. We ran a comprehensive sensitive search covering major electronic databases, clinical trial registries and grey literature. 2 teams of 2 reviewers screened titles and abstracts of included studies and assessed their risk of bias using standardized forms. We used meta-analysis to pool data for mortality and re-bleeding outcomes.

Results: Of 9827 citations, we assessed 254 full-texts for eligibility. 1 RCT and 3 observational studies address the primary question; all assess low dose aspirin, but timing of its resumption varied. None compare different times of aspirin resumption. The RCT suggests that early aspirin resumption may reduce mortality; HR = 0.29; 95% CI [0.06–0.65]; moderate certainty of evidence.
Meta-analysis of 3 observational studies suggests that aspirin resumption may reduce the risk of rebleeding: pooled HR = 0.79; 95% CI [0.60-1.02]; very low certainty of evidence. We assessed if the relative effect of resuming aspirin is modified by whether people were using it for secondary or primary prophylaxis. In those on aspirin for secondary prophylaxis, resuming aspirin may reduce mortality to a large extent (HR = 0.56; 95% CI [0.31–1.00]) compared to those taking it for primary prophylaxis (HR = 4.07; 95% CI [0.54–30.74]), but studies were characterized by high heterogeneity (p = 0.06 for subgroup effect). The RCT suggests that aspirin resumption may increase re-bleeding: HR = 1.90; 95% CI [0.60–6.00]; moderate certainty of evidence, while meta-analysis of 2 observational studies suggests it may reduce re-bleeding: pooled HR = 0.82; 95% CI [0.35–1.91]; very low certainty of evidence. Meta-analysis of 2 studies shows no increased re-bleeding risk: pooled HR = 1.23; 95% CI [0.44–3.42]; very low certainty of evidence.

Concluding a protective strategy soon after NVUGIB is of very low certainty based on observational studies and moderate certainty based on 1 RCT. The available evidence is not informative as to the optimal timing of aspirin resumption. High quality RCTs are needed to address the optimal timing of aspirin resumption in patients with NVUGIB.

Disclosure: Nothing to disclose.

### P0481 OPTIMAL ENDOSCOPY TIMING ACCORDING TO THE SEVERITY OF UNDERLYING LIVER DISEASE IN PATIENTS WITH ACUTE VARICEAL BLEEDING

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Introduction: Current guidelines recommend endoscopic therapy to be performed within 12 hours for acute variceal bleeding (AVB). However, the optimal timing of endoscopic therapy for AVB remains unclear.

Aims and Methods: The aim of this study was to examine the relationship between the endoscopy timing and clinical outcomes in AVB, with emphasis on Forrest classification and endoscopic therapy. From January 2010 to June 2015 in 3 center, 1287 patients with varices confirmed as the source of bleeding by endoscopy were evaluated. The primary outcome was a composite of 6-week rebleeding and mortality. We stratified patients according to the model for end-stage liver disease (MELD) score and analyzed the association between the endoscopy timing and primary composite outcome.

Results: In 411 patients, the overall composite outcome rate was 30.9% (n = 127) at 6 weeks. Patients who underwent urgent endoscopy (<12 hours) had a significantly higher composite outcome than patients who underwent endoscopy (>12 hours) (34.4% vs. 19.1%; p = 0.005). Low-risk patients who underwent urgent endoscopy were more likely to reach the composite outcome (adjusted OR, 0.84 per 4 hours; 95% CI, 0.67-0.98; p = 0.027). However, time to endoscopy did not have a significant impact on outcomes in high-risk patients. These findings persisted even after adjustment for baseline characteristics between the urgent and non-urgent groups.

Conclusions: Our results are significant and are associated with a poorer outcome in patients with AVB, especially in low-risk patients. This result provides a treatment strategy according to the severity of underlying liver disease in patients with AVB.

Disclosure: Nothing to disclose.

### P0482 FORREST CLASSIFICATION DOES NOT PROPERLY ASSESS REBLEEDING RISK OR MORTALITY IN HIGH-RISK UPPER GI BLEEDING

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Introduction: Forrest classification has been the most endoscopic used 1 in upper GI bleeding. The 6 stages risk assessment establishes the higher risk in Forrest Ia patients with Forrest IIa and Forrest I, regarding rebleeding risk, because it has been previously suggested that a visible vessel might entail a higher risk of rebleeding. Upper GI bleeding from Virgen de las Nieves University Hospital is a prospectively collected database from January 2013. For this study, patients up to January 2017 were included. For every patient 150 clinical and biochemical variables are recorded. Variables were compared with SPSS 17 software (SPSS Inc. Chicago, IL) by means of the Chi-square test.

Results: 414 patients were included (65.5% males) with non variceal upper GI bleeding. Mean age was 65 years (range 19-97). The main upper GI bleeding etiologies were duodenal ulcer in 29%, gastric ulcer in 22%, acute gastric erosions in 13%, Mallory-Weiss and esophageal ulcers in 8%. 34 patients died (8.2%) and 69% had a relevant comorbidity. An endoscopic therapy with 2 methods (injection plus clipping or argon plasma coagulation) was applied to every patient.

Mortality did not significantly differ between Forrest Ib patients and Forrest IIa (19.6% vs. 20.8%). Regarding rebleeding, despite the proportion of rebleeding patients with Forrest IIa ulcers almost doubled Forrest Ib (20% vs. 10%), the statistic test did not reach statistical significance, neither did regarding the need for surgery (16% vs. 6.5%, p = n.s.). Moreover, when mortality rates in patients with Forrest Ib and Ib were compared we found no significant differences, an trend toward a higher mortality in Forrest IIa patients (15.4% vs. 21.7% IIa). A significant absence of statistical differences was observed for the rest of outcomes studied: rebleeding (23.1% Ia vs. 16.7% IIa) and need for surgery (23.1% Ia vs. 12.5% IIa).

Conclusion: Our study shows that Forrest classification seems an inadequate predicting tool for rebleeding in its actual formulation. In view of our results Forrest IIa patients should probably be considered of a higher risk than Forrest Ib, and closer to Forrest Ia. We might hypothesize that the presence of a visible vessel carries a higher risk of rebleeding, as the presence of more than 4 vessel, close to the vessel, more local coagulation and more coagulation of capillaries, more easily coagulated through endoscopy and even natural mechanisms.

Disclosure: Nothing to disclose.

### P0483 RISK FACTORS OF POOR PROGNOSIS AND IMPAIRMENT OF ACTIVITIES OF DAILY LIVING IN PATIENTS WITH HEMORRHAGIC GASTRODUODENAL ULCERS


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Introduction: Although most of hemorrhagic gastroduodenal ulcers (HGU) can be safely treated with endoscopic procedures, some patients with HGU could have poor prognosis owing to comorbidities and medications for antiocoagulation. In this study, risk factors of poor prognosis including mortality and impairment of activities of daily living (ADL) in patients with HGU were examined. In particular, prognosis of elderly HGU patients (≥75 years old) was evaluated in comparison to that of non-elderly (<75 years old) patients.

Aims and Methods: The medical records of 580 patients with endoscopically confirmed HGU (430 men, 159 women; mean age 66.7 years; range 25–95 years) were retrospectively reviewed. Clinical backgrounds and outcomes were compared between patients ≤75 years old (n=394) and ≥75 years old (n=186).

Results: Of 580 patients, 75% patients were elderly HGU patients. The primary outcome was a composite of 6-week rebleeding and mortality. In elderly patients compared to non-elderly (<75 years old) patients, age ≥75 years old (n=28.0 days), and impairment of ADL were evaluated in 28.0 days after occurrence of hemorrhage and, impairment of ADL. Impairment of ADL was defined as admission to care facilities after hospital discharge or requirement of home modification for rehabilitation at home. Evaluated clinical factors were endoscopic features, non- intervention endoscopic procedures, comorbidities, symptoms, medications, vital signs, and blood test results.

Conclusions: There were significant differences in overall mortality (3.8% vs. 7.6%), hospitalization period (16.2±29.3 days vs. 22.8±28.0 days), and mortality of ADL (1.3% vs. 6.7%) between patients <75 years old and those ≥75 years old. Multivariate analysis revealed that independently significant risk factors for overall mortality were age (≥75 years) (odds ratio [OR] 2.25, 95% confidence interval 1.06–4.74), and renal disease (OR 3.38, 95% CI, 1.42–8.01). Risk factors of mortality within 30 days after hemorrhage were age (≥75 years) (OR 3.40, 95% CI, 1.21–9.56), need for interventional endoscopic procedures (OR 3.91, 95% CI, 1.08–14.1), and renal disease (OR 4.3, 95% CI, 1.40–13.2). Finally, risk factors of impairment of ADL were use of proton pump inhibition or prior to hemorrhage (OR 5.83, 95% CI, 2.1–16.2), heart disease (OR 3.06, 95% CI, 1.11–8.3), and age (≥75 years old) (OR 5.07, 95% CI, 1.73–14.9).

Conclusion: High mortality and impairment of ADL were more likely to be observed in elderly HGU patients compared to non-elderly patients. In particular, comorbidity of renal disease and heart disease was a risk of poor prognosis in those subjects. Prophylactic approaches for HGU and early improvement of ADL after HGU occurrence are particularly important in elderly patients with comorbidities.

Disclosure: Nothing to disclose.

### P0484 PALBI - THE PLATELET-ALBUMIN-BILIRUBIN SCORE - A BETTER PREDICTOR OF OUTCOME OF ACUTE VARICEAL BLEEDING

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Introduction: The albumin-bilirubin (ALBI) score eliminates the need for subjective variables required in the Child-Turcotte-Pugh (CTP) classification and has been validated as a prognostic indicator for patients with HCC. Incorporating platelet count to reflect portal hypertension in the PALBI score improved

Disclosure: Nothing to disclose.
validity in predicting outcome of patients with HCC undergoing resection and ablative therapies.

Aims and Methods: We aimed to evaluate the PALBI score compared to the CTP class for predicting the outcome of acute variceal bleeding. Data of 1517 patients presenting with acute variceal bleeding were analyzed. The CTP class and PALBI score were calculated to mortality. PALBI score was calculated as: $2.02^{*}\log_{10}\text{platelets} + (0.37^{*}\log_{10}\text{bilirubin}) + (0.04^{*}\text{albumin}) + (3.48^{*}\log_{10}\text{platelets}) + (1.01^{*}\log_{10}\text{bilirubin})$. Areas under the receiver-operator characteristics curve (AUROC) were calculated for survival.

Results: PALBI score was more significant in comparison to ALBI, and PALBI-1 patients survived. 332 Patients died during the admission (0.39%), PALBI grade 1, 43 patients (2.8%) PALBI grade 2, 957 patients (4.5%), 434 (29.2%) CTP B and 1014 (66.8%) CTP C; 6 patients had no score. Mean age was 52 years old; 77.5% were males. There were 69 CTP-A patients (4.5%), 432 (29.2%) CTP-B patients, and 278 (18.4%) CTP-C patients.

Conclusion: PALBI better predicts early mortality of patients with acute variceal bleeding than CTP score.

Disclose: Nothing to disclose

Reference

P0485 UPPER GASTROINTESTINAL BLEEDING NOT ASSOCIATED TO PORTAL HYPERTENSION: ASPECTS OF EPIDEMIOLOGY AND MANAGEMENT IN A SOUTHERN SPANISH AREA
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Introduction: The aim of the research was to evaluate different epidemiological and management aspects of Upper Gastrointestinal Bleeding not associated to Portal Hypertension (UGBNPH) in a Southern Spanish Hospital (Cádiz, Spain).

Aims and Methods: Retrospective research including every patient admitted to Gastroenterology Department of Puerta del Mar Hospital (Cádiz), between January 2016 and December 2016, because of UGBNPH.

We analysed different variables: gender, age, cardiovascular risk factors such as Arterial Hypertension (AHT), Diabetes Mellitus (DM) and Dyslipidemia (DLP); concomitant treatment with Proton Pump Inhibitors (PPIs), Antiplatelets, Antithrombotics, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Antidepressants; clinical and endoscopic findings; red blood cells and iron requirement, and Helicobacter pylori investigation. We also analysed short and medium term survival rates and recurrence rate in 1-year period.

Results: We included 75 patients admitted because of UGBNPH (56% men), with an average age of 69 years old (men 66, women 74).
We did not find significant differences by gender when analyzing DM (33.3%), with higher frequency of AHT among women (62.5% vs 27.3%) and DLP among men (22.7% vs 0%).
We did not find significant differences by gender when analyzing concomitant treatment with PPIs (43.3%), Antiplatelets (6.7%), Antithrombotics (3.3%), NSAIDs (0%) and Antidepressants (23.2%).

Clinical debut as Hematemesis (66.7%) and Melena (63.3%) was similar in frequency. Regarding Endoscopic findings, in both genders, we found more Esophageal Variceal bleeding as etiology (70%) compared to Portal Hypertension Gastropathy bleeding (33%).

87.5% of admitted patients needed red blood cell transfusion (vs 59.1% of admitted men), with 2.9 packed red blood cells as average (vs 4 packed red blood cells in men). We only began iron therapy in 20% of patients admitted.
Short-term survival rate was 90% (men 86.4%; women 100%) and medium-term survival rate (1 year after admission) was 90%. Bleeding recurrence rate in 1-year period was higher among women (50%) compared to men (36.8%) and related more often to Portal Hypertension Gastropathy (35.8%).

Conclusion: In our research, when analyzing Upper Gastrointestinal Bleeding not associated to Portal Hypertension, cirrhotic men of medium age was the more commonly affected demographic group. Esophageal Variceal bleeding is the most usual etiology in both genders, however Portal Hypertension Gastropathy bleeding has the highest recurrence rate. Regarding red high blood cells transfusion rate we should consider the use of iron therapy in more cases. Finally, short-term prognosis is favorable in our population.

Disclose: Nothing to disclose

P0487 PREDICTOR OF MORTALITY IN UPPER GASTROINTESTINAL BLEEDING IN PATIENTS ALREADY HOSPITALIZED FOR ANOTHER CONDITION: A PROSPECTIVE STUDY
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Introduction: Upper gastrointestinal bleeding (UGIB) is one of the main causes of hospital admission and urgent endoscopy in Gastroenterology departments and represents a true emergency, associated with significant morbidity, mortality and healthcare costs. Several predictors of in-hospital mortality have been identified.

1. We did not find significant differences by gender when analyzing AHT (53.3%), with higher frequency of AHT among women (62.5% vs 27.3%) and DLP among men (22.7% vs 0%).
2. We did not find significant differences by gender when analyzing concomitant treatment with PPIs (43.3%), Antiplatelets (6.7%), Antithrombotics (3.3%), NSAIDs (0%) and Antidepressants (23.2%).
3. Clinical debut as Hematemesis (66.7%) and Melena (63.3%) was similar in frequency. Regarding Endoscopic findings, in both genders, we found more Esophageal Variceal bleeding as etiology (70%) compared to Portal Hypertension Gastropathy bleeding (33%).
4. 87.5% of admitted patients needed red blood cell transfusion (vs 59.1% of admitted men), with 2.9 packed red blood cells as average (vs 4 packed red blood cells in men). We only began iron therapy in 20% of patients admitted. Short-term survival rate was 90% (men 86.4%; women 100%) and medium-term survival rate (1 year after admission) was 90%. Bleeding recurrence rate in 1-year period was higher among women (50%) compared to men (36.8%) and related more often to Portal Hypertension Gastropathy (35.8%).

Conclusion: In our research, when analyzing Upper Gastrointestinal Bleeding not associated to Portal Hypertension, cirrhotic men of medium age was the more commonly affected demographic group. Esophageal Variceal bleeding is the most usual etiology in both genders, however Portal Hypertension Gastropathy bleeding has the highest recurrence rate. Regarding red high blood cells transfusion rate we should consider the use of iron therapy in more cases. Finally, short-term prognosis is favorable in our population.
PATIENTS WHO FAILED INITIAL P0488 RISKS OF UPPER GASTROINTESTINAL BLEEDING IN C.-G Guo1, K.S Cheung1, L Chen1,

Disclosure: Nothing to disclose. More studies in this sense are needed.

bleeding and its management. It is obvious that IPs have poorer outcomes, and management of IPs who develop UGIB have been derived essentially from studies on OPs bleeding, whereas few data are available that focus on in-hospital bleeding and its management. It is obvious that IPs have poorer outcomes, and better understanding of the reasons is essential to develop a specific management. More studies in this sense are needed.

Disclosure: Nothing to disclose.

References

P0488 RISKS OF UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WHO FAILED INITIAL HELICOBACTER PYLORI ERADICATION THERAPY: A PROBABILITY SCORE MATCHING STUDY
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Introduction: Upper gastrointestinal bleeding (UGIB) is a leading cause of hospitalization which is still associated with significant mortality. Although Helicobacter pylori (HP) eradication and the use of gastroprotective agents could lower the risk of UGIB, the actual bleeding risk in patients who had received HP therapy remains unclear, particularly those who failed initial HP eradication.

Aims and Methods: This was a propensity score matched cohort study to determine the risk of UGIB in HP-infected patients who had received a course of clarithromycin-containing triple therapy for HP eradication between Jan 2003 and Dec 2012. Patients were identified from the territory-wide electronic health database of the Hong Kong Hospital Authority. The follow-up period commenced from 60 days after the HP therapy until the occurrence of UGIB, death or the end of the study (30 Jun 2016). The primary outcome was the occurrence of non-variceal UGIB. Failed initial HP eradication was identified by the need of repeat HP eradication therapy including repeated first-line therapy, a second-line or third-line therapy. Covariates included baseline characteristics, comorbid conditions and concurrent medications. As medication usages could change over time, the follow-up period was split into intervals of 3-month and drug usage was defined in each interval as more than 7 days use. To reduce the indications bias for gastroprotective agents, the last 6-week before the index date of events or censoring were excluded when retrieving proton pump inhibitors (PPI) and histamine type-2 receptor antagonists (H2RA) prescription records. Propensity score (PS) matching was used to select controls for each failed eradication patient by the ratio of 1:5. Cox proportional hazards model was used to adjust the confounders, in which medications were included as time varying variables. Hazards ratios (HR) and corresponding 95% confidence intervals (CI) were presented.

Results: 70,869 patients who had received HP eradication therapy were included in PS matching, with 5,593 patients in the failed initial eradication group and 70,869 patients who had received HP eradication therapy were included. Data collection is still ongoing. A total of 101 internal medicine wards took part in the study. For the purpose of this study, we have identified all possible diagnoses of GIB (upper and lower), describing the length of stay (LOS), mortality rate, and possible risk factors of GIB, including drugs (i.e., anti-platelet agents, anti-coagulants, selective serotonin reuptake inhibitors), smoking habit, alcohol abuse, obesity, index of comorbidity (through the Cumulative Illness Rating Scale [CIRS]), and common chronic diseases (i.e., diabetes mellitus, chronic heart failure, liver cirrhosis, and chronic obstructive pulmonary disease). Odds ratio, 95% confidence interval, and statistical significance were evaluated for all variables.

Results: The REPOSI registry includes 4486 (6-year time span). Among these, at least a diagnosis of GIB was reported in 120 patients (mean age 79.47, F:M 0.9:1), with a crude prevalence of 2.7%. Upper GIB occurred in 72 patients (mean age 79.98, F:M 0.9:1), and both upper/lower GIB in 3 patients. The pooled LOS of patients with GIB was 11.7±8.1 days. 4 patients with GIB died in hospital (3.3%) and eight died within the next 3 months (7.2%). Notably, the use of acetylsalicylic acid (ASA) and anti-coagulants (either vitamin K antagonists and direct oral anti-coagulants) was not associated with GIB (p=ns). Multivariate analysis for all the possible risk factors of GIB is shown in Table. Non-ASA anti-platelet agents (OR 2.77), CIRS index of comorbidity > 3 (OR 2.38), anaemia (OR 2.81), and liver cirrhosis (OR 5.87) were statistically associated with GIB (p < 0.01).

Conclusion: We here show for the first time that a high index of comorbidity (>3) is associated with high odds for GIB. GIB carries both an in-hospital and 3-month high mortality rate. The use of non-ASA anti-platelet agents should be discussed and carefully evaluated in elderly patients.

Disclosure: Nothing to disclose.
Aims and Methods: This study aimed to quantify oesophageal mucosal MCs inclusions and their spacial relationship with allent nerves in reflux disease patients. Distant oesophageal biopsies from 10 patients with ‘true’ NERD and 11 patients with ERD were stained for CGRP and toluidine blue. The position of CGRP positive nerves was determined as number of cell layers from the lumen. Similarly, the number of MCs per high power field (HFP: X50 magnification) and their position in the epithelium was recorded.

Results: The median age was 55.5 years (range: 28–75, 6M:4F) for NERD patients and 59 years (range: 38–75, 7M:4F) for ERD. The median density of MCs/HFP was 0.17 (CI: 0.08–0.5) for ERD vs 0.50 (CI: 0.3–0.8) for ERD (p = 0.01). There was no correlation between oesophageal acid exposure and density of MCs inclusion in NERD (r = 0.09). The MCs were more superficially located (17–25 cell layers) compared to ERD (25 cell layers), p = 0.01. There was no correlation between the position of the MCs and the nerve fibres amongst both groups (r² = 0.2, p = 0.05).

Conclusion: Although there are differences between the density of MCs infiltration and position of the MCs in the epithelium between NERD and ERD, we could not find a good correlation between the position of nerves and the position of the MCs. Therefore, the spacial relationship of the MCs and the mucosal allent nerves in NERD appears to be different to IBS with possible pathophysiological implications.

Disclosure: Nothing to disclose

References

P0491 THE EFFECT OF A SINGLE AND REPEATED DOSES OF MEMANTINE ON GASTRIC MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS

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Introduction: Memantine, currently available for the treatment of Alzheimer’s disease, is an competitive antagonist of the N-methyl-D-aspartate type of glutamate receptors. Under normal physiologic conditions, these unstimulated receptor ion channels are blocked by magnesium ions, which are displaced after agonist-induced depolarization. In humans, memantine administration is associated with different gastrointestinal dysmotility side effects (vomiting, diarrhea, constipation, motor-mediated abdominal pain), thus limiting its clinical use. Memantine treatment of these motility disorders has not been clarified yet. Pigs can be used in various preclinical experiments due to their relatively similar gastrointestinal functions compared to humans.

Aims and Methods: The aim of this study was to evaluate the impact of a single and repeated doses of memantine on porcine gastric myoelectric activity evaluated by means of electrogastrography (EGG). 6 adult female experimental pigs (Sus scrofa f. domestica, mean weight 41±7.5 kg) entered the study for 2 times. The animals received after a single intragastric dose of memantine (20 mg). In the second part, EGG was accomplished after 7 days intragastric administration (20 mg per day). All EGG recordings were performed under general anaesthesia. Basal (15 minutes) and study recordings (120 minutes) were accomplished using an EGG stand (MMS, Enschede, the Netherlands). Running spectral analysis based on Fourier transform was used. Results were expressed as dominant frequency of gastric slow waves (DF) and power analysis (areas of interest).

Results: Single dose of memantine significantly increased DF, from basic values (1.65±1.05 cycles per min.) to 2.86 cpm after 30 min. (p = 0.008), lasting till 75 min. (p = 0.014). Basal power (median 452; inter-quartile range 280–1312 μV²) raised after 15 min. (median 827; IQR 224–2769; p = 0.386; NS), lasting next 30 min. Repetitively administered memantine caused important gastric arrhythmia. Basal DF after single and repeated administration was not different, however, a DF increase in the second part was more prominent (up to 3.18±2.16 after 15 and 30 min, p < 0.001). In comparison with a single dose, basal power was significantly higher after repetitively administered memantine (median 3940; IQR 695–13023 μV²; p < 0.001). Next dose of 20 mg memantine in the second part induced a prominent drop of power after 15 min. (median 541; IQR 328–2280 μV²; p < 0.001), lasting till 120 min. (p < 0.001).

Conclusion: Single and repeated doses of memantine caused gastric arrhythmia and long-lasting low power after repeated administration might explain possible gastric dysmotility side effects in the chronic use of memantine.

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Disclosure: Nothing to disclose

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P0492 RELATIONSHIP BETWEEN ABUSE AND GASTROINTESTINAL SYMPTOMS IN NON PATIENT WOMEN

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Introduction: The relationship between abused women and specific gastrointestinal symptoms has been widely investigated. However, the relationship between abuse and the prevalence of gastrointestinal symptoms and the association with the time of perpetration, type, and severity of abuse is not clear (Y). Most women suffered from childhood and adulthood sexual and physical abuse. In 78% of LC the ASM was < 2 vs 36% of V (ASM > 4 in 54%). Controls lawyers women reported a mean of 4.9 GI symptoms (median 4; IQR 2–8) vs 4.6 of severely abused women (median 4; IQR 2–7). Controls lawyers women with an ASM ≥2 reported significantly more GI symptoms (median 6.5; IQR 3–11 vs median 3; IQR 1–7) (p = 0.002 vs < 2). Severely abused women with an ASM > 3 reported more GI symptoms than those reporting only one type of abuse. Conclusion: Symptoms in abused women mainly concern the abdomen and the GI tract. A history of severe, combined sexual and physical abuse is associated with a higher number of GI symptoms

Disclosure: Nothing to disclose

References
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P0493 MOTOR ACTIVITY OF ESOPHAGUS AND STOMACH IN PATIENTS WITH AMYOTROPIC LATERAL SCLEROSIS: AN OBSERVATIONAL STUDY

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Introduction: Patients with Amyotrophic lateral Sclerosis (ALS) may be affected by severe dysphagia, emerging in more than 80% of patients during the advanced phases of the disease and can affect all stages of swallowing with the need to resort to enteral nutrition via Percutaneous Endoscopic Gastrostomy. Previous studies have reported oesophageal and gastric dysmotility by manometry, although a large proportion of these patients have been described in small case reports, little is known about alterations of esophageal and gastric motor activity.

Aims and Methods: To assess motor function of esophagus and stomach, 12 ALS patients (4F/8M, age 46±13 yrs), receiving shelter in anti-violence associations and 46 lawyers controls (29–80 yrs), receiving shelter in anti-violence associations and 46 lawyers controls (29–80 yrs), were included as a control group. The severity of abuse was expressed as the Abuse Severity Measure (ASM) (2). The association between abuse characteristics and the number of symptoms, was assessed by Poisson regression model.

Results: In controls lawyers (LC) 65% of women suffered from physical and or sexual abuse in childhood and or adulthood vs 100% of severely abused women (V). Amongst the population, women having suffered from both sexual and physical abuse reported a higher number of GI symptoms than those reporting only one type of abuse. Conclusion: Symptoms in abused women mainly concern the abdomen and the GI tract. A history of severe, combined sexual and physical abuse is associated with a higher number of GI symptoms

Disclosure: Nothing to disclose

References
1. Pallotta N et al. UEGJ 2014;
Achalasia/Esophagogastric junction dysfunctional motility: a prospective observational trial to validate the utilization of esophageal pressure topography (EPT) as a monitoring tool during esophageal manometry

Aims and Methods: To validate the reliability of esophageal pressure topography (EPT) as a monitoring tool during esophageal manometry. To evaluate the association between EPT and the different manometric patterns of achalasia.

Results: A total of 250 patients were enrolled in the study. The mean age of the patients was 48.2 ± 17.1 years, with 56% being male. The EPT analysis showed a high level of agreement with the conventional manometric patterns of achalasia, with a Cohen's kappa coefficient of 0.85. The EPT analysis was able to accurately identify the presence or absence of concomitant esophageal motility disorders, with a sensitivity and specificity of 91.3% and 96.2%, respectively. The EPT analysis also showed a strong association between the different manometric patterns of achalasia and the presence of concomitant esophageal motility disorders, with a p-value of < 0.001.

Conclusion: EPT is a reliable monitoring tool during esophageal manometry for the diagnosis of concomitant esophageal motility disorders in patients with achalasia. It can be used to accurately identify the presence or absence of concomitant esophageal motility disorders, providing valuable information for the management of these patients.

Disclosure: Nothing to disclose

References
diagnosed with esophageal spasm during STM (n = 11 [3.0%]) compared to SWS (6/363 [1.7%]). n = 0 [0.0%] and n = 0 [0.0%] respectively. n = 120 (1%). The median procedure time was 48 minutes (18–240). Operative time was significantly less in cases where new triangular knife with water jet was used as compared to those in whom old triangular knife was used (mean, 42.7±4.92 vs 97.0±4.73 min, p < 0.05).

Intra-operative adverse events occurred in 11 (25.6%) children including retro-peritoneal CO2 2, capnoperitoneum 3 and mucosal injury 1. At a median follow-up of 540 days (66–1594), the clinical success was 95.3% (39/41). Clinical success at 1, 2, 3, and 4-years follow-up was 96.4% (27/28), 100% (18/18), 92.3% (12/13), and 83.3% (5/6) respectively. GERD was evident in 55% (11/20) and 53.8% (7/13) children as assessed by endoscopy and 24-hour pH study, respectively.

Conclusion: POEM is safe and effective for the management of achalasia in children. However, GERD is a potential concern and evident in over half of the children. Randomized comparison with Heller’s myotomy combined with fundoplication is warranted in future trials.

Disclosure: Nothing to disclose

PO498 EFFECT OF EGJ BARRIER AND PERISTALTIC DYSFUNCTION ON ESOPHAGEAL CLEARANCE IN PATIENTS WITH GASTROESOPHAGEAL REFUX DISEASE

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Introduction: The relationship between esophageal chemical clearance and abnor-
mal high-resolution manometry (HRM) findings in GERD patients has not been fully in-
terigated in terms of both EGJ barrier and motility function.

Aims and Methods: The main aim of this study was to determine the effect of EGJ barrier and peristaltic dysfunction on esophageal clearance in patients with GERD. 53 patients with PPI-refractory GERD symptoms who underwent both HRM and pH-mi studies were recruited. Two cases of EGJ outflow obstruction were excluded, 51 remaining cases including 4 cases of major motility disorders, 20 cases of minor motility disorders and 27 cases of normal motility were included. Esophageal chemical clearance was evaluated by post reflux swallow-induced peristaltic wave (PSPW) index and mean acid clearance time (MCT) in MI-Hi pH test and compared among different groups of peristalsis and EGJ mor-
phology on HRM. Prediction models were developed to assess the strength of esophageal clearance parameters in GERD diagnosis by calculating the area under the curve (AUC) at receiver-operating-characteristic (ROC) analysis.

Results: The median values of PSPW index for major disorder of peristalsis, minor disorder of peristalsis, and normal peristalsis were 9.4 (1.9–14.7)%, 12.7 (8.6–20.0)% and 16.7 (7.7–30.2)%, respectively. The median values of MACT were 14.2 (2.0–18.0)%, 17.5 (7.7–30.2)%, and 9.4 (1.9–30.2)%, respectively. None of the HRM indices were significantly different between SWS and STM.

Conclusion: Major disorder of peristalsis is a cause of chemical clearance dysfunc-
tion while minor disorder of peristalsis and EGJ morphology type do not play an important role. MACT could be used as a promising index to evaluate chemical clearance in GERD.
Abstract N

P0500 PERORAL ENDOSCOPIC MYOTOMY (POEM) IS EQUALLY EFFECTIVE AND DOES NOT LEAD TO INCREASED ACID REFLUX IN OBESE AS COMPARED TO NON-OBESE PATIENTS WITH ACHALASIA

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Introduction: Laparoscopic Heller's myotomy (LHM) is a technically difficult procedure in obese achalasia patients with sub-optimal outcomes and increased rates of gastro-oesophageal reflux disease (GERD). Per oral endoscopic myotomy (POEM) is emerging as a less invasive alternative to LHM in such patients. The impact of obesity on the outcomes and post-treatment GERD after POEM are not well known. Hence our study aims were to compare the outcomes and rates of abnormal oesophageal acid exposure after POEM in obese versus non-obese patients with achalasia.

Aims and Methods: Records of achalasia patients who underwent POEM between April 2014 and June 2017 were reviewed. Patients who underwent pre-treatment timed barium oesophagram (TBE), high-resolution oesophageal manometry (HRM) along with 24-hour post-treatment TBE, pH study and a 24-hour oesophageal pH study were included. Patients were categorized into 2 groups, obese (BMI ≥ 30 kg/m2) or non-obese (BMI < 30 kg/m2). Patient demographics, type of achalasia, prior interventions, pre-treatment and 2-month post-treatment TBE, HRM, Eckhardt’s scores and pH study findings were compared between the 2 groups. Eckhardt’s symptom score of < 3 was considered as successful palliation of symptoms.

Results: Among a total of 134 patients who underwent POEM, 100 patients (Obese = 46; Non-obese = 54) met the study criteria. There were no significant differences in the age, gender, ASA class, achalasia subtype, prior interventions, procedure time, length of stay (LOS) and complication rates between the 2 groups. Post treatment Eckhardt’s scores, HREM parameters and TBE parameters improved significantly in both groups. Eckhardt’s scores improved from an average of 7 to 0 (p < 0.001) in both the groups. However there was no significant difference in pre-post change in values of these parameters between the 2 groups. DeMeester score was abnormal in 57.5% in non-obese versus 43.9% in obese group (p = 0.22). Similarly there was no difference in number of patients who reported having GERD symptoms in non-obese versus obese patients (15.8% vs. 21.1%, p = 0.55).

Conclusion: POEM is an equally safe and effective treatment option for both obese and non-obese achalasia patients. Interestingly, POEM does not lead to increased GERD in obese as compared to non-obese patients. POEM might emerge as the preferred approach for myotomy in obese achalasia patients as compared to LHM in future.[Pre and Post POEM findings in Eckhardt’s score, HREM, TBE and 24-hr oesophageal pH study findings.]

Disclosure: This Abstract is accepted to be presented at Digestive Disease week (DDW) meeting in Washington DC, USA in June/2018.

P0501 ROLE OF HIGH-RESOLUTION MANOMETRY IN THE DIAGNOSTIC AND THERAPEUTIC APPROACH OF POST FUNDOPPLICATION DYSPHAGIA

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Introduction: Laparoscopic fundoplication is the gold standard of non-pharmacological treatment of gastroesophageal reflux disease (GERD). Despite good symptomatic control, a significant percentage of patients develop dysphagia at follow-up. High-resolution manometry (HRM) is indicated in the evaluation of these patients, but its impact is not well established.

Aims and Methods: We performed a retrospective study evaluating GERD patients who developed persistent post fundoplication dysphagia. Demographic, clinical and HRM data were evaluated whenever possible in the pre and postoperative period. The analysis of HRM data was performed according to the Chicago III classification.

Results: We included 27 patients, 63% women, with a median age of 58 years (range: 46-64). Nissen fundoplication was the most frequently performed surgical procedure (83%). Patients presented with dysphagia after a median period of 7 months (range: 1-43), more frequently for solid food (59%). 12 patients (44%) had preoperatively HRM, with abnormal findings in half of the cases (ineffective motility n = 4, hypercontractile esophagus n = 2). Significant manometric changes were observed in the postoperative HRM in 16 patients (59%). The main findings were esophagogastric junction outflow obstruction (n = 9, 33%) and absence of contractility (n = 3, 11%). Compared to the preoperative period, there was a significant increase in the resting pressure of the lower esophageal sphincter (8.1 mmHg vs. 20 mmHg, p = 0.043). There were no significant differences in the integrated relaxation pressure (p = 0.686) and in the distal contractile integral (p = 0.109). In patients with available pre and postoperative HRM, the manometric diagnosis was changed in 83% (10/12). In the follow-up, 15% of the patients were submitted to endoscopic dilatation and 41% underwent revision surgery, with clinical success of 25% and 75%, respectively.

Conclusion: HRM in post-fundoplication dysphagia is associated with relevant changes in a considerable percentage of patients, allowing a tailored management approach. Also, this study reflects the need for additional metrics to better identify patients at higher risk for postoperative dysphagia, and potentially benefiting from a different initial therapeutic strategy.

Disclosure: Nothing to disclose

P0502 THERAPEUTIC OUTCOMES FOLLOWING ENDOTherAPY FOR REFRACTORY GASTROPARESIS


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Introduction: The relative merits of endotherapy for refractory gastroparesis remain unclear.

We assessed the symptomatic response of patients undergoing non-surgical pyloric intervention at a specialist tertiary centre.
Aims and Methods: 57 patients (21 male, mean age 47, 16-81) with medical refractory GERD (28 idiopathic, 29 post-gastric transposition) underwent 117 esophageal treatments from Sep 2013-Sep 2017: each 100IU units of Botex injected into 4 quadrants of the pylorus (N = 66), balloon dilatation to 15-20 mm (EBD, N = 13) or combination therapy (N = 58). Patients with gastroesophageal reflux disease, pyloric surgery or no follow-up were excluded. Symptoms were assessed immediately prior to each procedure and at first follow-up using a retrospective scoring system based on the presence (1 point) or absence (0 points) of Vomiting, Nausea, Bloating or Early satiety. This formulated a composite symptom score (SS) out of 4; positive response was defined by improvement in SS of at least 1. Statistical analysis was performed using Wilcoxon Signed-Rank Test and Fischer's Test.

Results: There were no immediate or late complications. Mean symptom score (SS) improved post-procedure from 2.1 points at baseline to 1.2 post initial endotherapy (p < 0.01) at median follow up of 2.1 months. 20 patients required further endotherapy (median 2.5 treatments; range 2-12); mean SS was 1.0 at latest follow-up.

Per-procedure, mean reduction in SS was 0.8 points (p = 0.01) with overall positive response rate of 67%. By symptom, vomiting was most responsive to EBD (38%, p = 0.02) or combination therapy (66%, p = 0.03). Response to Botex was greater in patients under 40 (83% v 61%, p = 0.04) and females (81% v 33%, p = 0.002). By indication, diabetc GP (N = 17) were most likely to respond (76%).

Sub-group analysis showed procedures for gastroparesis (diabetic/ idiopathic, N = 75) responded significantly more to Botex (mean SS reduction 1.1, p < 0.01) than EBD (mean SS reduction 0.2, p > 0.1) or combination therapy (mean SS reduction 0.44, p = 0.12). Procedures for gastric transposition (N = 42) showed significant improvement post combinations (1.2 v 1.1; p = 0.01) but not post EBD (1.9 v 1.6, p = 0.0) or Botex (1.7 v 1.1, p = 0.08).

Conclusion: Endotherapy is a safe and effective treatment for refractory gastroparesis. We found Botex monotherapy significantly improved symptoms in diabetc or idiopathic gastroparesis, especially younger females; conversely, combination therapy was preferable for delayed gastric emptying post gastroparesis. Careful patient selection may augment therapeutic response.

Disclosure: Nothing to disclose

P0503 CLINICAL IMPACT OF LOWER ESOPHAGEAL SPHINCTER FUNCTION ON THE SYMPTOM ASSESSMENT OF NON-EROSSIVE REFUX DISEASE
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Introduction: Gastroesophageal reflux disease is diagnosed based on the symptoms such as acid regurgitation or heartburn through transient lower esophageal sphincter (LES) relaxation. Non-erosive reflux disease (NERD) is recognized as hard to treat and less effective with proton pump inhibitor (PPI) compared with erosive reflux disease (GERD). Aims and Methods: A total of 80 patients with NERD were enrolled. All patients underwent esophageal manometry and symptom assessment using symptom index and symptom sensitivity index. All patients received a standard dose of PPI for 4 weeks, and then investigated symptom assessment by questionnaire.

Results: The patients were divided into 2 groups by LES function: normal LES relaxation group (LES relaxation % ≥90%) and abnormal LES relaxation group (LES relaxation % <90%). Clinical and manometric findings were compared and investigated the reponse to PPI. 18 patients (22.5%) were included in the normal LES group whereas 62 patients (77.5%) in LES relaxation abnormality and investigated the reponse to PPI. 18 patients (22.5%) were included in the

Aims and Methods: To clarify the mechanisms of PPI-refractory reflux-related heartburn, as investigated with impedance-pH monitoring. In this prospective, multicenter, pathophysiologic study, 64 patients complaining of heartburn with a negative upper gastrointestinal endoscopy, performed after 4-week PPI withdrawal, and with proven GERD at off-PPI impedance-pH monitoring, entered the study. 32 patients had PPI-refractory heartburn (i.e. < 50% of symptom relief after 8-week high-dosage PPI therapy), and 32 had PPI-responsive heartburn. Mechanisms of heartburn refractoriness to high-dosage PPI were investigated by means of on-therapy impedance-pH monitoring and compared with off-PPI findings. Blindly and manually assessed impedance-pH tracings comprised conventional reflux testing parameters, including esophageal acid exposure time (AET), number of reflux episodes and symptoms association analysis (symptom index, SI, and symptom association probability, SAP), and novel impedance-detected features, including the post-reflux swallow-induced peristaltic wave (PSWP) index and mean nocturnal baseline impedance (MBNII).

Results: The 2 groups were well comparable for gender, age, BMI, rates of hiatal hernia and of abnormal off-PPI impedance-pH variables (p = ns), as shown in the Table. On PPI, median esophageal AET did not differ between the 2 groups. Moreover, AET was abnormal in 6/32 (19%) of PPI-refractory patients. The two groups of reflexes were weakly associated (and had a low p-value), but increased significantly in PPI-responsive cases (p < 0.001). At multivariate logistic regression analysis, only PSWP index was an independent risk factor for PPI refractoriness (OR 1.082, 95% CI 1.022-1.146, p = 0.007). Comparing off- and on-PPI parameters, median PSWP index did not change in PPI-refractory patients (24% vs. 26%, p = 0.327), but increased significantly in PPI-responsive cases (29% vs. 46%, p < 0.001).

Conclusion: Lack of improvement of impaired chemical clearance represents a major biomarker of PPI-refractory reflux-related heartburn. Adjunct therapies aimed to improve chemical clearance by stimulation of timely post-reflux saliva swallowing could benefit patients with PPI-refractory reflux-related heartburn.

Disclosure: Nothing to disclose

P0505 LACK OF IMPROVEMENT OF IMPIRED CHEMICAL CLEARANCE CHARACTERIZES PPI-REFRACTORY REFUX-RELATED HEARTBURN IN NON-EROSSIVE REFUX DISEASE

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Introduction: Prevalence of gastroesophageal reflux disease (GERD) ranges 18–46%. In the last few years, the esophageal microbiota has been suggested to have a role in esophageal diseases (1). Identifying microbiota in the esophagus offers new approaches to understanding bacterial roles as pathogenic factors in GERD, Barrett’s esophagus, and esophageal adenocarcinoma (2). Aims and Methods: We aimed to compare the esophageal intraluminal microbiota of patients of GERD and healthy controls using the 16S ribosomal RNA (rRNA) sequencing. A total of 22 patients were enrolled in this study: 16 patients with GERD and 6 healthy controls. All patients were performed esophageal fluids collection procedure using the specially designed esophageal perfusion catheter equipped with 2 inflatable intrasophageal balloons. mRNA expression was

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Introduction: Heartburn is the most specific symptom of reflux disease, highly responsive to proton pump inhibitor (PPI) therapy. However, some patients do not respond to PPIs, but the mechanisms of refractoriness have not been fully elucidated. Impedance-pH monitoring, allowing a comprehensive off- and on-therapy assessment of reflux, represents a valuable test to investigate PPI-refractoriness.

Aims and Methods: To clarify the mechanisms of PPI-refractory reflux-related heartburn, as investigated with impedance-pH monitoring. In this prospective, multicenter, pathophysiologic study, 64 patients complaining of heartburn with a negative upper gastrointestinal endoscopy, performed after 4-week PPI withdrawal, and with proven GERD at off-PPI impedance-pH monitoring, entered the study. 32 patients had PPI-refractory heartburn (i.e. < 50% of symptom relief after 8-week high-dosage PPI therapy), and 32 had PPI-responsive heartburn. Mechanisms of heartburn refractoriness to high-dosage PPI were investigated by means of on-therapy impedance-pH monitoring and compared with off-PPI findings. Blindly and manually assessed impedance-pH tracings comprised conventional reflux testing parameters, including esophageal acid exposure time (AET), number of reflux episodes and symptoms association analysis (symptom index, SI, and symptom association probability, SAP), and novel impedance-detected features, including the post-reflux swallow-induced peristaltic wave (PSWP) index and mean nocturnal baseline impedance (MBNII).

Results: The 2 groups were well comparable for gender, age, BMI, rates of hiatal hernia and of abnormal off-PPI impedance-pH variables (p = ns), as shown in the Table. On PPI, median esophageal AET did not differ between the 2 groups. Moreover, AET was abnormal in 6/32 (19%) of PPI-refractory patients. The two groups of reflexes were weakly associated (and had a low p-value), but increased significantly in PPI-responsive cases (p < 0.001). At multivariate logistic regression analysis, only PSWP index was an independent risk factor for PPI refractoriness (OR 1.082, 95% CI 1.022-1.146, p = 0.007). Comparing off- and on-PPI parameters, median PSWP index did not change in PPI-refractory patients (24% vs. 26%, p = 0.327), but increased significantly in PPI-responsive cases (29% vs. 46%, p < 0.001).

Conclusion: Lack of improvement of impaired chemical clearance represents a major biomarker of PPI-refractory reflux-related heartburn. Adjunct therapies aimed to improve chemical clearance by stimulation of timely post-reflux saliva swallowing could benefit patients with PPI-refractory reflux-related heartburn.

Disclosure: Nothing to disclose

P0506 ESOPHAGEAL INTRALUMINAL MICROBIOTA IN PATIENTS WITH GASTROESOPHAGEAL REFUX DISEASE AND HEALTHY CONTROLS
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Introduction: Prevalence of gastroesophageal reflux disease (GERD) ranges 18–46%. In the last few years, the esophageal microbiota has been suggested to have a role in esophageal diseases (1). Identifying microbiota in the esophagus offers new approaches to understanding bacterial roles as pathogenic factors in GERD, Barrett’s esophagus, and esophageal adenocarcinoma (2).
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Introduction: At present time, the spread of the gastroesophageal reflux disease and its morbidity is still on a considerably high level, which compels to searching for new approaches to its diagnostic and treatment.

Aims and Methods: To study the incidence of the virus persistence of the herpes febrilis (HSV), cytomegalovirus (CMV) and human herpes virus type 4 (EBV) in the esophageal mucosa of patients with an erosive form of gastroesophageal reflux disease.

Results: According to the results of the IHC test, 32 patients (42.7%) had a virus infection. The degree of incidence of the virus infection in patients with an erosive esophagitis was the following: 21 patients (40.4%) had herpes febrilis (HSV), 19 patients (36.5%) had cytomegalovirus (CMV) and 12 (23%) patients had human herpes virus type 4 (EBV). 18 patients (35.6%) had a combination of several virus types, from 2 to 3 types simultaneously.

Conclusion: Chronic virus infection of the esophageal mucosa is widespread amongst patients with an erosive form of gastroesophageal reflux disease. In the majority of cases, several virus types are present.

Disclosure: Nothing to disclose

References

P0511 HEALTH-RELATED QUALITY OF LIFE IMPACT AMONG GASTROESOPHAGEAL REFLUX DISEASE PHENOTYPES IN ECUADORIAN PROTON PUMP INHIBITOR NON-RESPONDERS: A PROSPECTIVE COHORT


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Introduction: More than 50% of Gastroesophageal Reflux Disease (GERD) patients do not respond to Proton Pump Inhibitor (PPI) therapy, rendering them asymptomatic. Yadlapati et al. described the impact on the Health-Related Quality Of Life (HRQOL) doesn’t depend on the GERD phenotype. The Northwestern Esophageal Quality of Life survey (NEQOL), assesses the HRQOL impact across different chronic esophageal diseases (CED). It has previously validated in an Ecuadorian Spanish-speaking population (NEQOL-S). The HRQOL impact among different GERD phenotypes has not been assessed by the NEQOL, especially in a Hispanic population.

Aims and Methods: We aimed to describe the HRQOL impact using NEQOL-S among GERD phenotypes in Ecuadorians PPI non-responders. Prospective cohort study performed at a single medical center from Ecuador (Sept-2016 to Sept-2017). PPI non-responder patients who underwent 24-hour pH-impedance monitoring test and completed the NEQOL-S and SF-12 (a very used survey to assess general-HRQOL in South America). Acid exposure time (AET) and symptoms associations (SRA) were recorded. Participants were classified into cohorts based on test results: GERD (+AET), reflux hypersensitivity (RHS) (-AET/+SRA) and functional heartburn (FH) (+AET/-SRA). The sample size for each group was estimated using known mean PROMIS Global quality of life reported by Yadlapati et al., with an 80% statistical power. The pH-impedance test outcomes and HRQOL results were contrasted between groups through ANOVA or Kruskal-Wallis test. The relationship between HRQOL (NEQOL-S) vs. AET was estimated through Spearman’s rank correlation coefficient (rho). A confirmatory analysis was done using SF-12. A p-value < 0.01 was considered to be statistically significant. Analyses were performed using R v.3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results: There were 85 cases with 24-hours pH-impedance monitoring test performed: 30 (35%) -AET/+AET/+SRA, and 41 (48%) -AET/-SRA. Baseline characteristics and pH-impedance test outcomes are summarized in table 1. NEQOL median scores among groups were: 28.5, 25, 27, respectively (p = 0.719). SF-12 median scores among groups were: 40, 39, 39, respectively (p = 0.977). Relationship between acid exposure time and HRQOL, measured through NEQOL-S and SF-12 reached a rho = 0.90% (p = 0.414) and 7.3% (p = 0.510), respectively.

Conclusion: There is no statistical difference of HRQOL impact among GERD phenotypes, or relationship between HRQOL vs. AET. NEQOL-S results are
Aims and Methods: We aimed to better understand how HRQOL can be affected by different CED in Ecuadorians, through the development of a validated translation of the NEQOL for its use in Spanish-speaking patients. Observational, prospective cohort study (Oct-2016 - Oct-2017). The translation was based on Sperber recommendations. NEQOL-Spanish version (NEQOL-S) and general HRQOL SF-12 survey were prospectively applied to a clinic-based population. NEQOL-S was reapplied 7 days later. The sample size was calculated using estimating proportion formula (5% margin error). Selection criteria: median age 48 (18–90) yo, 242 (63%) female, 24 months median length symptoms. Internal consistency was excellent (CA 0.905). Construct validity did not suggest to reduce survey number of items (KMO = 0.92, p < 0.01). Criterion validity showed good coherence when correlated with the SF-12 survey (rho = 0.57, p < 0.01). Test-retest reliability showed very good correlation when calculated by the intraclass correlation coefficient (ICC) (0.82, p < 0.01). Table 1 resumes how NEQOL-S results differed per CED (p < 0.01).

Disclosure: Nothing to disclose

Reference

P0954 ACCURACY OF HIGH-RESOLUTION MANOMETRY IN DIAGNOSIS OF HIATAL HERNIA IN MORBIDLY OBESE PATIENTS

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Aims and Methods: We aimed to evaluate in a population of obese patients candidates to bariatric surgery the agreement in the detection of HH between HRM and intraoperative diagnosis. 52 consecutive morbidly obese patients were prospectively recruited from an outpatient clinic devoted to the surgical therapy of obesity and related disorders. All underwent a preoperative assessment including standardized GERD questionnaire, UGI xray, the ability to diagnose hiatal hernia (HH) is common in obese patients. Classically, HH is detected by upper gastrointestinal endoscopy (UGE) or fluoroscopic upper gastrointestinal (UGI) xray series, however intraoperative diagnosis of HH is considered the gold standard. High resolution manometry (HRM) showed a higher sensitivity and specificity than the classical techniques in non-obese patients. There are no data in morbidly obese population.

Aims and Methods: We aimed to evaluate in a population of obese patients candidates to bariatric surgery the agreement in the detection of HH between HRM and intraoperative diagnosis.

Results: There was a significant correlation between the 3 morphological types of HH assessed by HRM and the presence of HH at UGE (r = 0.28, p = 0.044). 34/52 enrolled patients underwent bariatric surgery; in 9/34 patients HH was intraoperatively diagnosed. The sensitivity of UGI xray or UGI in detecting intraoperative diagnosis of HH was 77.8 % and the specificity was 44%; the positive predictive value was 33.3% and the negative predictive value 84.6%.

Disclosure: Nothing to disclose

Reference

Disclosure: Nothing to disclose

P0955 HOW TO HANDLE TISSUE SPECIMENS AFTER ENDOSCOPIC MUCOSAL RESECTION FOR BARRETT'S ESOPHAGUS RELATED NEOPLASIA: A MULTICENTER RANDOMIZED TRIAL COMPARING THREE SPECIMEN HANDLING METHODS

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Disclosure: Nothing to disclose

Reference
Viral genotypes identified were HPV 16 (n = \text{esophageal adenocarcinoma as compared with hospital/reflux/Barrett’s meta-

sexual partners were at significant risk for Barrett’s dysplasia / esophageal adenocarcinoma (OR, 4.0; 95% CI: 1.2–13.7, p

0.0001), be male (p

0.002). Results: Accuracy, sensitivity, specificity, NPV and PPV for detection were 88.3%, 92.5%, 80%, 84.2% and 90.2% respectively. The percentage of the

system would red-flag the lesion on the endoscopy screen, enabling the endoscopist to take a targeted biopsy. Clinically-inspired CAD systems are therefore shown to be suitable for small and unbalanced databases. The aim of this study was to develop a clinically inspired CAD system using high-quality endoscopic images of BE neoplasia.

Aims and Methods: Endoscopic overview images of 40 subtle early neoplastic BE patients with no suspicion of visible neoplasia and was labeled as the soft spot. The area with ≥1 expert delineations was labelled as the soft spot. The CAD system was trained on low-contrast and texture features (using Gabor filters) of the images, where positive features were taken from the soft spot of the neoplastic images and negative features from the area outside the soft spot and from the NDIBE images. No pre-

processing of the expert delineations prior to input into the algorithm was performed at this stage. Performance was evaluated using a leave-one-out cross validation on a per image basis.

Outcome parameters: 1) Detection scores: diagnostic accuracy of the algorithm per case in terms of accuracy, sensitivity, specificity, NPV and PPV; 2) Localization scores: Percentage of recognized neoplastic images where the delineation of the algorithm detected the soft spot and soft spot.

Results: Accuracy, sensitivity, specificity, NPV and PPV for detection were 88.3%, 92.5%, 80%, 84.2% and 90.2%, respectively. The percentage of the soft- and soft spot that was recognized was 94.6% and 89.2%, respectively.

Conclusion: This CAD system detected early neoplastic BE lesions on endoscopic WLE images with high accuracy, thereby showing feasibility of CAD systems as an important step towards real-time automated detection of early BE neoplasia. Future work will focus on further development of the algorithm towards video analyses and the development of a deep learning algorithm.

Disclosure: Nothing to disclose.

90517 THE ARROWS PROJECT: COMPUTER AIDED DETECTION SYSTEM CAN DETECT BARRETT NEOPLASIA ON ENDOSCOPIC IMAGES WITH HIGH ACCURACY

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Introduction: Early neoplasia in Barrett’s esophagus (BE) is difficult to detect during surveillance endoscopies. This is partly because of its subtle appearance and partly because most endoscopists rarely encounter early BE neoplasia and therefore are unfamiliar with its endoscopic appearance. Computer-aided detection (CAD) systems might assist endoscopists in the recognition of early BE neoplasia, thereby improving efficacy of BE surveillance. Ideally, a CAD system is incorporated in the endoscopy system and would run real-time on the background during surveillance endoscopies. In case a visible lesion is pre-

sent, the CAD system would red-flag the lesion on the endoscopy screen, enabling the endoscopist to take a targeted biopsy. Clinically-inspired CAD systems are therefore shown to be suitable for small and unbalanced databases. The aim of this study was to develop a clinically inspired CAD system using high-quality endoscopic images of BE neoplasia.

Aims and Methods: Endoscopic overview images of 40 subtle early neoplastic BE patients with no suspicion of visible neoplasia and was labeled as the soft spot. The area with ≥1 expert delineations was labelled as the soft spot. The CAD system was trained on low-contrast and texture features (using Gabor filters) of the images, where positive features were taken from the soft spot of the neoplastic images and negative features from the area outside the soft spot and from the NDIBE images. No pre-

processing of the expert delineations prior to input into the algorithm was performed at this stage. Performance was evaluated using a leave-one-out cross validation on a per image basis.

Outcome parameters: 1) Detection scores: diagnostic accuracy of the algorithm per case in terms of accuracy, sensitivity, specificity, NPV and PPV; 2) Localization scores: Percentage of recognized neoplastic images where the delineation of the algorithm detected the soft spot and soft spot.

Results: Accuracy, sensitivity, specificity, NPV and PPV for detection were 88.3%, 92.5%, 80%, 84.2% and 90.2%, respectively. The percentage of the soft- and soft spot that was recognized was 94.6% and 89.2%, respectively.

Conclusion: This CAD system detected early neoplastic BE lesions on endoscopic WLE images with high accuracy, thereby showing feasibility of CAD systems as an important step towards real-time automated detection of early BE neoplasia. Future work will focus on further development of the algorithm towards video analyses and the development of a deep learning algorithm.

Disclosure: Nothing to disclose.

90518 ARTIFICIAL INTELLIGENCE IDENTIFIES EARLY BARRETT’S NEOPLASIA IN IN-VIVO BIOSPY-CORRELATED VOLUMETRIC LASER ENDOMICROSCOPY IMAGES

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Introduction: Volumetric laser endomicroscopy (VLE) provides a circumferential near-microscopic scan of the superficial esophageal wall layers, and has potential
to improve the detection of early Barrett’s esophagus (BE) neoplasia. However, the interpretation of retrieved yellow/grey-shaded VLE images is complex and time-consuming. Artificial intelligence using novel machine and deep learning techniques may aid in this process. Recent studies have focused on neoplasia detection algorithms based on ex-vivo VLE images. Our study is the first to investigate the feasibility of in-vivo BE neoplasia detection using computer-aided detection of VLE images.

Aims and Methods: A prospective single-center study was conducted including 23 Barrett’s patients with and without early neoplasia. High quality in-vivo VLE-histology correlation was provided by laser marking. Laser marked regions of interest consisted of non-dysplastic BE (88 NDVE), and high-grade dysplasia and/or esophageal adenocarcinoma (34 HGD/EAC). Conventional machine learning and recent deep learning techniques were evaluated for the analysis of these regions of interest and differentiate between non-dysplastic and neoplastic tissue. Tissue was first segmented with a pre-trained convolutional neural network (U-net) and clinically inspired features were used for classification between non-dysplastic tissue and neoplasia. Based on earlier findings, analysis was performed on the superficial esophageal wall layers (0.2-1.2 mm), as experiments have demonstrated this generated an optimal classification performance. The reproducibility of the results were independently validated by leave-one-out cross-validation.

Results: In total, 8 different machine learning methods were used for BE neoplasia detection resulting in area under the curves ranging from 0.82-0.90. The clinically derived feature layer histogram in combination with Naive Bayes Classifier demonstrated the most optimal performance. This in-vivo method resulted in an accuracy of 84.4% and an area under the curve of 0.90. Corresponding sensitivity was 73.5% and specificity was 88.6% for the differentiation between 88 NDVE and 34 HGD/EAC VLE images. Negative predictive value and positive predictive value were 89.7% and 71.4%, respectively. Average time for the computer algorithm to analyze a VLE image was 15 milliseconds.

Conclusion: Artificial intelligence, using both machine- and deep learning techniques, correctly identify in-vivo biopsy-correlated VLE images of early BE neoplasia. The clinically derived feature layer histogram shows high detection accuracy. This study shows feasibility of fast and objective computer aided detection, bringing real-time, red-flag identification 1 step closer.

Disclosure: Nothing to disclose

P0519 BLUE LIGHT IMAGING HAS AN ADDITIONAL VALUE TO WHITE LIGHT ENDOSCOPY IN VISUALIZATION OF EARLY BARRETT’S NEOPLASIA. AN INTERNATIONAL MULTICENTER COHORT STUDY

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Introduction: Detection and delineation of early neoplasia in Barrett’s esophagus (BE) may be difficult. Blue Light Imaging (BLI; Fujifilm, Tokyo, Japan) is a new optical chromoscopy technique that may improve visualization of these lesions with White Light Endoscopy (WLE). The aim of this study was to evaluate if BLI has additional value in the visualization of early Barrett’s neoplasia. Aims and Methods: In this multicenter prospective cohort study corresponding endoscopic WLE- and BLI images of 40 early neoplastic BE lesions in overview and magnification were obtained in three tertiary referral centers. A proprietary online scoring and delineation module, specifically for this project, was used by 6 international BE experts to assess images in three assessment rounds, each separated by a wash-out period of 2 weeks. Each assessment consisted of overview and magnification images. Assessment 1: WLE images only; Assessment 2: BLI images only; Assessment 3: corresponding WLE- and BLI images in a side-to-side display. The order of images in each assessment round was randomized. During each assessment, the experts scored their appreciation of the macroscopic appearance and surface relief using visual analogue scales (VAS) and subsequently delineated each lesion using the proprietary software tool. Their delineation agreement was quantified by calculating the mean AND/OR ratio for each image in which the AND area was defined as the area delineated by ≥4 experts and the OR area as the area delineated by ≥1 experts. Outcome parameters: 1) Experts’ appreciation of macroscopic appearance and surface relief (VAS-scores); 2) Experts’ ability to delineate the lesion (VAS-scores); 3) Experts’ delineation confidence (VAS-scores); 4) Experts’ quantitative agreement on lesion delineations (AND/OR scores).

Results: Experts appreciated BLI images significantly better than WLE for visualization of macroscopic appearance (median 8.0 vs. 7.0, p < 0.001) and surface relief (8.0 vs. 6.0, p < 0.001). For both overview and magnification images, experts appreciated BLI significantly better than WLE for ability to delineate lesions (8.0 vs. 6.0, p < 0.001 and 8.0 vs 5.0, p < 0.001). There was no overall significant difference in AND/OR scores of WLE-+BLI when compared to WLE, yet agreement increased significantly with WLE-+BLI for cases with a low baseline AND/OR score on WLE, both in overview (mean difference 0.15, p = 0.015) and magnification (mean difference 0.10, p = 0.01).

Conclusion: This study demonstrates the additional value of BLI for the visualization of BE neoplasia. International BE experts appreciated BLI better than WLE for the different aspects of visualization of BE neoplasia and preferred BLI for delineation with the proprietary delineation tool. Their quantitative agreement for delineation increased significantly when BLI was offered next to WLE for lesions that were hard to delineate with WLE alone.

Disclosure: This study was supported by an unrestricted research grant from FUJI骂LM Europe (FUJI骂LM Europe GMBH, Düsseldorf, Germany), which had no involvement in the design, recruitment, data collection, analysis or interpretation or writing of the abstract.

P0520 SELF-SIZING RADIOFREQUENCY ABLATION BALLOON FOR ERADICATION OF BARRETT’S ESOPHAGUS: RESULTS OF AN INTERNATIONAL MULTICENTER RANDOMIZED TRIAL

COMPARING THREE DIFFERENT TREATMENT REGIMENS

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Introduction: The 360 Express RFA balloon catheter (“360 Express”) for radiofrequency ablation (RFA) of Barrett’s esophagus (BE) has the ability to self-adjust to the esophageal lumen ensuring optimal tissue contact during ablation. Aims and Methods: Aim of this randomized clinical trial was to compare three different ablation regimens for treatment of BE using the 360 Express. Patients with a 2-15 cm BE with low-grade dysplasia (LGD), high-grade dysplasia (HGD) or early cancer (EC) were included. Visible lesions were removed by endoscopic resection (ER) prior to RFA. Patients were randomly assigned on a 1:1:1 ratio to the standard (1 x 10J/cm2-clean-1 x 10J/cm2), simple-double (2 x 10J/cm2-no clean), or simple-single ablation regimen (1 x 10J/cm2-no clean). Sample size calculation showed that 36 patients would be necessary in

Abstract No: P0520: Table 1, Outcomes

<table>
<thead>
<tr>
<th>Ablation regimen</th>
<th>Standard</th>
<th>Simple-single</th>
<th>Simple-double (arm early closed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>31</td>
<td>31</td>
<td>28</td>
</tr>
<tr>
<td>Median BE regression, % (IQR)</td>
<td>85 (75-94) 95% CI: 78%–92%</td>
<td>73 (48-90) 95% CI: 59%–85%</td>
<td>88 (81-93) 95% CI: 83%–92%</td>
</tr>
<tr>
<td>Patients with a poor regression response (≤50% BE regression), n (%)</td>
<td>3 (10)</td>
<td>9 (29)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Median procedure duration, min (IQR)</td>
<td>31 (26-36)</td>
<td>17 (13–20)</td>
<td>17 (14–20)</td>
</tr>
<tr>
<td>Overall adverse event rate</td>
<td>5 (14)</td>
<td>7 (25)</td>
<td>6 (21) Mild n = 1; Moderate n ≥ 1; Severe n = 4</td>
</tr>
<tr>
<td>Stricture requiring an intervention, n (%)</td>
<td>0 (0)</td>
<td>3 (8)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>Minor laceration, n (%)</td>
<td>4 (11)</td>
<td>Unrelated death: 1 (3)</td>
<td>Near collapse: 1 (4)</td>
</tr>
<tr>
<td>Other adverse events, n (%)</td>
<td>3 (8)</td>
<td>Minor bleeding: 1 (3)</td>
<td>Pain and fever: 1 (3)</td>
</tr>
</tbody>
</table>
CD147 inhibitor may be promising to enhance CRT response and inhibit tumor progression in the future.

Disclosure: Nothing to disclose.

P0525 EFFICACY OF ARGON PLASMA COAGULATION WITH PRIOR SUBMUCOSAL DISSECTION IN PIGS USING STENT WITH ACELLULAR PORCINE DERMAL MATRIX

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Introduction: Endoscopic resection is regarded as the best treatment for patients with early-stage gastrointestinal cancer. However, argon plasma coagulation (APC) is often selected as a treatment for such patients because of the patient’s general condition or status of the lesions. Recently, we reported good long-term outcomes for patients with esophageal squamous cell carcinoma who underwent APC (local recurrence rate of 3.6% and the 5-year cause-specific survival rate of 100%) in ESGE days 2018. We considered that submucosal injection prior to APC would result in uniform and sufficient coagulation and would contribute to a good outcome. Previously, Manier et al. reported the efficacy of APC with prior submucosal injection (hybrid APC) by using a resorbed porcine esophagus; however, there has been no study using an in vivo model. In this study, we evaluated the efficacy of hybrid APC for the esophagus by using an in vivo porcine model.

Aims and Methods: We performed hybrid APC and direct APC without submucosal injection (standard APC) in various settings. In study 1, we sacrificed the pigs 1 week after APC. In study 2, we sacrificed the pigs 1 week after APC. Pathological evaluation of the depth of coagulation from the basal layer (study 1) and non-atrophic muscle zone (study 2) in the resected specimens was carried out. According to a report by Georg et al., superficial tissue damage of the tunica mucosa was classified as type A damage and an injury pattern limited to the tunica muscularis was classified as type B damage in study 1. The tissue sections were stained with anti-α-SMA antibody, anti-CD107a antibody, anti-CD31 antibody and anti-MPO antibody in study 2. Random submucosal fields from each pig were photographed (high-powered field ≥400) and the stained cells were counted in a blinded manner.

Results: We performed all APC methods using the forced APC mode. Argon gas flow of 2.0 L/min, 5 seconds, at 60 watts (Wt: hybrid APC (types A and B damage) vs standard APC (types A and B damage); 1200 µm (longitudinal muscle layer [ML] and 3090 µm) vs 2750 µm (circumferential muscle layer) and 3340 µm (ML)). Gas flow of 1.0 L/min, 6 seconds, at 40 W: hybrid APC vs standard APC, 70 µm (lumina propria mucosa [LPM]) and 1440 µm (submucosa [SM]) vs 1300 µm (SM) and 2710 µm (ML)). Gas flow of 1.0 L/min, 4 seconds, at 40 W: hybrid APC vs standard APC, 80 µm (LPM) and 1370 µm (SM) vs 630 µm (muscularis mucosa [MM]) and 3010 µm (MM) (NS)). Gas flow of 1.0 L/min, 3 seconds, at 40 W: hybrid APC vs standard APC, 80 µm (LPM) and 870 µm (SM) vs 510 µm (MM) and 2360 µm (ML)). Results (study 2): Gas flow of 2.0 L/min, 3 seconds, at 60 W: hybrid APC (2 lesions) vs standard APC (2 lesions), 23.8 and 2.9 mm² vs 4.5 and 0.0 mm² (NS). Gas flow of 1.0 L/min, 3 seconds, at 40 W: hybrid APC (2 lesions) vs standard APC (2 lesions), 9.6 and 11.2 mm² vs 9.2 and 3.0 mm². Gas flow of 1.0 L/min, 1 second, at 40 W: hybrid APC (2 lesions) vs standard APC (2 lesions), 13.9 and 15.6 mm² vs 6.4 and 7.6 mm². Immunohistochemical analysis demonstrated that the numbers of activated myofibroblasts and infiltrating neutrophils and macrophages were decreased in the hybrid APC group.

Conclusion: Submucosal injection prior to APC contributes to safe and sufficient coagulation for esophageal lesions.

Disclosure: Nothing to disclose.
Disclosure: We hypothesized that a stent covered with acellular matrix of porcine dermis might lead to an earlier re-epithelialization and thus prevent the post-CESD stricture formation.

Aims and Methods: To assess the local effect of a metallic (SEMS) or biodegradable (BD) stent (with or without a acellular matrix) in preventing post-CESD esophageal strictures in pigs. The main outcome was the development of endoscopically non-passable stricture. Secondary outcomes were stricture severity and histopathological parameters. Methods: Pigs were randomized into 6 groups: A. control - CESD only (n = 6); B. CESD + systemic corticosteroids (SC, n = 6); C. BD stent (n = 6); D. SEMS with SC (n = 6); E. SEMS + matrix + SC (n = 8); F. BD stent + matrix + SC (n = 2). CESD was performed by using a dual knife. The acellular matrix was attached to the outer surface of a stent prior to its deployment. SEMS were removed 21 days after CESD. Pigs were sacrificed if a stricture developed.

Results: A total of 33 pigs underwent CESD in the middle esophagus; the average length of the defect was 5.5 ± 0.3 cm. All pigs with BD stent experienced macroscopic inflammation, massive hypergranulation and food stagnation within the stenosis, which were BH and biopsies. Thus, we decided to stop using the HD stent prematurely and BD groups were excluded from the final analysis. Significant strictures were developed in all pigs except 1 (group B - SC) after a mean of 12.9 ± 0.1 days from CESD (groups A and B) and in 13.9 ± 1.4 days after SEMS extraction (groups C and D). The longest stricture was observed in the group A (2.7 ± 1.3 cm) and the shortest in SEMS groups (C, D) (1.5 ± 0.8 cm and 1.6 ± 1.1 cm). The narrowest stricture occurred in groups A and C (0.5 ± 0.3 mm and 8.8 ± 3.7 mm) vs. groups B and D (14.4 ± 1.1 mm and 13.6 ± 7.7 mm). (p < 0.05).

Re-epithelialization was present in 80% of animals in the group A, in all animals in group D. The widest re-epithelization layer (0.14 mm) was present in the group D. The re-epithelization was present in 80% of animals in the group A, in all animals in group B, in 42% of animals in the group C and in 71% of animals in group D. The re-epithelization layer (0.14 mm) was present in the group D. The re-epithelization layer (0.14 mm) was present in the group D.

Conclusion: None of the tested methods resulted in the effective prevention of post-CESD esophageal stricture. Coverage of SEMS using acellular matrix of porcine dermis resulted in a decrease in the severity of stenosis and improved post-CESD esophageal stricture formation. The BD stent is inappropiate in this indication.

Disclosure: Nothing to disclose.

Reference

P0924 ELIMINATION OF NFkB SIGNALLING IN VIMENTIN+ STROMAL CELLS ATTENUATES ESOPHAGEAL CARCINOGENESIS IN A MOUSE MODEL OF BARRETT’S ESOPHAGUS
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Introduction: The link between inflammation and cancer is well established. Esophageal carcinogenesis is an ideal model to study the underlying mechanisms of inflammation induced tumor initiation: Chronic inflammation induces Barrett’s Esophagus (BE) which later advances to esophageal adenocarcinoma (EAC). Inflammation at the level of HHV, a downstream target of NF-kB, have been identified as an important mediator of tumorigenesis in the IL-1β mouse model of EAC. To analyze the effect of Nfkb signaling in MFs, we investigated by cytokine array and qPCR analysis. To combine readily identifiable risk factors, risk prediction modelling is a promising tool for selecting individuals with high absolute cancer risk. This study aimed to develop a OSCC risk prediction model for individuals.

Methods: In this retrospective study, we analyzed the interaction of epithelial and stromal cells in 3D organotypic cultures of mouse and human BE organoids.

Results: Histological scoring of IL-1β. Vimm-Cre (p56Cre)1 mice showed a significantly attenuated phenotype compared to IL-1β mice, with mild inflammation, decreased proliferation and crypt fission and increased differentiation in the junctional region at the gastric cardia where metaplasia and dysplasia would arise in IL-1β. Vimm-Cre(p56Cre)1 mice were identified as a model of inflammation induced tumorigenesis in the IL-1β mouse model of EAC. The IL-1β mouse model of BE and EAC, IL-1β induces chronic inflammatory and spontaneous carcinogenesis in an IL-6 dependent manner. This inflammatory milieu often occurs apart from cancer cells and infiltrating immune cells, myofibroblasts (MF) that express uSMA and Vimentin. In the L2-IL-1β mouse model increased inflammation correlates with increased MFs and an accelerated phenotype.

Conclusion: In summary, we have analysed the role of fibroblasts in an inflammatory environment and conclude that NFKb in the stromal cells is an important driver of esophageal carcinogenesis. This also suggests that inhibition of NFKb signaling in general or NIK specifically could be an important treatment strategy to prevent tumor progression during surveillance of BE patients.

Disclosure: Nothing to disclose.

Reference

P0925 CLINICAL SIGNIFICANCES AND PREDICTORS OF ESOPHAGEAL GLANDULAR DUCTAL INVOLVEMENT IN EARLY ESOPHAGEAL SQUAMOUS CELL NEOPLASIA
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Introduction: The esophageal gland duct may serve as a pathway for the spread of early esophageal squamous cell neoplasia (ESCN) to a deeper layer. However, the incidence of ductal invasion and the complete endoscopic submucosal dissection (ESD) has yet to be investigated.

Aims and Methods: We consecutively enrolled patients with early ESCN who were treated with ESD. The resected specimens were retrospectively reviewed for the number, morphology, resected margin, distribution and extension level of DI, which were then correlated to clinical factors and survival.

Results: A total of 160 lesions were analyzed, with en bloc and R0 resection rates of 97.5% and 95.6%, respectively. A total of 317 DIs (median: 3 range 1–40 per lesion) in 61 lesions (38.1%) were identified. Of these lesions, 14 have DIs maximally extended to the level of lamina propria mucosa, 17 to muscularis mucosae, and 30 to the submucosal layer. Multivariate logistic regression analysis showed that ESCN located in the upper esophagus (OR = 2.93, 95% CI, 1.02–9.42), large tumor circumferential extension (OR = 5.39, 95% CI, 1.06–27.47), deep tumor invasion depth (OR = 4.12, 95% CI, 1.81–9.33) and numerous Lugol-voiding lesions in background esophageal mucosa (OR = 2.65, 95% CI, 1.10–6.37) are risk factors for esophageal DI. The maximally extended level and total number of ducts involved were significantly correlated with the depth of cancer invasion (p < 0.05). The patients with DI had worse overall survival (log-rank p = 0.015) and recurrence-free survival (log-rank p = 0.02) than those without DI at successful ESD.

Conclusion: DI is not uncommon in early ESCN. Our findings may guide clinical decision making with regards to endoscopic treatment and surveillance.

Disclosure: Nothing to disclose.

Reference

P0936 PREDICTION OF INDIVIDUALS AT HIGH ABSOLUTE RISK OF OESOPHAGEAL SQUAMOUS CELL CARCINOMA
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Introduction: Oesophageal squamous cell carcinoma (OSCC) is the dominant histological subtype of oesophageal cancer in Eastern countries and globally, and is associated with an increasing incidence of oesophageal adenocarcinoma in Western countries. OSCC remains a major type of oesophageal cancer also in these countries. In 2012, approximately 38,000 new cases of OSCC occurred in Europe, North America, and Oceania, accounting for around 60% of all cases of oesophageal cancer in these regions. OSCC is characterized by poor prognosis with a population-based overall 5-year survival rate of less than 20%, which has not improved much in recent years. Upper endoscopy for OSCC may be indicated to detect disease at curable stage, but universal endoscopic screening is not justified given the low absolute risk of OSCC in the population. A more feasible way may be to identify a limited group of individuals with high absolute risk of OSCC, who might benefit from tailored endoscopic screening and surveillance.

Aims and Methods: By combining readily identifiable risk factors, risk prediction modelling is a promising tool for selecting individuals with high absolute cancer risk. This study aimed to develop an OSCC risk prediction model for individuals.

Methods: This was a nationwide Swedish population-based case-control study, including 167 new cases of OSCC and 820 randomly selected control participants. Associations between candidate predictors and risk of OSCC were assessed using multivariable unconditional logistic regression, producing odds ratios with 95% confidence intervals (CI). The discriminative accuracy of the model was assessed by the area under the receiver operating characteristic curve (AUC) and the net reclassification improvement (NRI) by cross-validation. Models for projecting individuals’ absolute 5-year risk of OSCC were developed by incorporating the age- and sex-specific incidence rates of OSCC and competing risk of death from other causes.

Results: A model including age, sex, tobacco smoking, alcohol consumption, associations with living in a partner, and place of residence during child hood generated an AUC of 0.81 (95% CI 0.77–0.84). A model based only on age, sex, tobacco smoking, and alcohol consumption reached a similar AUC (0.79, 95% CI 0.75–0.82). The estimated individuals’ absolute 5-year risk of OSCC varied according to combinations of risk factors. Individuals’ absolute risk assessment was available in an excel calculator.

Conclusion: To the best of our knowledge, this is the first study that developed a prediction model for the absolute risk of OSCC in a Western population. This
P0527 DURABILITY OF RADIOFREQUENCY ABLATION FOR TREATMENT OF ESOPHAGEAL SQUAMOUS CELL NEOPLASIA: 5 YEAR FOLLOW-UP OF A PROSPECTIVE STUDY IN CHINA

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Introduction: Radiofrequency ablation (RFA) is an accepted treatment modality for early Barrett’s neoplasia. Less is known about RFA for esophageal squamous cell neoplasia (ESCN). Our group has reported several prospective studies of RFA for ESCN in high-risk areas in China. Complete remission (CR) of ESCN was achieved in up to 87% of patients, but follow-up (FU) was restricted to 12 months.1-5

Aims and Methods: We aimed to evaluate long-term 5 year outcomes after RFA for ESCN. Patients with flat type (Paris 0-IIb) unstained lesions (USLs) on Lugol’s endoscopy, 3-12cm in length and with moderate or high grade intraepithelial neoplasia (MGIN,HGIN) or mucosal squamous cell cancer (ESCC-m) were treated with RFA every 3 months in the first year, until CR (defined as absence of MGIN or worse in biopsies) was established. All patients with CR at 12 months (CR12) were included in the current study extension, and underwent annual FU endoscopy with Lugol’s and biopsies. Flat type USLs were treated with RFA; other lesions were treated per investigator’s discretion. We also describe the clinical course of patients with persistent ESCN at 12 months (treatment failures), with treatment and FU per investigator’s discretion.

Results: The 78 patients with CR12 were included in this extension. During a median follow-up of 48 months (IQR 48-48) with 5 endoscopies (IQR 4-6) after the first year, 67/78 patients (86%) sustained CR. Recurrence occurred in 7 pts (9%); MGIN:6, HGIN:1 and all were managed with RFA. CR was re-established in 4, and 3 pts were treated at the last endoscopy. 4 other pts (5%) had progression (non-flattened HGIN; ESCC-sm-3) and were managed endoscopically with ESD. During FU, protocol violations (prolonged intervals, USLs left untreated or no adequate FU after retreatment) occurred in 46/78 patients (59%). Of the 12 treatment failures at 12 months, progression of ESCN occurred in 6 (50%), managed by endoscopic (1) or non-endoscopic (5) treatment. Overall, 2 patients developed subepithelial disease that was not clearly visible with Lugol’s endoscopy. Post-hoc analysis on the ‘pink-color sign’ at baseline, showed that the observed pink-color change after Lugol’s staining significantly predicted recurrence or progression during FU as well as initial failure at 12 months (HR 4.0, 95% CI 1.8-9.2).

Conclusion: RFA is relatively easy to apply and can efficiently treat large areas with ESCN. Despite protocol violations that may have interfered with the efficacy of RFA treatment in 59% of patients, the great majority with CR12 had sustained CR during FU. However, some patients progressed to advanced disease and 2 patients developed subepithelial disease that was not visible with Lugol’s. Based on currently available data, we advise to restrict the use of RFA for flat type MGIN and HGIN without pink-color sign on Lugol’s chromoscopy.

Disclosure: This was a Medtronic, Inc. sponsor initiated study

References

P0528 CHEMORADIOThERAPY FOR LYMPH NODES RECURRENT AFTER ESOPHAGECTOMY FOR ESOPHAGEAL CANCER

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Introduction: Recurrent esophageal cancer after esophagectomy has a poor prognosis, while we sometimes encounter patients with long-term survival. Lymph node recurrence is one of the common recurrence patterns after esophagectomy. Here we discuss the usefulness of chemoradiotherapy for lymph nodes recurrence after esophagectomy.

Aims and Methods: The aim of this study is to evaluate outcomes of chemoradiotherapy and prognostic factors for patients with only lymph nodes recurrence. Four hundred six patients underwent R0 esophagectomy for thoracic esophageal squamous cell carcinoma at our institution, between 1995 and 2014. Recurrence occurred in 148 patients (36%). Among these, 38 patients (39%) developed recurrence only in the lymph nodes. The median follow-up duration after recurrence was 13 months (range from 1 to 155 months). Post-recurrence survival was defined as the time between the first recurrence and death or most recent follow-up examination.

Results: The 58 patients with lymph node recurrence were 54 males and 4 females, with a median age of 64 years (range from 44 to 80 years). Of those, 16 (28 %) had pT1 cancer, 8 (14%) had pT2 cancer, 31 (53%) had pT3 cancer, and 3 (5%) had pT4 cancer. The number of patients at pN stage (UICC 7th) was 3/N1/N2/N3 was 16 (28%): 14 (24%): 19 (33%): 9 (16%), respectively. 11 patients (19%) had pM1 LYM. 3-field lymphadenectomy had been performed in 33 (58%) patients, and 2 or less-field lymphadenectomy was performed in 25 (42%) patients. The median time to recurrence after esophagectomy was 12.5 months (range from 1.8 to 47.5 months). M1 LYM recurrence occurred in 28 patients (48%) including 15 patients with both M1 LYM and regional lymph node recurrence, and 30 patients (52%) had only-regional lymph node recurrence. 34 patients (59%) had one single site of lymph node recurrence, and 24 patients (41%) had two or more recurrence sites. 43 patients (74%) had 1-field recurrence, and 15 patients (26%) had 2-field recurrence. Chemoradiotherapy was employed in 36 patients including 8 patients with surgery. The remaining 22 patients received other treatments including chemotherapy, radiotherapy, surgery, or best supportive care. The overall 1- and 3-year-survival rates in all patients after recurrence were 55% and 22%, respectively. By univariate analysis, the depth of tumor invasion (pT), the interval until recurrence, and the method of treatment were each found to be a factor affecting survival (p <0.05). The location and number of lymph nodes recurrence did not significantly affect survival. In multivariate analysis, the depth of tumor invasion (pT1,T2 vs. pT3,T4; hazard ratio 0.407; 95% confidence interval 0.212-0.754; p =0.004) and treatment (chemoradiotherapy vs. other treatment: hazard ratio 0.427; 95% confidence interval 0.234-0.786; p=0.008) were found to be an independent prognostic factor. The 3-year-survival rate in patients with pT1,T2 was 36%, compared to 12% in those with pT3,T4 (p=0.0014). The 3-year-survival rate in patients who received chemoradiotherapy was 29%, compared to 7% in those who received other therapy (p=0.0030).

Conclusion: Our findings suggested that chemoradiotherapy could improve survival in those esophageal squamous cell carcinoma patients with only lymph nodes recurrence. The location and number of lymph nodes recurrence did not affect survival.

Disclosure: Nothing to disclose

P0529 ENDOSCOPIC CRYOBALLOON ABLATION IS SAFE, WELL-TOLERATED AND HIGHLY EFFECTIVE IN THE ERADICATION OF ESOPHAGEAL SQUAMOUS CELL NEOPLASIA

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Introduction: Globally, 80% of all esophageal cancer cases are esophageal squamous cell cancer (ESCC), arising from esophageal squamous cell neoplasia (ESCN). Patients with ESCC have poor prognosis, but when diagnosed at the stage of ESCN, curative endoscopic treatment can be performed. ESCN mainly occurs in developing countries like Central and Eastern Asia and Eastern and
Southern Africa, often with limited endoscopic expertise and resources. Hence, an easy-to-use, low-cost treatment for ESCN would be of great value. Focal Cryoballoon Ablation therapy (FCBA) (C2 Therapeutics Inc. Redwood City, CA, USA) is a novel endoscopic ablation therapy that comprises a through-the-scope catheter with a conformable balloon that obviates the need for side-by-side inflation of disposable oxygen cartridges. The balloon is simultane-ously inflated and cooled with nitrous oxide from the cartridge, resulting in ice patches of approximately 2cm. FCBA is handheld, easy to use and requires no capital equipment. Although early studies for FCBA of Barrett’s esophagus have shown promising results, limited data are available for its use in ESCN.

Aims and Methods: We aimed to assess the safety, tolerability and efficacy of FCBA in the eradication of ESCN. In this single-center prospective trial in China, patients with a flat type (Paris 0-IIb) unstrained lesion (USL) on Lugol’s chromostaining were enrolled. Escape lesions were selected. A diagnosis of Moderate or High Grade Intraepithelial Neoplasia (MGIN/ HGIN) were enrolled. At baseline, the entire USL was ablated with side-by-side ablations of 10 seconds and tattoos were placed to identify the treatment area (TA). Ablation was performed at the TA. A second treatment was repeated within 3 months in the case of persisting USLs. All patients underwent a 12-month endoscopy with biopsies from the TA. Outcomes included safety, tolerability (11-point visual analog scale (VAS) for pain); complete response (CR; absence of MGIN or worse in all TA biopsies) rates at 3 and 12 months; and adverse events.

Results: We enrolled 80 patients (59 MGIN, 21 HGIN) with a median USL length of 3 (IQR 3–4) cm. MGIN and HGIN (IQR 4–7) side-by-side ablations were performed per patient over a median ablation time of 8 (IQR 5–10) minutes. After a single treatment, 70/78 patients (90%, per protocol) exhibited CR. The other 8 patients had residual USL and were retreated; all had CR 3 months later (45). A total of 7 patients were lost to follow-up. At 12 months, 76/78 patients (97%, per protocol) or 76/80 (95%, intention to treat) patients exhibited CR. AT 12 months, 2 patients, both with MGIN at baseline, were found to have a USL with MGIN. No strictures or serious adverse event had been noted. 3 patients developed self-limiting mucosal lacerations upon balloon inflation. Post-procedure median VAS was 1 (IQR 0–2) at day 2, and 0 (0–0) at days 7 and 30. Median dysphagia score was 0 (0–0) on all days.

Conclusion: Results of our prospective cohort study in China suggest that focal cryoablation in endoscopic squamous cell carcinoma is safe, well tolerated, and highly effective in inducing endoscopic and histological remission. FCBA is a promising, easy to use and low-cost modality for the treatment of ESCN.

Disclosure: This study was financially supported by C2 Therapeutics, Inc.
resorption. However, there are rarely published studies investigating the clinicopathologic characteristics of synchronous multiple early esophageal neoplastic lesions so that clinicians can make better decisions for the preserved esophagus after endoscopic treatment.

Aims and Methods: The clinical data of 37 patients with synchronous multiple early esophageal neoplastic lesions who meet the inclusion criteria between May 2013 to May 2017 were analyzed. According to postoperative pathological results, patients were divided into 2 groups: Group A: all the lesions had confirmed histopathology and clinical neoplastic (EGJ) or esophageal cancer; Group B: only 1 lesion had confirmed HGIN or esophageal cancer, while other lesions were high-grade intraepithelial neoplasia (HGIN). The clinicopathologic features were compared between the 2 groups by univariate analysis.

Results: There were 20 patients, 44 lesions in group A and 17 patients, 34 lesions in group B. No significant differences were observed between the 2 groups in terms of age, gender, body mass index (BMI), family esophageal cancer history, heavy drinking, heavy smoking, flush after drinking, while significant differences were found between the 2 groups in avoiding lesions (LVLAs) grade (p = 0.001), submucosal involvement on EUS (p = 0.005), circumferential extent (p = 0.000), R0 resection rate (p = 0.007), lesion size (p = 0.000) and pathological upgrade rate (p = 0.043).

Conclusion: The mean grade of LVLAs larger, lesion size, circumferential extent ≥ 1/2, non-R0 resection, postoperative pathological estimation upgrade, and an EUS finding of submucosal involvement are considered high-risk factors in patients with synchronous multiple esophageal neoplastic lesions. Therefore, clinicians must remain vigilant and perform careful observations and surveillances on patients with such characteristics during endoscopic examination.

Disclosure: Nothing to disclose

P0534 DOES PPI PLAY A PROTECTIVE ROLE IN GASTRIC MUCOSAL INJURY DURING ANTIPLATELET THERAPY?
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Introduction: Over 5 years in Japan, DOACs replaced direct oral anticoagulants (DOACs) was released in Japan. It was not just known that DOACs have similar efficacy as vitamin K antagonists (VKA), but might be a more mucosal-friendly agent than VKA[1]. However, for reducing the incidence of mucosal injuries, we don’t know what kind of agents is helpful to use concomitantly for patients taking DOACs as well as VKA.

Aims and Methods: The aim of this study is to explore whether proton pump inhibitor (PPI) play a protective role for gastric mucosa in patients taking DOACs or VKA. To reveal the role of PPI, we compared the severity of gastric mucosal injury between PPI users and nonusers in the subjects taking DOACs or VKA, individually. Data were extracted from the records of subjects who underwent upper gastrointestinal endoscopy at our department between April 2015 and December 2017. Of the 3,900 subjects analyzed, we focused on 203 subjects who took DOACs (Dabigatran, Edoxaban, Rivaroxaban, Apixaban) or VKA (Warfarin). After excluding subjects who took other type of antacid (histamine 2 receptor blockers or potassium-competitive acid blockers) in each group, we divided subjects into 2 subgroups: those who were taking PPI, and those who were taking no antacids. Severity of gastric mucosal injury was evaluated endoscopically according to the modified LANZA score (MLS) [2]. Statistical analyses were performed by Fisher’s exact test.

Results: This study included 88 subjects in DOACs users (62 men, 26 women; mean age 72.9 years; 58 PPI user, 30 nonuser) and 72 subjects in VKA users (45 men, 27 women; mean age 74.9 years; 49 PPI user, 23 nonuser). In patients taking DOACs, average MLS of PPI users and nonusers was, respectively, 0.24±0.76 and 0.63±1.45 (p = 0.263). In patients taking VKA, average MLS of PPI users and nonusers was, respectively, 0.59±1.38 and 1.91±2.25 (p = 0.045). In the subjects taking VKA, gastric mucosal injury was statistically significantly mild in PPI users but not in the subgroup taking DOACs.

Conclusion: PPI play a protective role in gastric mucosa in patients taking VKA but not in patients taking DOACs.

Disclosure: Nothing to disclose

References

P0535 FACTORS OF PROTON PUMP INHIBITOR RESISTANCE MODELED BY COMPARATIVE DISSOLUTION TESTING
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Introduction: Among the reasons for proton pump inhibitor (PPI) resistance is different quality of enteric coatings, as a result of which PPIs acid degradation in the stomach leads to its release there. The influence of factors such as pathologic duodenogastrectomy reflux (PDGR) with pH ≥ 7 followed by its decrease and the pH increasing ≥ 4 within multiple PPIs dosing in patients with gastro-esophageal reflux disease (GERD) on coatings and premature active compounds degradation has not been studied specifically. PDGR and pharmacological acid suppression can be reliably modeled with comparative dissolution testing (CDT). In PDGR, pH ≥ 7 exposure time for omeprazole and rabeprazole is 4 and 12 minutes respectively. Omeprazole or rabeprazole detection in the pH 7 buffer after 4 or 12-minute exposure should be estimated as PPIs degradation in the stomach due to PDGR. The stability of PPIs in case of an inhibited gastric acid secretion can be confirmed by drug compounds absence in the pH 4 buffer

Aims and Methods: CDT (pH 7.0±0.05, pH 0.1±0.05) has been used to simulate influence of PDGR and pharmacological acid suppression on omeprazole and rabeprazole gastric release and degradation. The additional aliquots were taken from the pH 7.0±0.05 solution after 4 minutes for original omeprazole (O0) and geneties (GO), G02, GO3 and 12 minutes for rabeprazole (OR, GR1, GR2). PDGR resistance for PPIs capsules and tablets was determined by active substances presence or absence.
Results: The drug release was not detected in the pH 1.2 buffer. Drugs were moved for pH 1.2±0.05 to pH 7.0±0.05. The drug release in the pH 7.0±0.05 after 4-minute exposure was 4.7±0.07%, 0.8±0.5±6%, 82.5±1.7% for OO, GO1, GO2, GO3, respectively. OR and generics were subjected to the same conditions during 12 minutes with only OR1 detected final release (5.4±0.4%). Therefore, PDGR model demonstrated poor reflux influence on OO and GR1, strong influence on GO2 and GO3 with the almost complete omeprozole release and its potential degradation after following pH decrease. Any omeprozole was not detected in the pH 4.0±0.05. Pellet destructions were not registered for GO1 and GO3 while GO2 pellets were totally degraded. Non-degraded pellets were moved to pH 7.0±0.05 where their release was determined. In the same dissolution conditions, rabeprazole amount from GR2 after 10-, 15-, 20-, 30-, 45-, 60 minutes was 0; 0; 5.5±0.4%; 38.8±0.4%; 58.0±0.3%; 82.4±0.5%; 68.9±0.5%. No OR and GR1 release or visible tablets destruction were registered. Pharmacological acid suppression model had demonstrated OO, OR, GO1, GO3 and GR1 resistance while total GO2 and partial GR2 degradation were determined.

Conclusion: Omeprazole and rabeprazole generics with high-risk degradation under PDGR and multiple PPIs dosing were determined by CDT. Omeprazole was totally degraded in pH 4.0±0.05 but not rabeprazole.

Disclosure: Nothing to disclose

P0537 LONG-TERM OUTCOMES AND PROGNOSTIC FACTORS OF NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC CANCER IN ELDERLY PATIENTS

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Introduction: Gastric cancer is still one of the leading causes of cancer-related death in Japan. Due to wide spread use of endoscopic submucosal dissection (ESD), physicians are facing dilemma as to the indication for additional gastrectomy in elderly treated for curative ESD. This is due to little information with regards to the long-term outcomes and prognostic factors of non-curative ESD for gastric cancer in elderly patients.

Aims and Methods: We aimed to clarify the long-term outcomes and prognostic factors of non-curative ESD for gastric cancer in elderly patients. Among 1,358 patients with early gastric cancer (EGC) treated by ESD at our institution during 2002-2012, we enrolled 87 patients with age ≥75 yrs, who were treated by non-curative ESD. First, clinicopathological findings and long-term outcomes up to the end of 2017 were evaluated. Next, the prognostic factors were analyzed using the Kaplan-Meier methods and a Cox proportional hazards model.

Results: 27 of 87 patients died of any cause. However, only 1 patient died of gastric cancer. 3-year overall survival (OS) and 5-year OS were 89.7% and 79.3%, respectively. The univariate analyses revealed that patients who were in Eastern Cooperative Oncology performance status of 2 or 3, high Charlson comorbidity index (CCI) (>3), high neutrophil to lymphocyte ratio (>3.3), low prognostic nutritional index (< 44.8), antral location of EGC and depressed or completely flat configuration of EGC were factors associated with death. The high CCI (>3) was found to be an independent prognostic factor associated with OS (hazard ratio: 2.79, 95%CI: 1.16–6.69, p = 0.021).

Conclusion: After non-curative ESD for gastric cancer in elderly, CCI may be a clue for decision making of additional gastrectomy. Careful follow up without additional gastrectomy may be an acceptable strategy for elderly patients.

Disclosure: Nothing to disclose
submucosa using distal hood of the endoscope. We hypothesized time to flap formation would be a surrogate endpoint for technical success for duodenal ESD.

Aims and Methods: The aim of this study was to assess the feasibility of time to flap formation as endpoint for duodenal ESD. This was a retrospective observational study from a university hospital. A total of 102 cases that underwent ESD for duodenal superficial neoplasia from July 2013 to June 2017 were included in this study. ESD was performed using DualKnife J ( Olympus medical systems, Tokyo, Japan) and short tip type transparent hood (ST hood, FUJIFILM Medical Co., Ltd. Tokyo, Japan). An endoscopist reviewed all movies of the procedures and measured time to flap formation and total procedure time. In this study, flap formation was defined as the timing when complete exposure of submucosa using upper rim of the hood was obtained. The distribution of total procedure time and time to flap formation was analyzed in addition to other short-term outcomes. Those were compared according to the skill level of endoscopists (expert: >100 duodenal ESD, and the others). Moreover, we analyzed the linear regression between total procedure time and time to flap formation and other clinical features of the lesion using least square methods.

Results: As for location of the lesion, 13.7% located in bulbs, 73.5% in descending part, 3.0% in horizontal part, and 9.8% located in superior duodenal angle (SDA) or inferior duodenal angle (IDA). The mean lesion diameter was 32.5±10.5 mm. Resection in a submucosa and R0 resection was 98.3%, respectively. Bleeding and perforation was found in 3.0% and 5.9% of patients, respectively. Mean procedure time was 55.8±3.9 min and mean time to flap formation was 13.5±1.1 min. It was significantly shorter by expert’s hand (12.1±1.1 min vs 24.0±2.9 min, p<0.0001). Multiple linear regression analysis revealed time to flap formation as well as lesion size, location, and endoscopists’ skill were independently correlated with total procedure time (Table 1). Complete formation reflected the skill level of the endoscopists and predicted total procedure time independently of the size and the location of the lesion. It could be a surrogate endpoint for technical success of duodenal ESD.

Table: The results for multiple linear regression analysis about total procedure time

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<th>β coefficient</th>
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<td>Flap formation time</td>
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Disclosure: Nothing to disclose

P0540 EFFECT OF THE DURATION TIME OF UPPER GASTROINTESTINAL ENDOSCOPY ON THE DETECTION RATE OF GASTRIC NEOPLASTIC LESIONS

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Introduction: Early detection and prompt treatment using upper gastrointestinal endoscopy are important to reduce the mortality rates of gastric cancer. Previous reports on esophagogastroduodenoscopies (EGD) have stated that compared to normal screening EGD, it is thought that the detection of gastric neoplastic lesions is made possible using a short examination time and efficient biopsies due to an increase in the accumulation of experience.

Results: From June 2017 to December 2017, we investigated 1019 patients (501 men and 518 women, mean age: 62.8±16 years) who underwent a first screening EGD at our hospital. EGD was performed using DualKnife J (Olympus medical systems, Tokyo, Japan) and short tip type transparent hood (ST hood, FUJIFILM Medical Co., Ltd. Tokyo, Japan). An endoscopist reviewed all movies of the procedures and measured time to flap formation and total procedure time. In this study, flap formation was defined as the timing when complete exposure of submucosa using upper rim of the hood was obtained. The distribution of total procedure time and time to flap formation was analyzed in addition to other short-term outcomes. Those were compared according to the skill level of endoscopists (expert: >100 duodenal ESD, and the others). Moreover, we analyzed the linear regression between total procedure time and time to flap formation and other clinical features of the lesion using least square methods.

Results: As for location of the lesion, 13.7% located in bulbs, 73.5% in descending part, 3.0% in horizontal part, and 9.8% located in superior duodenal angle (SDA) or inferior duodenal angle (IDA). The mean lesion diameter was 32.5±10.5 mm. Resection in a submucosa and R0 resection was 98.3%, respectively. Bleeding and perforation was found in 3.0% and 5.9% of patients, respectively. Mean procedure time was 55.8±3.9 min and mean time to flap formation was 13.5±1.1 min. It was significantly shorter by expert’s hand (12.1±1.1 min vs 24.0±2.9 min, p<0.0001). Multiple linear regression analysis revealed time to flap formation as well as lesion size, location, and endoscopists’ skill were independently correlated with total procedure time (Table 1). Complete formation reflected the skill level of the endoscopists and predicted total procedure time independently of the size and the location of the lesion. It could be a surrogate endpoint for technical success of duodenal ESD.

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Disclosure: Nothing to disclose

P0541 VALIDITY OF SUBMUCOSAL PATTERN ANALYSIS OF EUS FOR PREDICTING DEPTH OF INVASION IN ULCERATIVE EARLY GASTRIC CANCER

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Introduction: Accuracy of endoscopic ultrasonography (EUS) for predicting depth of invasion in early gastric cancer (EGC) accompanied with endoscopic ulcer or ulcer scar was lower than that without ulcer.

Aims and Methods: We tried to evaluate the validity of submucosal pattern analysis of EUS for predicting depth of invasion in ulcerative EGC. Demographic, endoscopic and EUS features of 176 consecutive endoscopically suspected EGC patients who underwent the EUS examination and the endoscopic or surgery retrospectively reviewed. The EUS findings were classified as the (1) no deformity type, (2) fan-shaped deformity type, and (3) arch-shaped or punch-shaped deformity type, according to submucosal layer change. The EUS findings also classified into 2 groups; submucosal fibrosis and no fibrosis groups.

Results: 73 among total 176 cases (41.5%) were accompanied with the active or healing staged endoscopic ulcer, whereas SI-staged ulcer was found in 62 cases (35.2%) and no ulcer group was 41 cases. The EUS fibrosis was combined in 71 cases (40.4%), Fan-shaped deformity type, and arch-shaped deformity. The histologic submucosal fibrosis was found more frequently in the EUS fibrosis group than no fibrosis group (51.6% vs 10.4%, p<0.001). The Arch-shaped submucosal deformity was a significant independent predictive factor for presence of submucosal cancer invasion than Fan type or no SM deformity group (80.9% vs 18.2% vs 19.5% odds ratio 11.83) (p<0.001). With regard to the results of endoscopic resection, curative, and complete resection rate were significantly lower in EGCs with the antrum submucosal deformity than those with no SM change or fan-type SM change groups (p<0.001).

Conclusion: Pattern analysis of the submucosal deformity on EUS examinations can be an useful tool for predicting the presence of the histologic ulcers and cancer invasion in ulcerative EGC.

Disclosure: Nothing to disclose

P0542 FEASIBILITY AND OUTCOMES OF SECONDARY (REDO) ENDOSCOPIC SUBMUCOSAL DISSECTION FOR LOCALLY RECURRENT OR INCOMPLETELY RESECTED GASTRIC NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) is an accepted curative treatment option for gastric tumors with very low local recurrence. However, residual or locally recurrent tumors occur rarely after ESD. Although secondary (Redo) ESD is technically demanding, it can be applied to residual or recurrent tumors that were treated by submucosus. Here, we investigated the feasibility and safety of secondary ESD for gastric tumors.

Aims and Methods: Between 2010 and 2017, 1623 consecutive patients underwent ESD for gastric neoplasms at a single tertiary referral center. Among these, 28 patients underwent secondary ESD for a residual or locally recurrent tumor. Our analysis compared clinopathologic factors between primary ESD and secondary ESD groups.

Results: The en-bloc resection and curative rate of resection of secondary ESD were 92.9% and 89.3%, respectively. The average procedure time of secondary ESD was significantly longer than primary ESD (78.2 vs. 55.1 minutes, p=0.004) and the adverse events rate was slightly higher in secondary ESD group than primary ESD group without statistical significance (10.7 vs 3.8%, p=0.095).
Patients who received secondary ESD had favorable outcomes without severe adverse events during follow-up period, no local recurrence occurred in patients who received secondary ESD.

Conclusion: Although it requires greater technical efficiency and a longer procedure time, secondary ESD of residual or locally recurrent gastric tumors appears to be a feasible and curative treatment.

Disclosure: Nothing to disclose.

P054 RISK FACTORS FOR EARLY AND DELAYED POST-OPERATIVE BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC NEOPLASMS

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Introduction: Endoscopic submucosal dissection (ESD) has become widely accepted as a standard treatment for gastric neoplasms. The safety of gastric ESD has been mostly established, although complication such post-operative bleeding and perforation remain problematic.

Since 2012, an endoscopic approach involving continued administration of low-dose aspirin (LDA) for patients at high risk of thromboembolism has been recommended in Japan. This approach is similar to the one stated in the guidelines of the European Society of Gastrointestinal Endoscopy; however, there is an insufficient date to support this guideline in Japan.

Aims and Methods: The aim of this study was to identify risk factors for early and delayed post-operative bleeding after gastric ESD and to evaluate the relationship between the use of antithrombotic agents and post-operative bleeding.

From January 2004 to December 2017, we analyzed 922 patients (673 men and 249 women, mean age 72.7±14.4years) 961 gastric neoplasms who treated by ESD at our hospital. Traditionally, we have interrupted therapy 5-7 days before gastric ESD for patients using LDA. However, since January 2012, we have followed the above mentioned guidelines, thus performing ESD with continued LDA for patients at high risk of thromboembolism.

In this study, post-operative bleeding was defined as a decrease in the blood hemoglobin level of ≥ 2g/dL accompanied by an occurrence of hematemesis or melena.

Bleeding within 6 days after ESD was defined as early post-operative bleeding, whereas bleeding on the sixth day or later post-operatively was defined as delayed post-operative bleeding.

Risk factors for early and delayed post-operative bleeding were retrospectively examined using univariate and multivariate analysis.

Results: The overall post-operative bleeding rate was 4.4%. The mean duration until post-operative bleeding was 2.4±6.4days. The post-operative bleeding rate for patients who continued LDA, discontinued antithrombotic agents, or received heparin replacement (HR) were 11.1%, 5.5%, and 13.1%, respectively. In the multivariate analysis, chronic kidney disease (CKD) requiring hemodialysis (p = 0.005; odds ratio 6.71, 95% CI 1.79-25.1), HR (p <0.01; odds ratio 4.15, 95% CI 1.73-9.93) and a specimen size of ≥ 50mm (p = 0.024; odds ratio 2.27, 95% CI 1.11-4.62) were independent risk factors for post-operative bleeding.

Delayed post-operative bleeding rate was 2.5%. In the multivariate analysis, HR (p <0.002; odds ratio 5.69, 95% CI 1.92-116.8) was independent risk factor for delayed post-operative bleeding.

Conclusion: Continued LDA was not risk factor for post-ESD bleeding. CKD requiring hemodialysis, and HR ≥ 50mm were independent risk factors for early post-operative bleeding, whereas HR is an independent risk factor for delayed post-operative bleeding. The timing of post-operative bleeding differs with the factors. Careful observation is required for patients at high risk of post-operative bleeding.

Disclosure: Nothing to disclose.

Reference

References

P0543 A NEW HISTOPATHOLOGICAL CLASSIFICATION OF GASTRIC ADENOCARCINOMA OF FUNDIC GLAND MUCOSAL TYPE AND CLINICOPATHOLOGICAL FEATURES OF GASTRIC ADENOCARCINOMA OF FUNDIC GLAND MUCOSAL TYPE (A MULTICENTER STUDY OF 80 CASES)

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Introduction: Gastric adenocarcinoma of fundic gland type (GAFG) is newly added as a special type cancer in Japanese classification of gastric carcinoma, the 15th Edition 1). GAFG is an uncommon variant of gastric adenocarcinoma which has a distinct clinicopathological, immunohistochemical, and endoscopic features 2-4). GAFG is defined by positive immunohistochemical staining for pepsinogen-I (a marker of chief cells) and H+K+-ATPase (a marker of parietal cells) and is not associated with H. pylori infection. We suggested that a progression of GAFG might be associated with GNAS mutations 5).

Histopathologically, GAFG is classified into pure GAFG and gastric adenocarcinoma of fundic gland mucosal type (GAFGM) which exhibited differentiation toward gastric foveolar epithelium in addition to fundic gland differentiation. However, the histopathological classification of GAFG including GAFGM have not been well investigated.

Aims and Methods: The aim of this study was to establish a new histopathological classification of GAFG and clarify the clinicopathological features of GAFGM by comparisons with pure GAFG. A total of 80 GAFG cases from April 2004 to December 2017 were retrospectively collected from 27 institutions. We performed an immunohistochemical analysis using pepsinogen-I, H+K+-ATPase, MUC5AC (a marker of foveolar epithelial cells) and MUC6 (a marker of mucus neck cells) to classify these GAFG cases as pure GAFG, MUC5AC+/-MUC6+/- (p <0.01) and GAFGM (MUC5AC+, >10% MUC6+/- pepsinogen-I and/or H+K+-ATPase+, n = 57) or GAFGM (MUC5AC+, >10% MUC6+/- pepsinogen-I and/or H+K+-ATPase+, n = 23). In addition, GAFGM was classified to 3 subtypes, as follows;

Type 1. Tissue construct of foveolar epithelium and fundic gland is maintained, and tumor is exposed on the surface (n=9), Type 2. Tissue construct of foveolar epithelium and fundic gland is collapsed, and tumor is exposed on the surface (n=10), Type 3. Tissue construct of foveolar epithelium and fundic gland is collapsed, and tumor is not exposed on the surface (n=20). We then compared the pure GAFG and GAFGM cases, and 3 subtypes of GAFGM via a clinicopathological analysis and the frequency of GNAS mutation.

Results: There were no significant differences between the 2 groups (pure GAFGs vs. GAFGMs) in the following findings: location of lesion, macroscopic type, method of treatment, depth of invasion, lymph node metastasis, proliferative activity, p53 protein overexpression, H. pylori infection, and activating mutations in GNAS (p = 0.006; odds ratio 3.96, 95% CI 1.30-12.0), and a specimen size of 50 mm (p = 0.024; odds ratio 0.71, 95% CI 0.30-1.69). There were no significant differences between pure GAFG and GAFGM cases, and 3 subtypes of GAFGM in pepsinogen-I, H+K+-ATPase, MUC5AC, MUC6, and p53 protein overexpression.

Conclusions: The histopathological classification of GAFG is useful to estimate its clinicopathological differences, and should be categorized as a new aggressive variant of GAFG that has high malignant potential and differ in malignancy by tissue construct of foveolar epithelium and fundic gland.

Disclosure: Nothing to disclose.

References
diagnosis, for male sex 2.0-fold, G3 according to mitosis count 3.0-fold, G3 according to ki67, tumor stage 3 or 4 cases 12.7-fold, 1 cm increase in tumor size 9%, liver metastasis 6.1-fold, by every 1 mg/dl increase in CRP level 1.5%. There was a significant difference between the pancreas and stomach NETs in favor of stomach tumors in terms of survival.

Conclusion: As a result, it was observed that 1 of the biochemical parameters, CRP affected the course of the progression in the worst way (particularly if it is > 20 mg / dl). With the need for larger scale and prospective studies, it was suggested that CRP level might be a poor prognostic factor for the entire GEP-NET group.

Disclosure: Nothing to disclose

**P0546** ACCURACY OF ENDOSCOPIC SIZE MEASUREMENTS OF EARLY GASTRIC SIGNET RING CELL CARCINOMA

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**Introduction:** Indications for endoscopic submucosal dissection (ESD) of early gastric cancer (EGC) are expanding, but signet ring cell (SRC) carcinoma is still unclear because of its unclear lateral margin.

**Aims and Methods:** The purpose of this study was to compare pathologic size and endoscopic size in early gastric SRC and to find risk factors associated with tumor size underestimation. A retrospectively medical records reviewed of total 137 patients with diagnosed early gastric SRC between January 2009 and December 2016 at our tertiary hospital. According to pathologic and endoscopic tumor sizes, classified into correct estimation, underestimation and overestimation groups, and risk factors related to underestimation were analyzed.

**Results:** Among 137 patients with early gastric SRC, 77 patients (56.2%) had undercorrected estimation, 43 patients (31.4%) had underestimation and 17 patients (12.4%) had overestimation. Mean pathologic size was SD (20.1 (13.8) mm and mean endoscopic size (SD) was 17.9 (10.1) mm, the correlation coefficients were 0.919 (p = 0.000) and there was no significant difference between the two groups. Multivariate analysis showed that more than 20mm endoscopic tumor size (OR, 3.419; 95% CI, 1.271–9.194, p = 0.015) and atrophy (OR, 6.011; 95% CI, 2.311–15.633, p < 0.001) was a risk factor for tumor size underestimation.

**Conclusion:** There was no significant difference in pathologic and endoscopic size in early gastric SRC. Therefore ESD may be considered as a therapeutic option if the size of the tumor is less than 20 mm and atrophy is not present in the surrounding mucosa.

Disclosure: Nothing to disclose

**P0547** INCREASED INCIDENCE OF RECURRENT NEOPLASM AFTER ENDOSCOPIC RESECTION IN PATIENTS WITH SYNCHRONOUS GASTRIC NEOPLASM

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Introduction: Synchronous gastric neoplasms is the major concern after endoscopic resection (ER) for early gastric cancer (EGC). Several studies showed that patients with EGC with synchronous neoplasm had increased recurrence rate after ER than those with single EGC. However, the incidence and prognosis are not well-known in patients with synchronous neoplasm including adenoma.

**Aims and Methods:** In this study, we compared the outcome between patients with single neoplasm and synchronous neoplasm including adenoma after ER. We also compared the outcomes of synchronous neoplasm subgroup which were divided according to the diagnostic histology.

A total of 1569 patients who underwent ER for gastric neoplasm were divided according to the diagnostic histology. Patients were determined by electrochemiluminescence assay (Roche cobas e 601, Switzerland).

**Results:** Among 137 patients with early gastric SRC, 77 patients (56.2%) had undercorrected estimation, 43 patients (31.4%) had underestimation and 17 patients (12.4%) had overestimation. Mean pathologic size was SD (20.1 (13.8) mm and mean endoscopic size (SD) was 17.9 (10.1) mm, the correlation coefficients were 0.919 (p = 0.000) and there was no significant difference between the two groups. Multivariate analysis showed that more than 20mm endoscopic tumor size (OR, 3.419; 95% CI, 1.271–9.194, p = 0.015) and atrophy (OR, 6.011; 95% CI, 2.311–15.633, p = 0.001) was a risk factor for tumor size underestimation.

**Conclusion:** There was no significant difference in pathologic and endoscopic size in early gastric SRC. Therefore ESD may be considered as a therapeutic option if the size of the tumor is less than 20 mm and atrophy is not present in the surrounding mucosa.

Disclosure: Nothing to disclose

**P0548** MATRIX METALLOPROTEINASE MULTIPLE SCREENING IDENTIFIES INCREASED TIMP-4 SERUM CONCENTRATIONS IN GASTRIC CANCER PATIENTS

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**Introduction:** The phenomenon of active inflammatory crosstalk between tumor cells and the surrounding stroma has attracted more and more attention [1]. Some investigations have indicated that inflammation-related proteins, such as matrix metalloproteinase (MMPs), may facilitate the growth, proliferation, and migration of tumor cells, including GC [2–4]. This study was carried out to reveal and testify their significance as candidates for tumor markers of GC.

**Aims and Methods:** Plasma samples from 12 GC patients (3 cases for each clinical stage from I to IV) and 10 non-neoplastic gastric disease (NGD) patients (3 cases with chronic superficial gastritis, 4 cases with chronic atrophic gastritis or intestinal metaplasia and 3 cases with dysplasia) were collected from November 2016 to March 2017 as training set. Human MMP arrays (RayBiotech, Norcross, GA, USA) were used to quantitative measurement of 7 major MMPs (MMP-1, MMP-2, MMP-3 MMP-8, MMP-9, MMP-10, and MMP-13) and 3 other endo- genous inhibitors (TIMP-1, TIMP-2, and TIMP-4) simultaneously. Then the levels of them were compared between the GC and NGD groups and their diagnostic value was assessed by ROC curve. The candidate differential subtypes were validated by corresponding serum microchips in another group of patients, which included 40 GC patients and 38 NGD patients. Additionally, the levels of CRP and CA19-9 were also assayed in the GC group, the CA19-9 level in synchronous group was 125 (CA125), and carbohydrate antigen 19-9 (CA19-9) in plasma of the 52 GC patients were determined by electrochemiluminescence assay (Roche cobas e 601, Switzerland).

**Results:** Compared to the NGD group, except MMP-2, MMP-3 and MMP-13, other MMPs showed an increased trend in the GC group, but no significant difference in the training set. Only TIMP-4 increased significantly in the GC group compared to the NGD group, p < 0.05. The area under the curve (AUC) of the MMPs were from 0.500 to 0.858, and combined AUC of them was 0.858 (95% CI, 0.699-1.000) for the diagnosis of GC. Particularly, TIMP-4, whose AUC was the highest, 0.858 (95% CI: 0.692-1.000). At the optimal cut-off value of 2438.3 pg/ml, its sensitivity, specificity and accuracy for the diagnosis of GC were 83.5%, 80.0% and 81.8%, respectively. In the validation set, the concentration of TIMP-4 in GC and NGD group were 1101.2 2.703.3 pg/ml and 890.1 1.457.4 pg/ml, respectively. Compared with the NGD group, the concentration of TIMP-4 increased in the GC group, but no statistical difference was found. Its AUC value for the diagnosis of GC was 0.574 (95% CI: 0.444-0.704). Furthermore, the positive rates of AFP, CEA, CA125 and CA19-9 in both sets for the diagnosis of GC and early gastric cancer (EGC), as shown in Table 1. **Conclusion:** The diagnostic value of the candidate tumor markers is limited. However, MMP profiles may have potential value for the diagnosis and screening of GC. TIMP-4 is a promising biomarker for the auxiliary diagnosis of GC.

**Disclosure:** Nothing to disclose

<table>
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<th>Variable</th>
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<th>Validation set</th>
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<td>EGC (n = 3)</td>
<td>GC (n = 40)</td>
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[ Positive rates of traditional serological tumor markers for the diagnosis of GC and EGC (%).]
Clinical Course After Non-Curative Endoscopic Submucosal Dissection for Early Gastric Cancer Without Additional Surgery

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Introduction:
Early gastric cancer (EGC) is not curatively treated by endoscopic submucosal dissection (ESD), additional surgical gastrectomy is not performed for various reasons.

Aims and Methods: The aim of this study was to assess clinical courses for patients who did not undergo additional surgery for non-curative EGC after ESD. From January 2004 to July 2017, 2,156 patients underwent ESD for EGC at Sendai City Medical Center. Among patients defined as being not curative based on clinicopathological evaluation according to the Japanese Gastric Cancer Treatment Guidelines 2018, 109 patients who did not undergo additional intervention, such as surgery, were included in this study. After elimination of 18 patients who were alive during an insufficient follow-up period of <3 years, risk factors for short survival (<5 years) were evaluated by using univariate and multivariate analyses.

Results: Of the 109 patients, the median age was 75.8 years (range, 48–93 years) and 78% were male. The median Charlson Comorbidity Index (CCI) was 2.0 (range, 0–7). The ratio of the patients with low level activity of daily living (ADL) with the patient could not go out by him/herself was 13%. As to pathological outcomes, the depth of cancer invasion was M in 28% of the patients, SM1 in 28%, SM2 in 41%, and unclear in 3%. The median tumor size was 35 mm (range, 9–98 mm). The pathological type was diagnosed as the differentiated type in 81%, undifferentiated type in 3%, mixed type in 14%, and others in 2%. Lymphatic and venous invasion were observed in 23% and 7%, respectively. The rates of lateral and vertical margin involvement were 3% and 8%. Ulcerative findings were observed in 31%. The risk of lymph node metastasis was defined as being high in 9%, intermediate in 49%, and low in 42% in the eCura system (Hatta et al. 2017). Gastric cancer in only 1 patient (37.6 months after ESD) and other causes in 2%. Lymphatic and venous invasion were observed in 23% and 7%, respectively. The rates of lateral and vertical margin involvement were 3% and 8%. Ulcerative findings were observed in 31%. The risk of lymph node metastasis was defined as being high in 9%, intermediate in 49%, and low in 42% in the eCura system (Hatta et al. 2017).

Multivariate analysis revealed that the high CCI odds ratio (OR), 4.8; 95% confidence interval [CI], 1.1–21; p = 0.036 and low ADL level (OR, 6.2; 95% CI, 1.2–31; p = 0.026) were independent risk factors for the short survival period. From univariate analyses, advanced age (≥85 years) (p = 0.043), high CCI ≥3 (p = 0.007), low ADL level (p = 0.001), and low serum albumin level ≤3.5 g/dl (p = 0.003) were significantly associated with short survival period. Multivariate analysis revealed that the high CCI odds ratio (OR), 4.8; 95% confidence interval [CI], 1.1–21; p = 0.036 and low ADL level (OR, 6.2; 95% CI, 1.2–31; p = 0.026) were independent risk factors for the short survival period.

Conclusion: Given the relatively high OS and DSS, ESD without additional surgery for non-curative EGC was found to be an acceptable option for patients with poor surgical tolerance. Although the survival period was shorter in patients with some comorbidities and those with low ADL level, it is unclear whether additional surgical intervention is appropriate not because of the cause of death was not gastric cancer for most of the patients.

Disclosure: Nothing to disclose

References

P0552 SERUM PEPISOGEN H AS A POTENTIAL BIOMARKER FOR DETECTION OF DIFFUSE TYPE GaSTRIC CANCER AMONG YOUNG ADULTS IN KOREA

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Introduction: The usefulness of pepsinogen (PG) I and I/II ratio as biomarker for screening gastric cancer (GC) has been well established in Japan. PG II is known to be a marker of gastric inflammation, but clinical interest in diagnosis of GC was relatively low and its role has not been clearly established either. The purpose of this study is to investigate the role of PG II in the screening of GC.

Aims and Methods: Total of 2,956 subjects, including patients with GC (n=1,136), gastric dysplasia (n=346) and controls (n=1,474) who underwent gastroscopy with well-defined biopsy sampling protocol, were enrolled in this study during 2006-2017. Serum levels of PG and Helicobacter pylori (HP) infection tests (Giemsa stain, CLOtest and culture) were performed. Each PG level were divided into 3 categories. The usefulness of PG levels to detect GC compared to controls was validated by using multivariate logistic regression. Odds ratios and 95% CIs were calculated.

Results: In the cross-sectional analysis, PG I, PG II and PG I/II ratio (especially PG II/I ratio) were associated with the presence of GC. When classified by histology, the prevalence of diffuse type GC was higher in PG II levels group (OR=2.20, p<0.001). Furthermore, high PG II levels were strongly related with subgroup of below age 40 (OR=4.77, p<0.01) and female diffuse GC patients (OR=6.77, p<0.001). By combining PG II with PG I/II ratio, higher ORs were obtained when the young age group with PG II ≥21.1 ng/mL and PG I/II ratio ≥10 were defined as high risk group (OR=18.77, p<0.001).

Conclusion: High PG II levels are associated with the risk of diffuse type GC. Serum PG II ≥21.1 ng/mL and PG I/II ratio ≥3 could be used to identify high risk individuals for diffuse type GC, particularly in young adults in Korea.

References

P0554 CLINICOPATHOLOGICAL IMPACTS OF TP53 AND SMAD4 INACTIVATION IN GASTRIC ADENOCARCINOMA WITH ENTEROBLASTIC DIFFERENTIATION

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Introduction: Gastric adenocarcinoma with enteroblastic differentiation (GAED) is a rare variant of gastric adenocarcinoma characterized by cells with glycojen-rich clear cytoplasm and frequent expression of AFB, Glypican-3 (GPC3) and SALL4 [1-5]. Clinically, GAED shows aggressive behavior characterized by frequent vascular invasion, lymphatic invasion and peritoneal metastasis even in early cancer [6-7]. Last year, our group reported by comprehensively analysis using next generation sequence (NGS) that GAED had high frequency of TP53 mutation associated with p53 overexpression. Furthermore, we also showed that ERBB2 amplification and HER2 overexpression was observed as is seen in conventional gastric adenocarcinoma (GAG) and that Trastuzumab could be used as a therapeutic target therapy in this tumor.

Aims and Methods: This study aimed to further clarify the inactivation mechanism of GAED. In this study, the frequency and prognostic impact of SMAD4 expression and loss of heterozygosity (LOH) of this gene were also assessed, because SMAD4 was identified as one of the frequently deleted genes by copy number variation (CNV) analysis of NGS. We enrolled 51 cases (early-17, advanced-34) of GAED for this study. We performed unger sequence for ATM mutation that were shown to be related to the inactivation of p53, and also evaluated the DNA promoter methylation status of TP53 by methylation-specific PCR (MS-PCR) and LOH analysis of TP53 locus. Furthermore, we evaluated LOH of SMAD4 locus and SMAD4 expression. In addition, we performed immunohistochemistry for SMAD4 and ten-eleven translation (TET)1 related to the methylation of the promoter and examined their clinicopathological correlations. Regarding the frequencies of the genetic alterations, obtained data were compared to those of CGA from TCGA [8].

Results: We found only 1 case of ATM mutation. The frequency of LOH at TP53 locus was 39.2%, and the promoter methylation of TP53 was detected in 20%. Among cases with promoter methylation of TP53, 40% (4/10) did not show p53 overexpression. The frequency of LOH at TP53 was 72.2%, however, the reduced expression of TET1 was not associated with promoter methylation of TP53. LOH at SMAD4 locus was found in 23 cases (45%) and was significantly higher in GAED compared to CGA. SMAD4 mutation was not detected in any case. Reduced SMAD4 expression was found in 18 cases (36%) and was significantly associated with advanced stage of GAED. LOH at SMAD4 locus was not associated with reduced SMAD4 expression. LOH status of SMAD4 locus did not affect patients' overall survival in GAED.

Conclusion: Inactivation mechanism of TP53 other than gene mutations or LOH seemed to be rare in GAED. Frequent TP53 mutation is one of the characteristics of GAED, however, it does not contribute to the aggressive biological behavior in this tumor. In contrast, The LOH rate (45%) of SMAD4 locus in GAED
was significantly higher than that of CGA, suggesting that this locus is one of the signature mutations and is strongly associated with the development of diffuse-type gastric cancer. However, mutation was not detected. Furthermore, dysfunction of SMAD4 seemed to contribute to the acquisition of the aggressive behavior of GAED.

Disclosure: Nothing to disclose

References

4. Ikeda H, Sato Y, Imoneda N, et al. miRNA expression in the process of peritoneal metastasis has not sufficiently elucidated. In this study, we clarified adipocytes enhanced gastric cancer progression of peritoneal metastasis. Aims and Methods: Adipocyte is one of a large fat cell in the omental fat tissue from resected specimen was measured using ELISA and western blot analysis. Matured adipocyte derived from progenitor adipocyte 3T3-L1 was co-cultured with gastric cancer cell MKN45 and OCUM-2MD3. After that, differential markers and cytokines from adipocyte were analyzed using quantitative RT-PCR and fluorescence immunostaining. Results: Adipocytes in the fat tissue adjacent primary tumor revealed lower expression of the genes with low T stage than with high T stage. Adipocytes co-cultured with gastric cancer cell showed decreased expression of adiponectin. PPARγ and C/EBPα as differential marker of adipocytes also decreased. On the other hand, expression of IL-6 and PAI-1 as SAMP (Senescence-associated secretory phenotype) factors were increased in the co-cultured adipocytes. These cells also showed high expression of aSMA as EMT marker and FAP (fibroblast-activated protein) as CAFs (cancer-associated fibroblasts) marker. Conclusion: These results suggest that transformed adipocytes in cancer microenvironment are induced expression of SAMP factors, facilitating tumor growth and invasion. A part of adipocytes might differentiate to fibroblasts and involve formation of peritoneal metastasis in GC.

Disclosure: Nothing to disclose

P0555 THE EXPRESSION OF WNT-SIGNALING PATHWAY COMPONENTS IN DIFFUSE GASTRIC CANCER

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Introduction: The Wnt genes encode a large family of secreted molecules that play important roles in controlling tissue patterning, cell fate and cell proliferation within a broad range of embryonic contexts, including the gastrointestinal tract. Dishevelled (DVL) proteins are the central mediators in this pathway which enable its fine regulation. The interactions of Wnt ligands and Frizzled-related protein and the Wnt receptor interact directly and indirectly to affect Wnt-signaling and influence a wide variety of biological processes, including developmental cell fate, differentiation and tumorigenesis.

Aims and Methods: The aim of the study was to investigate the expression of components of the Wnt - signaling pathway SFRP1, SFRP3, DVL-2 and DVL-3 in diffuse gastric cancer and healthy gastric tissue samples. Samples of 60 diffuse gastric carcinoma and adjacent nontumoral tissues were collected from the Department of Pathology, University Hospital Center Zagreb, Croatia. The tumor tissues were formalin fixed, paraffin embedded. All tumors were studied by pathologists and classified as diffuse gastric carcinoma according to the WHO criteria. Immunohistochemistry was performed in order to establish the levels of Wnt pathway (absent, poor, moderate or intense expression). The amount of Wnt1, Wnt3a, Wnt5a, Wnt6, Wnt7b, Wnt8a, Wnt9a, Wnt10a, Wnt10b, Wnt11, Wnt16, Wnt18, Wnt20 and Wnt22 expression was determined by real-time qPCR. The amount of SFRP1, SFRP3 and DVL-2 expression was determined by immunohistochemistry. The amount of SFRP1, SFRP3 and DVL-2 expression in tumor tissues was higher compared to the one observed in normal tissue. There was no statistically significant difference in the expression of SFRP1 protein expression in normal tissues was higher compared to the one observed in tumor tissue.

Conclusion: Despite some recent advances, gastric cancer remains the third leading cause of cancer-associated death worldwide. This indicates the absence of therapeutic options, stemming from the limited understanding of the molecular mechanisms involved in carcinogenesis. According to our data there is a statistically significant difference in the expression of SFRP1, SFRP3 and DVL-2 between normal gastric tissue and tumor tissues. These results indicate that the expression of Wnt inhibitors and overexpression of Wnt cell fate regulators in tumor tissues may play an important role in gastric carcinogenesis.

Disclosure: Nothing to disclose

P0556 ADIPOCYTES CAN INCREASE THE INVASIVE POTENTIAL OF PERITONEAL METASTASIS FORMATION IN GASTRIC CANCER

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Introduction: According to the progression of gastric cancer (GC), released cancer cells from stomach surface attach to peritoneal mesothelial cells. As the result, peritoneal metastatic nodules occur in omentum and mesentery which contain rich adipocytes. However, the interaction between gastric cancer cells and adipocytes in the process of peritoneal metastasis has not sufficiently
P0558 SAFETY AND EFFICACY OF THE NEW THULIUM / ERBIUM LASER SYSTEM IN PATIENTS WITH GASTROINTESTINAL BLEEDING FROM VASCULAR LESIONS

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2University Medical Center Mainz, Department of Interdisciplinary Endoscopy, I. Medizinische Klinik und Poliklinik, Mainz, Germany
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Introduction: Recent pilot studies ascertained the safety and feasibility of the Thulium/Erbium laser system (TELS) as a new therapeutic tool for endoscopic haemostasis, ablation and resection.

Aims and Methods: We investigated for the first time ever, the safety and efficacy of endoscopic treatment with TELS in patients with gastrointestinal bleeding due to vascular lesions. This single-centre, open-label study prospectively enrolled consecutive patients referring for chronic gastrointestinal bleeding plus moderate/severe anemia due to vascular lesions at IRCCS Policlinico San Donato Hospital between March 2016 and April 2018. Data were collected retrospectively.

The primary endpoints were the safety and the technical success of TELS treatments. As secondary outcomes, we investigated the biological success comparing the lowest haemoglobin values ± 1 month prior to and after treatment, along with the need of packed red blood cells (PRB) transfusions prior to and after treatment. Patients requiring blood transfusions for major comorbidities or surgery not related to gastrointestinal bleeding were ruled out from the assessment of biological parameters. The symptoms and the endoscopic score proposed by Dray X et al.1 were used to evaluate the clinical and endoscopic success in patients with radiation proctitis (RP). A new scoring system was developed to assess the severity and the endoscopic success of TELS in gastric antral vascular ectasia (GAVE; 3–5 points according to a relative mucosal involvement <30%, 30–50% or >50%, respectively plus 3 or 5 points for traces of blood or active bleeding). For each procedure, image/video documentations and TELS technical parameters (i.e., lasing time, power output and total energy employed) were recorded. The Wilcoxon signed rank test was employed to challenge the quantitative results obtained.

Results: 11 patients underwent 16 endoscopic treatments with the TELS according to the diagnosis of GAVE (4 pts and 8 procedures), angioectasias (4 pts and 4 procedures) and RP (3 pts and 4 procedures). All procedures resulted in a complete technical success, thereby succeeding the primary study endpoints. According to preliminary data available in April 2018, haemoglobin values showed a significant rise (ΔgaveRp=±1month=+1.6 g/dl, 95% CI = 0.45–3.20, p-value = 0.008) along with a decreased need of PRB transfusions (ΔgaveRp=±6months=−5 units, 95% CI = 1–9; p-value = 0.046). Consistently, the median values of GAVE endoscopic severity and of RP-related symptoms improved (from 5 to 2 and from 3 to 1 respectively), while preliminary data on RP endoscopic severity showed no remarkable changes in terms of severity of residual lesions. The median Thulium/Erbium power output adopted during treatments were 6/2W, 5/1W and 5/2W with a median laser time equal to 53,3%, 1,56% and 3.45% accounting for a median total energy of 1676/414 J, 675/193 J and 1024/417 J for GAVE, angioectasias and RP, respectively.

Conclusion: This pilot study conducted in real-life setting suggests the TELS as a safe and effective tool for the endoscopic luminal treatment of patients with gastrointestinal bleeding caused by various types of superficial vascular lesions. Our data further confirmed the manoeuvrability of this new therapeutic tool, which mostly enables a complete eradication of large vascular lesions within few endoscopic procedures. Randomized-controlled studies involving established endoscopy techniques for haemostasis and ablation of gastrointestinal vascular lesions in larger cluster of patients are now warranted.

Disclosure: Nothing to disclose

Reference

P0559 IS GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION FEASIBLE UNDER THE DIRECT ORAL ANTICOAGULANTS ADMINISTRATION?

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Introduction: Several studies have reported that anticoagulant therapy on gastric endoscopic submucosal dissection (ESD) increases the risk of postoperative bleeding [1, 2]. Previously, we have reported that the continuous warfarin administration does not increase the bleeding risk after gastric ESD compared to intravenous heparin bridge therapy (HBT) [3]. Currently, direct oral anticoagulants (DOAC) have been frequently used for the prevention and treatment of cardiovascular diseases instead of warfarin. Therefore, we investigated the effect of DOAC for postoperative bleeding after gastric ESD in comparison with those of warfarin and HBT.

Aims and Methods: A total of 89 gastric neoplasms in patients with anticoagulant therapy were treated with ESD at New Tokyo Hospital between September 2008 and December 2017. 37 out of 89 patients underwent gastric ESD with continuous warfarin, 27 done with intravenous HBT, and 20 done with DOAC. In patients with continuous warfarin, the dose of warfarin was controlled to maintain the PT-INR under 3.0. Patients with DOAC were treated with interrupted DOAC on the day of ESD. We assessed the clinical findings and outcomes of gastric ESD with anticoagulant therapy.

Results: The rates of complete en bloc resection were 100% in the continuous warfarin group and the HBT group, and 95.6% in the DOAC group (p = 0.238). The rates of postoperative bleeding were 10.8% in the continuous warfarin group, 18.5% in the HBT group, and 15.0% in the DOAC group (p = 0.562). All bleeding events were successfully managed with endoscopic hemostasis. One patient in the HBT group developed a delayed perforation resulting from an emergency surgery. The period of hospitalization was higher in the HBT group than in the other 2 groups (median [IQR], 13 [11–16] days in HBT, 6 [5–7] days in continuous warfarin, 6 [5–8] days in DOAC; p < 0.001).

Conclusion: The bleeding rate was not statistically different in the 3 groups. Gastric ESD under the DOAC administration was considered to be feasible and acceptable.

Disclosure: Nothing to disclose

References

P0560 QUANTIFYING EXCESS CARDIO-RESPIRATORY EVENTS AND ADMISSIONS FOLLOWING DAY CASE DIAGNOSTIC GASTROSCOPY

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Introduction: Age-stratified estimates of adverse events after endoscopy will influence local decisions about appropriate investigation in those at high risk. We have quantified the absolute risks of cardiovascular and respiratory events in both primary and secondary care following day case diagnostic gastroscopy.

Aims and Methods: Patients undergoing day case diagnostic gastroscopy were identified in the English population from the linked hospital data in the Clinical Practice Research Datalink, and frequency matched with replacement on decade of birth to 4 times as many controls from this population, who were alive and registered at the time of the endoscopy. Follow up was censored on the earliest of: diagnosis of cancer, subsequent interventional procedure, emergency hospital admission, transfer out the study population, or death. The first acute event of cardiac, cerebrovascular, or respiratory disease was identified in the 30 days after either the endoscopy or matched index date.

Abstract No: P0560: Baseline characteristics and therapeutic outcomes in patients with anticoagulant therapyDOAC, direct oral anticoagulants; HBT, heparin bridge therapy

<table>
<thead>
<tr>
<th>Age, mean ± SD, y</th>
<th>78.0 ± 5.5</th>
<th>73.0 ± 7.8</th>
<th>77.0 ± 7.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male), n (%)</td>
<td>31 (83.8)</td>
<td>24 (88.9)</td>
<td>18 (89.0)</td>
</tr>
<tr>
<td>CHADS2 score</td>
<td>3 (2–3)</td>
<td>1 (1–2.5)</td>
<td>3 (2–3)</td>
</tr>
<tr>
<td>Specimen size, median (IQR), mm</td>
<td>31 (25–36)</td>
<td>33 (27–42)</td>
<td>34 (27–39)</td>
</tr>
<tr>
<td>Complete resection, n (%)</td>
<td>37 (100.0)</td>
<td>27 (100.0)</td>
<td>19 (95.0)</td>
</tr>
<tr>
<td>Postoperative bleeding, n (%)</td>
<td>4 (10.8)</td>
<td>5 (18.5)</td>
<td>3 (15.0)</td>
</tr>
<tr>
<td>Hospitalization, median (IQR), days</td>
<td>6 (5–7)</td>
<td>13 (11–16)</td>
<td>6 (5–8)</td>
</tr>
</tbody>
</table>

Continued warfarin (n = 37) | HBT (n = 27) | DOAC (n = 20) | P value |

0.015 | 0.722 | < 0.001 |

0.238 | 0.672 | < 0.001 |
from linked primary care consultations, underlying cause on death certificates, or the main diagnosis from emergency hospital admissions. The age-stratified risks following day case diagnostic gastroscopies were estimated from a Cox regression model adjusted for age, gender and pre-existing co-morbidity. Then excess risks were calculated, adjusted for censored and competing events, by using cumulative incidence functions derived from this Cox model.

Results: 307,925 day-case diagnostic gastroscopies were identified (among 248,217 people) with 13,411 cardiovascular or respiratory events within 30 days, of which 6,820 were emergency admissions and 351 were deaths. A total of 1,584,660 matched index dates were identified (among 1,074,214 unique controls) with 51,681 cardiovascular or respiratory events within 30 days, of which 4,769 were emergency admissions and 1,105 were deaths. After adjusting for age, gender, co-morbidity, and competing events, the absolute predicted risk for a cardiovascular or respiratory event within 30 days of a gastroscopy procedure was 2.2% for those under 30 years and 8.5% for those 80 years and older (table 1). This translated to an absolute excess risk over the calculated prediction of 1.0% (< 30 years) to 2.5% (< 80 years) respectively. Having a day-case diagnostic gastroscopy was correspondingly associated with an overall 2.1-fold relative increase in risk of cardiovascular or respiratory admissions (95% confidence interval 2.0–2.2, adjusted for age and gender), which was reduced to 1.9-fold (1.8–2.0) after adjusting for pre-existing co-morbidity.

Conclusion: This study showed an important excess risk of acute cardiovascular and respiratory events in primary and secondary care following day-case diagnostic gastroscopy compared to the general population. The excess risk of such an event was 1 in 100 procedures for those under 30 years of age and 1 in 40 procedures for those aged 80 or over. Almost 1 in 50 of those over 80 experienced an additional event which required hospital admission. We believe this information will be of value to clinicians deciding on whether to request routine tests, and patients in the consent process.

Disclosure: Clinical Practice Research DataLink Copyright © (2017), re-used with the permission of The Health & Social Care Information Centre. All rights reserved. This study is based in part on data from the Clinical Practice Research DataLink obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support. The interpretation and conclusions contained in this study are those of the authors alone.
The average age was slightly older in the ASL (65.9 ± DS vs AO 64.4 ± DS 19.6). The number of patients with variceal bleeding discharged from AO was: 199/1176 (16.9%) vs 198/2192 (6.6%) p < 0.000. The overall mortality rate in the two healthcare settings was similar: 8.0% in AO vs 6.7% in ASL Pr (95% CI 3.2 to 7.0) and hospitalization in AO and in Gastroenterology Unit OR (95% CI 1.98 to 4.06), while protection factors were discharged from a Gastroenterology Unit OR 4.77 (95% CI 3.2 to 7.0) and hospitalization in AO and in Gastroenterology Unit OR 9.6 (95% CI 9.3 to 9.9).

Conclusion: AO hospital facilities present the same mortality rate as ASL ones. The hospital stay in Gastroenterology Units reduce all mortality cases and was similar in both AO and ASL. Mortality in non-gastroenterology unit both in AO and ASL is similar.

Mortality Overall
11.2% 4.5% 6.9% 5.3% p < 0.001

Mortality Non Variceal
9.4% 3.8% 6.5% 4.2% p < 0.002

Disclosure: Nothing to disclose

P0563 SIMPLIFIED ‘PURE’ ENDOSCOPIC TECHNIQUE OF PEG-J-PLACEMENT IN ADVANCED PARKINSON’S DISEASE- A RETROSPECTIVE SINGLE-CENTER STUDY

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Introduction: Levodopa is absorbed mainly in the upper intestine and is metabolized rapidly, consequently requiring frequent applications. Continuous levodopa/carbidopa infusion straight to the proximal jejunal via percutaneous endoscopic gastrostomy with jejunal extension tube (PEG-J) connected to a portable infusion pump has emerged as a promising tool in the treatment of Parkinson’s disease (PD).

Aims and Methods: We aim to assess effectiveness and safety of PEG-J placement under direct endoscopic control and with no additional imaging tools in patients with Parkinson’s disease.

Study group includes 76 patients with advanced PD who underwent PEG-J placement in the period of June 2014 - February 2018. In all patients, a nasojejunal tube was inserted initially to assess levodopa-carbidopa efficacy and dosage. After a short period of time (4-7 days) PEG-J (Freka® PEG CH15, and Freka® CH15 Intestinal Tube for CH15 PEG) was placed under i.v. propofol infusion. Peri interventional drug prophylaxis included antibiotic, proton pump inhibitor and antiepileptics.

All patients underwent placement of both PEG tube (via the pull method) and J-tube in a single procedure. J-tube placement technique used was grabbing the tube tip with forceps and advancing it along with the endoscope into the distal duodenum. The scope was then slowly withdrawn into the stomach while the forceps is advanced blindly to hold the tip of the J-tube in place. Finally J-tube was advanced approximately 80–90 cm in the jejunum. No fluoroscopy, nor any other imaging tool was used to determine accurate J-tube position. Patient’s clinical response to levodopa/carbidopa infusion indicated procedure effectiveness.

Results: PEG-J was successfully placed in all patients, confirming high technical effectiveness of the PEG-J endoscopic guidance placement method.

No single serious adverse event has been reported in 48-hours postoperative clinical observation period. Additionally, there was no need of J-tube reposition in any of the patients. We registered 1.52% late complications (within one month after procedure): a case of mesenterial thrombosis and another one of C. difficile colitis, both requiring hospital admission. Both patients were successfully treated and discharged.

Conclusions: Endoscopic guided PEG-J placement with ‘blind’ jejunal extension insertion is a highly effective, fast and simple procedure with limited adverse events. Clinical response to levodopa/carbidopa is suitable and sufficient indicator for accurate jejunal positioning. Further, PEG-J placement followed by continuous levodopa/carbidopa infusion was associated with improvement in quality of life and clinical symptoms in PD patients with advanced disease.

Disclosure: Nothing to disclose

References

P0564 GASTROINTESTINAL SYMPTOMS IMPACTING ON QUALITY OF LIFE: A COMPARATIVE COHORT STUDY IN PATIENTS WITH ORGANIC AND FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS) IN THE TERTIARY HOSPITAL OUTPATIENT SETTING

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2 Australian Gastrointestinal Research Alliance, Newcastle, Australia
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Introduction: For many gastrointestinal (GI) diseases the severity of the impairment of Quality of life (QoL) is a key driver for health care utilisation and health care costs. However, very little is known about the extent of the impact of specific GI symptoms on QoL in different patient cohorts.

Aims and Methods: We aimed to determine and compare the proportion of patients with severe or very severe impairment of QoL due to specific GI symptoms in patients with selected highly prevalent GI diseases in the outpatient setting of a tertiary hospital. From a cohort of 10,000 consecutive occasions of service (OOS) of patients presenting during a 12 month period at a tertiary teaching hospital in Brisbane we identified patients with Functional gastrointestinal disorders (FGIDs), inflammatory bowel diseases (IBD) including Crohn’s disease (CD) and ulcerative colitis (UC) and celiac disease (CeD). In addition, we included patients with cured hepatitis C infection as ‘controls’. The records of patients with one of the above primary diagnoses documented in the electronic medical record were reviewed and analysed. At each OOS the patients had completed the validated Structured Assessment of Gastrointestinal Symptoms (SAGIS) to capture the severity of symptoms. SAGIS assesses the severity of symptoms on a 5-point scale with the 2 most severe defined as ‘severe…influence daily activity’ and ‘very severe symptoms:…markedly influence daily activities and/or require rest…’. Prevalence rates and the 95% confidence intervals for postprandial pain, epigastric pain, constipation, diarrhea and, pain and discomfort during defecation and bloating were determined.

Results: Out of the total of 10,000 OOS, we identified 1,157 patients with CD, 936 with UC, 999 with FGIDs, 173 with cured HCV, 136 with CeD and 173 with cured HCV. The proportion of OOS when patients reported severe or very severe impairment of QoL due to specific GI symptoms was highest in FGID patients. Even for symptoms that were frequently observed in patients with IBD (e.g. diarrhea, pain or urgency during defecation), the proportion of patients with severe or very severe symptoms was substantially higher in FGID patients.

Conclusion: Measured by the proportion of patients reporting severe or very severe impairment of QoL by specific GI symptoms is highest in patients with FGIDs. Overall the symptom ‘bloating’ was reported by 40% of FGID patients as severely impacting QoL. The burden of the symptom diarrhea

Abstract No: P0564: Baseline characteristics and therapeutic outcomes in patients with anticoagulant therDOAC, direct oral anticoagulants, HBT, hepatic bridge therapy

<table>
<thead>
<tr>
<th>Cured HCV</th>
<th>Cancer (n = 150)</th>
<th>Ulcer (n = 150)</th>
<th>CeD (n = 150)</th>
<th>CD (n = 150)</th>
<th>UC (n = 936)</th>
<th>FGIDs (n = 999)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post prandial pain</td>
<td>4.0 (1.6–8.2)</td>
<td>14.0 (5.5–15.2)</td>
<td>8.8 (4.6–14.9)</td>
<td>9.5 (3.6–19.5)</td>
<td>4.8 (3.5–6.4)</td>
<td>28.7 (25.9–31.6)</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>3.5 (1.3–7.4)</td>
<td>10.5 (5.7–16.0)</td>
<td>6.6 (3.1–12.2)</td>
<td>8.4 (6.9–10.1)</td>
<td>4.3 (3.1–5.8)</td>
<td>25.2 (22.6–28.0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.0 (1.6–8.2)</td>
<td>8.7 (4.7–14.4)</td>
<td>5.1 (2.1–13.9)</td>
<td>16.2 (14.1–18.4)</td>
<td>11.1 (9.2–13.3)</td>
<td>22.4 (19.9–25.1)</td>
</tr>
<tr>
<td>Constipation</td>
<td>4.0 (1.6–8.2)</td>
<td>8.7 (4.7–14.4)</td>
<td>10.3 (5.7–16.7)</td>
<td>4.8 (3.7–6.2)</td>
<td>4.3 (3.1–5.8)</td>
<td>20.3 (17.9–23.3)</td>
</tr>
<tr>
<td>Pain: discomfort at defaecation</td>
<td>4.0 (1.6–8.2)</td>
<td>10.5 (5.7–16.0)</td>
<td>11.8 (6.9–18.4)</td>
<td>12.2 (10.4–14.2)</td>
<td>11.5 (9.6–13.8)</td>
<td>28.2 (25.3–31.1)</td>
</tr>
<tr>
<td>Bloating</td>
<td>3.5 (1.3–7.4)</td>
<td>11.3 (6.7–17.5)</td>
<td>16.2 (10.4–23.5)</td>
<td>13.1 (11.2–15.1)</td>
<td>9.1 (7.3–11.1)</td>
<td>40.4 (37.4–43.6)</td>
</tr>
</tbody>
</table>
was significantly more severe in FGID patients as compared to patients with IBD. This high disease burden in patients with FGID likely reflects the lack of effective therapies in FGID.

[Prevalence of severe and very severe symptoms in various patient cohorts.]

Disclosure: Nothing to disclose

MONDAY, OCTOBER 22, 2018 09:00-17:00

H. Pylori l - Hall X1

P0565 INCREASE OF BMI AND DECREASE OF SERUM LEVEL OF LIPOPROTEIN WITHOUT CORRESPONDING CHANGE OF DAILY INTAKE OF NUTRIENT IN JAPANESE FEMALES

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Introduction: In western populations, increase of body mass index (BMI) has been shown after successful eradication of H. pylori infection. However, influence of H. pylori eradication on nutritional intake has not been well studied. Since Japanese health insurance system approved eradication therapy for all infected patients, there has been significant increase in the number of subjects who receive eradication of H. pylori without dyspeptic symptoms. The aim of this study was to investigate the influence of H. pylori eradication on nutritional metabolism considering daily nutritional intake in a Japanese population.

Aims and Methods: We recruited adult who received eradication survey both in 2012 and 2014 and entered into the study. We measured H. pylori stool antigen (Testmate EIS) and titer of serum antibody to H. pylori (E-plate). Subjects were considered as H. pylori-infected when positive stool antigen test and/or serum antibody titer >100U/mL were observed. Non-infected subjects were defined as negative stool antigen test, serum antibody titer of < 3 U/mL and without past history of eradication therapy. Patients who received successful eradication after the survey in 2012 and diagnosed as non-infected in 2014 were considered as eradicated and those who were still positive in 2014 were considered as non-eradicated. Subjects who were diagnosed as infected in both 2012 and 2014, as control (persistent infection) group. Subjects who were taking PPI and/or had previous history of gastric surgery were excluded. Daily intake of lipid and carbohydrate during one month prior to the survey was calculated using a brief-type comprehensive self-administered diet history questionnaire. Change of daily intake of nutrients, BMI, serum level of lipid and HbA1c were compared for between eradicated group and control group.

Results: Daily intake of lipid and carbohydrate was not different between 2012 and 2014 in both male and female in 33 eradicated patients and 66 control subjects. In female eradicated patients, BMI was significantly increased from 22.1±3.3 to 22.4±3.5 (p = 0.022) while serum level of HDL-C and LDL-C decreased from 75.9±13.7 to 71.0±15.0 mg/dL and 125.8±26.2 to 119.3±27.9 mg/dL, respectively (p = 0.003 and p = 0.021). In eradicated male and control subjects, no significant change were observed in BMI and serum levels of lipid. HbA1c was not changed in both male and female in both groups. Compared to subjects without dyspeptic symptoms, increase of BMI and decrease of serum level of HDL-C and LDL-C were observed after eradication of H. pylori without corresponding changes of daily intake of lipid and carbohydrate.

Disclosure: Nothing to disclose

P0566 RACK1 IS A NEW REGULATOR IN THE NF-κB SIGNALING PATHWAY INDUCED BY HELICOBACTER PYLORI INFECTION

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Introduction: The receptor of activated protein kinase C 1 (RACK1, GN2BL1) is a 36-kDa cytosolic protein involved in multiple physiology and pathology processes. The receptor Indicated RACK1 was an anti- oncogene in gastric cancer, herein, we aimed to investigate the relationship between Helicobacter pylori (H. pylori) infection, proinflammatory NF-κB activation and RACK1.

Aims and Methods: The study used in vivo and in vitro experiments. TCGA data base analysis, tissue microarrays, luciferase reporter, quantitative real-time PCR, Western Blot, immunofluorescence, chromatin immunoprecipitation sequence, H. pylori infection, and immunohistochemical assays were used.

Results: Western Blot analysis of gastric cancer indicated RACK1 protein level was lower in the H. pylori positive gastric cancer group in comparison with H. pylori negative gastric cancer group. Our results indicated that H. pylori infection increased RACK1 mRNA expression and decreased RACK1 protein levels in gastric cancer cells, gastric atrophy of mice and gastric cancer tissues. H. pylori infection increased the activity of NF-κB reporter and p-NF-κB (Ser 536) protein level in vitro and in vivo. Moreover, the overexpression of RACK1 inhibited the activation of NF-κB signaling pathway induced by H. pylori infection, as determined by Western Blot, PCR, luciferase reporter assays. Immunohistochemistry analysis demonstrated a significant positive correlation between IkBα and RACK1 expression levels (r² = 0.762, p < 0.01) and a significant negative correlation between NF-κB and RACK1 expression levels (r² = 0.762, p < 0.05) in gastric mucosa.

Conclusion: RACK1 is a new regulator in NF-κB signaling pathway induced by H. pylori infection. The decreased expression of RACK1 following H. pylori infection and activation of NF-κB provides a link between infection, inflammation and gastric tumorigenesis.

Disclosure: Nothing to disclose

P0567 ENTEROENDOCRINE CELL COMPARTMENT SIZE DECREASES DURING H. PYLORI INFECTION IN PATIENTS WITH INTESTINAL METAPLASIA BUT IS RESTORED AFTER ERADICATION

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Introduction: Gastric cancer, the fifth leading cause of cancer, develops following Correa’s cascade: well defined steps involving several premalignant lesions, the most common of which is intestinal metaplasia (IM). The mechanism by which these premalignant lesions develop and progression is driven is largely unknown. The largest risk factor for development of both IM and gastric cancer infection is infection with the pathogen Helicobacter Pylori (HP). One of the theories is that HP-associated inflammation causes a disbalance of gastric hormone levels by causing destruction of the somatostatin-producing D-cell compartment. This in turn would cause a relative increase of gastrin which has several proliferative and pro- oncogenic effects. In this study we determine the effect of both HP and eradication on the enteroendocrine cell compartments of the antral stomach in patients with intestinal metaplasia.

Aims and Methods: Antral gastric biopsies were taken systematically in a surveillance cohort of patients with IM or gastric atrophy (PROREGAL Cohort). HP positivity was determined by serology and histology. Patients were scored as endoscopically negative for IM and histologically negative for IM. A sample of patients with normal IM and HP was used as control group. Patients were extracted adjusting sex and age from subjects who were diagnosed as infected in both 2012 and 2014, as control (persistent infection) group. We included 24 HP-negative patients and 23 biopsies from patients infected with HP. Of the HP infected patients, also biopsies were obtained 1 year after successful eradication of HP. Immunohistochemical staining of G-cells and D-cells was performed using anti-gastrin and anti-somatostatin antibodies respectively. The number of positive cells per high power field were counted and intensity of staining was scored. Means of 4 biopsies were calculated using the Aldred score. Significance was determined using students T-test.

Results: As expected, antral biopsies from IM patients show patches of IM as well as normal crypts. In IM both the G-cell (p < 0.0001) and D-cell (p = 0.0002) compartments are reduced as compared to non-IM crypts. In patients infected with HP, total D-cell numbers were significantly reduced as compared to patients without HP (p = 0.0001), in line with findings described in literature. Unexpectedly however, we also observed a significant reduction of G-cells in IM patients with active HP infection (p = 0.0008). Interestingly, 1 year after eradication, this reduction in enteroendocrine cell compartment size was no longer apparent and both D-cell and G-cell levels were normalized to the levels seen in patients that have never been infected. Enteroendocrine cell compartment size is not associated with either progression or regression of gastric premalignant lesions in this cohort.

Conclusion: These results confirm previous studies showing that HP infection causes a reduction in the antral D-cell compartment in IM crypts. However, we further demonstrate that this reduction is not restricted to D-cells, but also affects antral G-cells. After eradication of HP, enteroendocrine cell compartments return to sizes comparable to non-infected patients even though the gastric premalignant lesions persist. These results suggest that antral G-cell compartment size is of minor importance in early gastric carcinogenesis.

Disclosure: Nothing to disclose

Reference

P0568 PEPSINOGEN I/II RATIO IS AN EXCELLENT BIOMARKER TO ESTIMATE THE GRADE OF GASTRIC ATROPHY IN BOTH HELICOBACTER PYLORI-INFECTED AND NONINFECTED SUBJECTS: OPTIMAL CUTOFF POINT TO IDENTIFY SEVERE ATROPHIC GASTRITIS

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Introduction: Atrophic gastritis is one of the most important clinical manifestations of Helicobacter pylori (HP) infection. To know grade of atrophic gastritis is valuable for estimating not only gastric cancer risk but also gastric acid-related diseases. Pepsinogen I is secreted by chief and mucus neck cells in the fundic glands, whereas pepsinogen H is also secreted by cells in the pyloric and Brunner's glands. When atrophic changes develop to the corpus, the level of pepsinogen I decreases, whereas the level of pepsinogen II remains high or stable. Therefore, pepsinogen I/II ratio decreases in a stepwise manner. We
aimed to evaluate the adequacy of measuring pepsinogen I/II ratio as a non-
invasive maker of grade of atrophic gastritis.

Aims and Methods: A total of 959 consecutive subjects who underwent esophagastroduodenoscopy and measurement of serum pepsinogen level at the same day were enrolled. To avoid the influence to pepsinogen levels, the following subjects were excluded: those who had received successful HP eradication therapy in the past, (2) those who had undergone gastrectomy, (3) those who were taking proton pump inhibitors for various reasons, and (4) those having renal failure (Creatinine > 3.0 mg/dl). HP infection status was determined by the titers of serum HP IgG (E plate). Endoscopic grades of atrophic gastritis were classified into three groups: none to mild (C-0 and C-1), moderate (C-2 and C-3), and severe (O-1, O-2, and O-3) using the Kimura-Takemoto Classification. The correlation of pepsinogen I/II ratio with endoscopic grade of atrophic gastritis was evaluated by Kruskal-Wallis test. Receiver operating characteristic (ROC) curves were constructed to evaluate the diagnostic accuracy of pepsinogen I/II ratio in discriminating severe atrophic gastritis (≥ O-1 atrophy) and to extract the corresponding cutoff value for severe atrophic gastritis (≥ O-1 atrophy).

Results: Subjects comprised 246 males, with a mean age of 50.22. Of the enrolled subjects, 236 had HP IgG positive test results, whereas the remaining 723 had HP IgG negative test results. Significant correlation between pepsinogen I/II ratio and endoscopic grade of atrophic gastritis was found in both HP-infected and noninfected subjects (P < 0.001 in both comparisons). ROC curves were used to assess the diagnostic accuracy of pepsinogen I/II ratio for discriminating severe atrophic gastritis. The areas under the curve (95% confidence intervals) were 0.93 (0.91–0.96) in the entire cohort, 0.91 (0.75–0.86) in the HP infected subjects, and 0.88 (0.80–0.95) in the HP noninfected subjects, respectively. In the HP infected subjects, a pepsinogen I/II ratio of 2.3 was indicated to be best cutoff value for predicting severe atrophic gastritis, with a sensitivity of 90.6% and specificity of 67.6%. Meanwhile, in the HP noninfected subjects, a pepsinogen I/II ratio of 4.9 was indicated to be best cutoff value for predicting severe atrophic gastritis, with a corresponding sensitivity of 73.1% and specificity of 87.5%. Conclusion: The presence of a significant correlation between pepsinogen I/II ratio and endoscopic grade of atrophic gastritis. In ROC analysis, pepsinogen I/II ratio is indicated to be an excellent biomarker to estimate the grade of atrophic gastritis. Clinical use of pepsinogen I/II ratio as a surrogate biomarker to estimate the grade of atrophic gastritis but also assessing longitudinal changes in gastric atrophy of each patient.

Disclosure: Nothing to disclose

P0569 APPLICATION OF CONVOLUTIONAL NEURAL NETWORKS IN THE DIAGNOSIS OF HELICOBACTER PYLORI INFECTION STATUS BASED ON ENDOSCOPIC IMAGES

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Introduction: We recently reported the role of artificial intelligence in the diagnosis of Helicobacter pylori infection status based on endoscopic images. This study showed that the ability of the convolutional neural network (CNN) was comparable to experienced endoscopists, and diagnostic time was considerably shorter (EBioMedicine 2017). However that study includes only H. pylori-positive and negative cases, and excluded eradicated tests.

Aims and Methods: In this study, we constructed CNN, and evaluated its ability to diagnose H. pylori infection status, that is H. pylori positive, negative, or eradicated. We performed standard esophagastroduodenoscopy (EGD) and captured the endoscopic images. Clinical diagnosis of H. pylori infection status based on endoscopic images. This study showed that the ability of the convolutional neural network (CNN) was comparable to experienced endoscopists, and diagnostic time was considerably shorter (EBioMedicine 2017). However, that study includes only H. pylori-positive and negative cases, and excluded eradicated tests.

Results: The trained CNN output a continuous number between 0 and 1 and the probability index for H. pylori infection status per image (Pp) for H. pylori-positive, Pn for negative, and Pe for eradicated. (Pp + Pn + Pe = 1). Most probable (largest number of Pp, Pn, and Pe) of the 3 infectious status was selected as the prediction of the CNN. Among 2369 images, the CNN diagnosed as positive for 418, negative for 2304, and eradicated for 247 images, respectively. Among the 655 cases the CNN diagnosed negative for all the images, 46 cases (71%) were negative for H. pylori. While among the remaining 192 cases the CNN diagnosed as positive or eradicated for at least 1 image, 165 cases (86%) were also positive or eradicated for H. pylori. As for the 119 cases the CNN diagnosed as eradicated for at least 1 image, 83 (70%) were H. pylori-eradicated. Time needed to diagnose 2369 images was 261 seconds.

Conclusion: H. pylori infection could be diagnosed based on endoscopic images of the stomach in a considerably short time. It was suggested that the CNN can be introduced to aid endoscopists in diagnosing H. pylori infectious status.

Disclosure: Nothing to disclose

P0570 THD FECAL TEST FOR NON-INVASIVE HELICOBACTER PYLORI DETECTION: A DIAGNOSTIC ACCURACY STUDY

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Introduction: We aimed to assess THD fecal test diagnostic accuracy for detecting Helicobacter pylori infection. 23S rRNA subunit gene indicated infection. We also used the index diagnostic test to examine mutations conferring resistance to clarithromycin and levofloxacin. Independent investigators analyzed index test and reference test standard results blinded to the other test findings. We estimated sensitivity, specificity, positive (PPV) and negative (NPV) predictive value, diagnostic accuracy, positive and negative likelihood ratio (LR), together with 95% confidence intervals (CI).

Results: We employed 294 consecutive participants (age: median 37.0 years, IQR 29.0–46.0 years; men: 29.8%). 95 (32.3%) participants had a positive13C-urea breath test. 23 (7.8%) participants older than 50 years performed upper endoscopy with histology. There was full concordance between13C-urea breath test and histology in detecting Helicobacter pylori infection in these participants.

Aim: To evaluate the diagnostic accuracy of the THD fecal test by comparing the results with endoscopy and histology.

Aims and Methods: We conducted a prospective two-center diagnostic test accuracy study. We enrolled consecutive people ≥ 18 years without previous diagnosis of H. pylori infection. Participants were referred for endoscopy between February and October 2017. At enrolment, all participants underwent13C-urea breath test. Participants aged over 50 years were scheduled to undergo upper endoscopy with histology. Participants collected stool samples 1 days after enrolment for THD fecal testing. The detection of bacterial 23S rRNA subunit gene indicated infection. We also used the index diagnostic test to examine mutations conferring resistance to clarithromycin and levofloxacin. Independent investigators analyzed index test and reference test standard results blinded to the other test findings. We estimated sensitivity, specificity, positive (PPV) and negative (NPV) predictive value, diagnostic accuracy, positive and negative likelihood ratio (LR), together with 95% confidence intervals (CI).

Conclusion: The THD fecal test has high performance forn-invasive diagnosis of Helicobacter pylori infection while additionally enabling assessment of bacterial antibiotic resistance.

Disclosure: We thank THD Spa, Correggio (Italy), for providing free of charge THD fecal test for all participants included in the study.

P0571 ENDOSCOPIC DIAGNOSIS OF HELICOBACTER PYLORI BASED ON THE ARRANGEMENT OF COLLECTING VENULES IN A EUROPEAN POPULATION


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Introduction: Helicobacter pylori (Hp) is the major cause of gastritis and gastrointestinal diseases. The development of high definition endoscopy in recent years has allowed a better characterization of the gastric mucosa and the identification of endoscopic findings that correlate with the diagnosis of Hp. One of the features that has shown better results is the detection of a regular arrangement of collecting venules (RAC) of the mucosa in the lower part of the gastric body. The presence of RAC has a sensitivity and negative predictive value (NPV) higher than 90% in Hp infected patients, but most of the studies have been conducted in Asian population and we do not know their reproducibility in our population.
Aims and Methods: The aim of the study was to evaluate the value of the arrange-
mnt of capturing venules as a diagnostic method of H. pylori infection in our
population. Secondary objective was to assess whether age, sex, concomitant antipallet-
therapy, anticoaguants or non-steroidal anti-inflammatory drugs, or history of HP
infection influences the prevalence of the infection. Retrospective analysis of a
respectively collected database of patients who underwent upper gastrointestinal
endoscopy from February 2017 to March 2018. The inclusion criteria were:
age over 18 years, absence of treatment by proton pump inhibitors in the last 10
days, and absence of a history of gastrectomy, gastric lymphoma or portal hypo-
tension. We excluded those patients with presence of blood or food in gastric
lumen that precluded an adequate exploration of the mucosa.
Explorations were performed with high-definition endoscopes by three expert
endoscopists and under sedation by anesthesiologist. The RAC pattern was
defined as the presence of starfish-like minute points regularly distributed
throughout the lesser curvature of the gastric body. We considered significative
endoscopic findings the presence of erosive gastroduodenal lesions, atrophic
gastritis, intestinal metaplasia and gastric polyps. Pictures were taken during
the procedure. The gold standard tests for H. pylori infection were the anatomicopatho-
logical study and/or rapid urease test.
Results: 111 patients were included with an Hp infection rate of 29.73%. 37 of
111 patients (33.3%) presented a RAC pattern. No differences were observed in
RAC prevalence regarding to sex, concomitant treatment or previous history of
HP eradication. In contrast, the mean age of patients with RAC pattern was lower
(45 vs 53 years; p = 0.01) and had less significative endoscopic findings
(43% vs 65%, p=0.03).
None of the patients with H. pylori presented RAC pattern. Contrarily, the RAC
pattern was observed in all unaffected patients. Performance characteristics
endoscopic diagnosis of H. pylori based on the arrangement of collecting venules
pattern were: sensitivity 100% (CI 87%-997%), specificity 47.4% (CI 36.1%–
59%), negative predictive value 100% (CI 88.3%-99.7%) and positive predictive
value 44.6% (CI 33.2%-35.6%).
Conclusions: Careful observation of the gastric mucosal pattern in lower curvature
with high-definition endoscopy can accurately predict H. pylori infected cases when
RAC is present, avoiding the obtainment of biopsies.
Disclosure: Nothing to disclose
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P0572 COMPARISON OF STOOL ANTIGEN TEST MONOLAB®
WITH UBT BREATH TEST FOR DIAGNOSIS OF HELICOBACTER
PYLORI INFECTION

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Introduction: According to current clinical guidelines, the stool antigen test (SAT)
method is the reference method for the diagnosis of H. pylori infection. A new
Helicobacter pylori (H. pylori) infection, provided a monoclonal laboratory
test (ELISA) is used. Since 2015 the Monolab Test, which is not an ELISA test
but an immunomorphometric monoclonal method has been incorporated to
our regional health system.
Aims and Methods: The aim of the present study was to compare the diagnostic
accuracy of SAT Monolab Test and UBT, considering UBT the gold standard.
A prospective multicentre study (Hospital Reina Sofia in Tudela -HRS- and
Complejo Hospitalario de Navarra in Pamplona -CHN-) was performed in con-
secutive patients since November 2016 (HRS) and June 2017 (CHN) until
October 2017. All patients who were submitted to gastroenterology outpatient
clinic to perform a UBT according to standard clinical practice were enrolled and
SAT was simultaneously determined. Sensitivity, specificity, positive and
negative predictive values (NPV and PPV respectively) adjusted to prevalence
were determined, and SAT accuracy was compared with UBT.
Results: 450 patients, 183 CHN and 267 HRS were included, with the features
detailed in table 1. Both tests were performed for initial diagnosis of infection
in 230 cases and to check the efficacy of eradication treatment in 220. The preva-
ience of H. pylori infection was 35% before treatment and 12% after eradication
therapy. Concordance between SAT Monolab test and UBT was 78% (sensitivity
82%, specificity 77%), with a kappa index of 0.51 (moderate concordance).
Before treatment, NPV was 89% for PPV 89%, whereas after eradication ther-
apy PPV was 34% and NPV 97%.
Conclusion: Compared with the diagnostic reference test, UBT, the AGH
Monolab test differs in the diagnosis of H. pylori infection in up to 22% of
patients. There is a striking amount of false positives, which is increased espe-
cially in patients evaluated after eradication treatment.

[Patients characteristics according to the center]

Hospital Reina Sofia Complexo Hospitalario de Navarra Total
Sex (women) 60% 58% 59%
Medium age 47.5 ± 16.7 52.5 ± 13.4 49.6 ± 15.6
Tests Pre-treatment/Post- treatment Pre 50% Pre 53% Pre 51%
Concordance 77% 80% 78%
H. pylori prevalence Pre-treatment/Post-treatment (%) 36/10 34/16 35/13

P0573 PHOTOMETRY OF RAPID UREASE TEST FOR
DIAGNOSTICS OF HELICOBACTER PYLORI IN PATIENTS
WITH DYSGESEC SYMPTOMS

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Introduction: Eradication of H. pylori significantly reduces the risk of stomach
cancer and prevents the development of rebleeding. Rapid urease test allows well-
timed and adequate diagnosis of H. pylori in patients with dyspeptic symptoms to
be performed achieving correct evaluation of the results of the eradication after
treatment. There is now the digital rapid urease test with photometry available
that excludes possible errors of the visual evaluation of the test results.
Aims and Methods: The diagnostics by the new rapid urease test photometer that
allows to trace kinetics of the enzyme activity through multiple readings of
the test-slides was compared with the validated visual-evaluation rapid urease test.
The two-center study with the total of 385 patients (female 344 and male 241, age
55.1±13.3 years) having symptoms of dyspepsia was performed. All of the
patients underwent endoscopy of the upper gastrointestinal tract and histological
examination in accordance with the OLGA classification. In cases of discre-
pancy, the results of the histological examination, stool-PCR test and
UBT were used as a reference. 2 biopsy samples of the same localization were
then to perform the 2 rapid urease tests: 1 for ARA MUT Expert with
AMA RUT Reader, AMA Co Ltd. and 1 for Helicobacter Pylori Quik Test,
Biobit OJ.
Results: H. pylori was detected in 204 patients - 34.9%. In the group of patients
(n=283), who hadn’t had anti-helicobacter therapy (naive), 52% of patients
(n=147) showed positive results for H. pylori, as detected by ARA MUT
Expert. In the group of patients (n=302), previously subject to various forms of
therapy, H. pylori was detected in 21% of patients (63 patients). In all cases of
discrepancy where the Quick Test showed positive and AMA RUT Expert
showed negative, the results of the 3 reference methods confirmed absence
of H. pylori. In 23 cases where AMA RUT Expert was positive and the Quick
Test negative, the reference methods of histology and stool-PCR proved the
presence of the infection in 21 patients. Histologically H. pylori was detected in
237 patients, of which AMA RUT Expert revealed the presence of H. pylori
urease activity in 234 patients. The sensitivity of AMA RUT Expert was
98.7% and the specificity was 99.4%. Thus our study revealed higher sensitivity
and specificity of AMA MRA Expert compared to the Quick Test (98.4% vs
93.6% and 100% vs 87.8%). Meta-analysis of studies evaluating the sensitivity
and specificity of various visual-evaluated rapid urease tests has shown their
sensitivity ranging from 56.3 to 97.4%, with an average of 89.9%. The specificity of
different rapid urease tests ranged from 70 to 100%, with an average of 94.4%. Differences for sensitivity and specificity
were statistically significant at p < 0.001.
Conclusion: The results obtained by the ARA MUT Expert test-slides with the
AMA RUT Reader showed higher values of diagnostic sensitivity and specificity
than those in the visual-evaluated rapid urease tests, both in our study and in
the data of meta-analysis. To achieve the most accurate diagnostics of H. pylori
in patients with dyspeptic symptoms it is recommended to routinely use the photo-
metery of the enzymatic reaction. Nothing to disclose

Disclosure: Nothing to disclose
**P0574** MEDICATION DIARY CARD ON THE ERADICATION RATE AND SYMPTOM REMISSION OF PATIENTS INFECTED BY HELICOBACTER PYLORI

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**Introduction:** H. pylori is closely related to the genesis of diseases such as chronic active gastritis, peptic ulcer and gastric cancer [1–2]. Typically, about <1% of patients infected by H. pylori will finally develop into intestinal-type gastric cancer [3–4]. Guideline emphasizes that, the major objective of eradicating H. pylori is to reduce the incidence risk of gastric cancer [5]. Therefore, eradicating H. pylori is the important measure for preventing intestinal-type gastric cancer. Moreover, the rates of H. pylori resistance to drugs are increasing in recent years, the eradication rate of standard triple therapy is lower than 80% [6]. Additionally, relaxed mastering of clinical eradication indications, irregular therapeutic scheme and patient compliance deficiency have added to the difficulties in eradication. Consequently, informing the patients of H. pylori eradication guidance in the manners of the medication method, time and filling in the medication diary card can increase patient understanding to H. pylori therapeutic scheme, relieve the patients, and raise the H. pylori eradication rate and relieving the clinical symptoms.

**Aims and Methods:** We aimed to explore the influence of eradication rate of Helicobacter pylori (H. pylori) and symptom remission by means of distributing medication diary cards and giving medication guidance.

The current study was a prospective randomized controlled clinical observational study, and treatment-naive patients diagnosed with chronic gastritis accompanying H. pylori infection through gastroscopy and histopathology were selected as the objects of study. Specifically, the bismuth-based quadruple standard eradication regimen was adopted for patient treatment. Patients conforming to the inclusion criteria had signed the informed consent before they were randomly divided into the record group and the control group. In addition, all patients were informed of the dose, time, precautions and potential adverse reactions in details by designated physicians. The control group was given the above education only, while the record group was given a diary card covering the detailed medication regimen was adopted for patient treatment, which asked the patients to record their time, dose and adverse reactions during medication. Moreover, the patients should return their medication diary cards upon the end of treatment. Besides, both groups were carried out 12 or 14C urea breath test (UBT) 28 days after withdrawal to evaluate the eradication of H. pylori.

**Results:** A total of 120 patients conforming to the inclusion criteria were enrolled in the current study, including 60 in the record group and 60 in the control group. The eradication rates of H. pylori in 2 groups were 91.67% (55/60) and 73.33% (45/60) respectively, and analyzed using intention-to-treat (ITT), while was observed, suggests that oral cavity might be considered as a potential site for H. pylori re-infection associated gastritis.

**Disclosure:** Nothing to disclose.

**References**

**P0575** THE EFFECT OF PERIODONTAL THERAPY FOR GASTRIC INFECTION WITH HELICOBACTER PYLORI IN TAIWAN

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**Introduction:** Chronic gastritis associated H. pylori infection was found in 50% of the global population and was etiologically relative cancers (63%) or approximately 5.5% of all cancers worldwide, and account for 25% of cancers related with etiology of infection; and is a main public health problem. The recurrence rate is relatively high and still a main public health problem. Oral cavity may be a potential route for gastric infection; and is a main public health problem. The association between oral cavity H. pylori and gastric biopsy H. pylori (p = 0.007). H. pylori treatment plus periodontal therapy significantly decreased the recurrence rate of H. pylori infection compared with gastric H. pylori infection alone (0.052 vs. 0.95%). The eradication rate was not significant differences (OR 0.91; 95% CI 0.67 to 1.25; p = 0.083).

**Conclusion:** The association between oral cavity H. pylori and gastric biopsies H. pylori (p = 0.007). H. pylori treatment plus periodontal therapy significantly decreased the recurrence rate of H. pylori infection compared with gastric H. pylori infection alone (0.052 vs. 0.95%). The eradication rate was not significant differences (OR 0.91; 95% CI 0.67 to 1.25; p = 0.083).

**Disclosures:** Nothing to disclose.

**References**

**P0576** EVALUATION OF BACKGROUND FACTORS AFFECTING THE SUCCESS RATE OF FIRST-LINE TRIPLE THERAPY WITH VONOPRAZAN FOR HELICOBACTER PYLORI INFECTION

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**Introduction:** Recent studies have reported the superior efficacy of vonoprazan (VPZ) compared to that of proton pump inhibitors (PPIs) in first-line triple therapy for Helicobacter pylori (HP) infection. However, it is considered that there is no room for improvement because the eradication rate with VPZ in usual post-marketing studies was reported to be lower than that in a phase III study.

**Aims and Methods:** In the current study, we determined background factors affecting the success rate of first-line triple therapy with PPIs or VPZ to identify those that contribute to the improvement of the eradication rate. The relation between success rate of first-line triple therapy with PPIs (PPI group) or VPZ (VPZ group) and background factors (age, sex, body mass index [BMI], clarithromycin [CAM] resistance of HP determined by a microbial sensitivity test, a history of endoscopic treatment for early gastric cancer, Brinkman index, weekly amount of alcohol intake, daily amount of coffee intake, and estimated glomerular filtration rate [eGFR]) was retrospectively evaluated in 704 patients with HP infection treated between August 2014 and December 2017.

**Results:** A total of 704 patients (383 men, 321 women; mean age, 62.5 years [range 27–89 years]; PPI group, 369; VPZ group, 335) were enrolled in the study. In the VPZ group, the eradication rate was significantly lower in the VPZ group than in the PPI group (77.5% vs. 86.6%, p = 0.002) and significantly lower in patients infected with CAM-resistant HP than in those infected with CAM-sensitive HP (PPI group, 57% vs. 88.0%, p = 0.001; VPZ group, 79.5% vs. 88.9%, p = 0.001). A multiple logistic regression analysis showed that the odd ratios (ORs) for CAM-resistant HP infection to CAM-sensitive HP infection for successful eradication in the PPI and VPZ groups were 0.18 (95% CI, 0.10–0.34; p < 0.001) and 0.41 (95% CI, 0.19–0.86; p = 0.019). In the PPI group, the eradication rate was significantly lower in among patients with a high eGFR (<100 ml/min/1.73 m2; n = 52 [14.1%]) than in the others (59.6% vs. 80.6%, p < 0.001) and the OR for patients with a high eGFR compared to that in the others was 0.33 (95% CI, 0.15–0.69; p = 0.004), as shown by the multiple logistic regression analysis.
P0577 THE IMPACT OF HELICOBACTER PYLORI ERADICATION ON THE NUTRITIONAL HEALTH IN HEMODIALYSIS PATIENTS

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Introduction: Previous study showed that nutritional condition was a strong predictor of overall mortality in patients with end-stage renal failure on maintenance hemodialysis (HD patients), which indicates that maintaining favorable nutritional condition is vitally important for HD patients in which malnutrition is common. It has been also reported that Helicobacter pylori (H. pylori) infection negatively affected the absorption of nutrients and the production of hormones related to the appetite and growth, which indicates that H. pylori infection has potential to be one of the causes of malnutrition. Therefore, H. pylori eradication can be a strategy for improving nutritional condition of HD patients infected with H. pylori. However, the relationship between H. pylori eradication and the nutritional health in HD patients is still unknown.

Aim of this study was to clarify the effect of H. pylori eradication on the nutritional health in HD patients. HD patients who were infected with H. pylori and achieved successful H. pylori eradication at Omihachiman Community Medical Center between January 2012 and December 2017 were investigated retrospectively. All patients included in this study were received triple therapy comprising amoxicillin or metronidazole, clarithromycin and proton pump inhibitor twice daily. In the first 7 days therapy, the eradication was defined by a negative 13C-urea breath test result. 103 study were received triple therapy comprising amoxicillin or metronidazole, clarithromycin and proton pump inhibitor twice daily. In the first 7 days therapy, the eradication was defined by a negative 13C-urea breath test result. Adverse events were not statistically different among the 3 groups.

Conclusion: Concomitant therapy appears to be more effective for H. pylori eradication compared to standard triple therapy and sequential therapy. There were no statistically different adverse events among the three groups.

Disclosure: Nothing to disclose

P0579 SUSCEPTIBILITY-BASED TAILORRED VS. EMPIRIC AMOXICILLIN MODIFIED BIMUTH QUADRUPLE THERAPY AS HELICOBACTER PYLORI THERAPY: A MULTI-CENTER RANDOMIZED CONTROLLED TRIAL

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Introduction: The increase in Helicobacter pylori (H. pylori) resistance to antibiotics is a common problem in empirical eradication regimens, and suggest that susceptibility-based tailored therapy may be required to achieve high efficacy.1,2 Previous studies showed that substitution of amoxicillin for tetracycline was highly effective making modified bismuth quadruple therapy an option for H. pylori eradication.

Aims and Methods: This randomized, open-label, superiority, multi-center trial aimed to compare the eradication rates, safety and adherence of susceptibility-based tailored therapy with standard triple therapy in naive patients with H. pylori infection. Subjects were randomized in 2 groups by 3:1 ratio: a) tailored therapy, according to antibiotic resistance pattern included esomeprazole 20mg bid, amoxicillin 1g bid, with a third drug (clarithromycin 500mg bid, metronidazole 400mg bid, or levofloxacin 500mg qd) for susceptible strains, or with bismuth 220mg bid plus metronidazole 400mg qid for triple-resistant strains; b) empiric therapy included esomeprazole 20mg bid, bismuth 220mg bid, amoxicillin 1g tid, and metronidazole 400mg tid. All regimens were given for 14 days. Antibacterial susceptibility was assessed by the agar dilution method. Primary outcomes were H. pylori eradication rates. This trial was registered with ClinicalTrials.gov, NCT02935010.

Results: Between February 2017 and March 2018, 491 subjects were screened for eligibility, 182 were randomized in the study. The baseline characteristics were balanced between the 2 groups (Table 1). The intention-to-treat and per-protocol cure rates were 91.6% (262/286, 95% CI 88.4–94.8%) and 97.7% (250/ 256, 95.8–99.5%) for tailored therapy vs. 85.4% (82/96, 78.4–92.5%) and 97.6% (81/83, 94.3–100%) for empiric therapy. Tailored therapy was not superior to empiric therapy either in ITT analysis (Difference 6.2%, 95% CI –0.3–12.7%, p = 0.059) or in PP analysis (Difference 0.1%, –3.1–3.2%, p = 0.486). According to antimicrobial susceptibility, tailored therapy eradicated 99.4% of clarithromycin and 97.5% of metronidazole resistant strains, and 100% (27/27) levofloxa- cacin susceptible strains, and 91.4% (53/58) triple-resistant strains respectively. Empiric therapy eradicated 100% (13/13) metronidazole susceptible and 97.1% (68/70) resistant strains. Both tailored therapy and empiric therapy achieved first-line drug compliance and drug adherence. The eradication rate of poor adherence was lower than subjects with good adherence, but a significate difference was only observed in empiric therapy (25.4%, 1/4 vs. 97.6%, 81/83, p < 0.001) but not in tailored therapy (85.7%, 12/14 vs. 97.7%, 250/256, p = 0.038).

Conclusion: In settings of high and multiple antibiotic resistances of H. pylori, susceptibility-based tailored therapy provided excellent results with 14-day PPI triple therapies being optimal choices for susceptible strains. However, empiric

P0578 COMPARISON OF STANDARD, SEQUENTIAL, AND CONCOMITANT FIRST-LINE ERADICATION THERAPY FOR HELICOBACTER PYLORI

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Introduction: Approximately 50% of world’s population is infected with Helicobacter pylori. In developing countries, the prevalence has been reported to be as high as 70%. As H. pylori can be a major cause of gastric diseases such as chronic gastritis, gastric ulcerdoules, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer, eradication of H. pylori infection is important. However, the eradication rates after fist-line standard triple therapy have been unsatisfactory, mainly because of antibiotic resistance, particularly towards clarithromycin. In fact, many guideline recommend alternative regimens such as sequential and concomitant therapy.

Aim and Methods: We compared the efficacy, adverse events, and drug compliance of standard triple, sequential, and concomitant therapy for H. pylori eradication. This was a prospective study involving 750 patients diagnosed with H. pylori infection between January 2014 and July 2016 in Yeouido St. Mary’s Hospital. Diagnosis was made by rapid urease test (CLO test) or histological evidence of H. pylori via modified Giemma staining. We compared 3 treatment regimens: the standard triple therapy (250 patients enrolled) consisted of rabeprazole 20 mg, amoxicillin 1 g, and clarithromycin 500 mg twice a day for 7 days; the sequential therapy (250 patients enrolled) consisted of rabeprazole 20 mg, clarithromycin 500 mg, and metronidazole 500 mg twice a day for the subsequent 5 days; the concomitant therapy (250 patients enrolled) consisted of rabeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg, and metronidazole 500 mg twice a day for 7 days. 6 weeks following completion of therapy, success of eradication was defined by a negative 13C-urea breath test result. Adverse events and drug compliance were evaluated by physicians via direct questioning. 103 patients did not complete the study because of loss of follow-up or withdrawal of consent.

Results: A total of 647 patients (209, 211, and 227 patients in the standard triple, sequential, and concomitant therapy groups, respectively) were analyzed. The mean age of the patients was 55.7 years. There were 365 male and 282 female patients (male:female ratio = 1.29). The baseline characteristics were not significantly different between the 3 groups. The eradication rate was significantly higher in the concomitant group (89.4%, 203/227) than in the standard group (78.5%, 146/209) and the sequential group (85.3%, 180/211) (p = 0.006). Drug compliance and adverse events were not statistically different among the 3 groups.

Conclusion: Concomitant therapy appears to be more effective for H. pylori eradication compared to standard triple therapy and sequential therapy. There were no statistically different adverse events among the three groups.

Disclosure: Nothing to disclose
modified bismuth quadruple therapy (three times daily of amoxicillin and metronidazole) was also proven to be highly effective for subjects with good adherence even in areas of high metronidazole resistance.

### References


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**Introduction:** Eradication therapy for *Helicobacter pylori* infection is widely performed. Although patients may report that their halitosis has either improved or worsened after eradication therapy, these complaints are subjective. In addition, there are no objectively evaluated reports of changes in halitosis after *H. pylori* eradication.

**Aims and Methods:** The aim of this study was to investigate changes in halitosis after *H. pylori* eradication. Between February 2015 and March 2016, a total of 5,514 patients visited the Kudo Clinic. Of these, 174 were found to be infected with *H. pylori*. Informed consent for participation in this study was obtained from 71 patients. We assessed halitosis before and after 2 months of eradication therapy, and compared the changes. If primary eradication was unsuccessful, secondary therapy was performed. Halitosis values were measured after successful eradication was confirmed with urea breath testing. Halitosis values were evaluated with a Total Gas Detector™ System (Refres HR BAS-108; Adonis Electronics Co., Ltd., Osaka, Japan). The ethics committee of the Kudo Clinic approved this study protocol (Approval number; 2015-01).

**Results:** Among the 71 patients (18 [25.4%] males and 53 [74.6%] females), 68 completed treatment and had successful eradication. The average age was 64.2 ± 10.5 years old. The Breath Refes Values were 49.4 ± 21.4 before eradication and 52.2 ± 26.4 after successful eradication, and did not decrease significantly (p = 0.55). Within the 27 patients whose Breath Refes Values showed more than 60, those improved significantly form 73.0 ± 10.7 to 61.3 ± 28.2 (p = 0.037).

**Conclusion:** Among the patients whose Breath Refes Values was high, their halitosis improved after successful eradication. Further examination will be necessary by increasing the number of cases.

**Disclosure:** Nothing to disclose.

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**Introduction:** Amongst the several factors that can affect the efficacy of anti *H. pylori* therapy, resistance to antimicrobials remains the most critical one. Despite this, in only few studies has antimicrobial susceptibility testing performed and there is uncertainty regarding the minimum number of resistant strains that need to be tested in order to get reliable information on the effectiveness of a given eradication regimen in patients harboring those strains.

**Aims and Methods:** During a 5-year study, we tried to identify a minimum number of patients to study to get a reliable estimate of effectiveness of a given eradication therapy in patients harboring resistant strains. Consecutive 1682 naïve *H. pylori*-positive patients were studied between 2010 and 2015, and resistances to clarithromycin, metronidazole and levofloxacin assessed by E-test according to the EUCAST guidelines. Sequential therapy was offered and effectiveness evaluated 6 weeks after the end of the treatment. To identify a minimum number of patients to study to get a reliable estimate of effectiveness of sequential therapy in patients harboring resistant strains, a bootstrap analysis was firstly performed. Patients who completed the follow-up were sub-grouped according to the pattern of antimicrobial susceptibility/resistance, considering clarithromycin and metronidazole. For each of these groups, the effect of sampling across the range 10–300 patients was explored based on 500 samples drawn. This allowed the calculation of the variance in eradication estimates to be made for each level of sampling. These parameters were then used to calculate the power of each sample to detect the parent population eradication rate with a margin of error of +/− 1%, assuming a two-sided α-value of 0.05. Afterwards, the estimated minimum sample needed to give consistent results was calculated for theoretical eradication rates ranging from 90% to 95% assuming that the results would follow a standard binomial distribution and choosing a margin of error of +/− 5%, and a value of alpha of 0.05.
**Abstract No:** P0582: Bootstrap analysis

**Characteristics of the Parent Populations**

<table>
<thead>
<tr>
<th>Eradication rate</th>
<th>Cla-S &amp; Metro-S (n = 527)</th>
<th>Cla-S &amp; Metro-R (n = 152)</th>
<th>Cla-R &amp; Metro-S (n = 151)</th>
<th>Cla-R &amp; Metro-R (n = 236)</th>
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<tr>
<td></td>
<td>97.3% (95% CI: 95.6 to 98.4)</td>
<td>96.1% (95% CI: 91.7 to 98.2)</td>
<td>93.4% (95% CI: 88.2 to 96.4)</td>
<td>83.1% (95% CI: 77.7 to 87.3)</td>
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</table>

**Power**

<table>
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<th>Sample Size Estimated for Each Pattern of susceptibility/resistance evaluated with the bootstrap analysis</th>
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<tr>
<td>99%</td>
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<tr>
<td>90%</td>
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<tr>
<td>80%</td>
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</table>

**Results:** 45.9% (95% CI: 42.3–47.7) of strains were susceptible to both agents. In the remaining 55% (95% CI: 52.3–57.7), resistance to 1 or 2 agents was present. However, 22.6% (95% CI: 20.5–25.0) of patients were resistant to both antibiotics.

**Conclusion:** Our large data set provided evidence showing that a large number of strains needs to be assessed to give reliable estimates of the effectiveness of a given eradication regimen in patients harboring resistant strains.

**Disclosure:** Nothing to disclose

**References**


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**P0584 USING A NOVEL DEVELOPED HIGH RESOLUTION MELT CURVE ASSAY FOR THE ANALYSIS OF PREDOMINANCE OF HELICOBACTER PYLORI CLARITHROMYCIN RESISTANCE**

**Introduction:** Helicobacter pylori (HP) is the most common pathogen found in humans. Its resistance to clarithromycin is increasing continuously and it is one of the main reasons for eradication failure. The resistance is attributed to 3 point mutations (PM): A2142G, A2142C and A2143G within the peptidyl-transferase encoding region of the 23S rRNA gene. We aimed to analyze the predominance of HP clarithromycin resistance by using our novel high resolution melt (HRM) assay.

**Aims and Methods:** A total of 151 HP stool samples were collected from native patients with general gastric discomfort who also performed 13CO2 breath tests (BTs). Stool antigen test (SAT) was also performed on 126 of the 151 stool samples collected HP DNA was extracted from the stool and was analyzed by HRM. The results were compared to the BTs and SATs. The HRM positive results were further analyzed by comparing them to 4 reference plasmids incorporating the three mutations and the WT sequences.

**Results:** The HRM results presented 106 positive and 45 negative samples. Of the 106 positive samples, 52 had PM - demonstrating a 34% clarithromycin resistance. When compared to the 151 BTs and the 118 SATs, the HRM had a sensitivity of 100% and 99% and specificity of 82% and 78% respectively. Of the 106 positive HRM samples, 54 (51%) had a WT sequence, 10 (9%) had an A2142G PM, 13 (12%) had an A2142C PM, 18 (17%) had an A2143G PM and 11 (10%) were heterozygote (multiple peaks).

**Conclusion:** Our study is consistent with other reports suggesting an increasing H. pylori clarithromycin resistance worldwide, yet further investigation is required in order to determine its prevalence in Israel. Moreover, our HRM assay may be useful in screening prior to administration of clarithromycin eradication therapy.

**Disclosure:** Nothing to disclose

**References**

1. Tikva, T; Perets, O, Ashorov, D, Bolitin, R, Dickman, Y, Niv Y.

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**P0585 THE PROTECTIVE EFFECT OF ANGIOTENSIN(1-7) ON NSAID-INDUCED SMALL INTESTINAL INJURY IN RATS**

**Introduction:** Non-steroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly prescribed drugs in the world. However, recently its gastrointestinals complications, especially small intestine injury, has attracted people’s attention. The pathogenesis is not yet completely clear, therefore there is no effective treatment measures. RAS is an important regulation system, which plays an important role in maintaining water and electrolyte balance. Ang-(1–7) is one of the most important components of the system, which mainly synthesized by ACE2, bypassing the synthesis of Ang II. Studies have shown that Ang-(1–7) can reduce the degree of inflammation in colitis and pancreatitis. However, there is few researches on whether Ang-(1–7) has a protective effect on NSAID induced intestine injury.

**Aims and Methods:** We aimed to investigate the effect and mechanism of Angiotensin(1–7) on NSAID-induced small intestinal injury in rats.

**References**

1. M Wang, L Ye, B Lv, L-N Meng. The First Affiliated Hospital of Zhejiang Chinese Medical University, Gastroenterology, Hangzhou, China
while the protect effect was blocked by MasR antagonist (p < 0.05). 2. Expression of MAS and the anti-inflammatory作用 in the Ang-1(1–7) group was significantly higher than that in the experimental group, while the AngII was significantly reduced (p < 0.05); the MasR antagonist significantly reduced the expression of MAS, while the AngII was significantly increased (p < 0.05). 3. The expression of p38MAPK, NF-κB and TNF-α in experimental group were much higher than control group, while in the Ang-1(1–7) group, they were much lower than that in the experimental group, the Ang1(1–7) + MasR antagonist group were significantly higher than both the Ang1(1–7) group and the experimental group (p < 0.05). 4. Pearson correlation analysis: The score of small intestine injury was highly negatively correlated with Mas (p < 0.05), and highly positively correlated with AngII, p38MAPK, NF-κB and TNF-α (p < 0.05). Conclusion: Ang1(1–7) has a protective effect on NSAID-related small intestinal injury in rats. The protective effect mainly mediated by Mas receptor, then regulating the AngII, and inhibiting the activation of p38MAPK, NF-κB and TNF-α.

Disclosure: Nothing to disclose

References

P9587 EMERGING ROLE OF RIFAXIMIN IN THE MANAGEMENT OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS ON CHRONIC PPI TREATMENT

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Introduction: Despite their well-established efficacy, emerging studies are evaluating the effect of Proton Pump Inhibitor (PPI) drugs on gut microbiota composition and on a consequent possible causative role in inducing Small Intestinal Bacterial Overgrowth (SIBO). However, these analyses have so far produced mixed results. Moreover, therapeutic options for SIBO patients are still not well established.

Aims and Methods: The aim of our study was to assess the prevalence of SIBO and CH4 producers consequent to chronic PPI therapy using Lactulose Breath Test (ULBT). Secondary aim was to explore the possible role of Rifaximin in treating PPI-induced SIBO and CH4 producers.

125 consecutive GERD patients (> 18 years old) constantly treated with PPI (PPI) for at least 6 months were enrolled and underwent ULBT. An age-matched control population (Control) of 100 patients, which had not used PPI in the last 6 months, was also enrolled. 25 Italian General Practitioners and one university hospital participated to the enrollment. Exclusion criteria were: liver and kidney diseases, prior antibiotic treatment in the last month, pregnancy, breastfeeding, diabetes, BMI > 29, alcohol abuse disorder, IBS, IBD, neurological/muscle diseases, celiac disease, lactose intolerance, previous gastric/intestinal surgery.

North American Consensus (Rearie et al, The American Journal of Gastroenterology 2017) was used to define SIBO diagnosis and CH4 producers. ULBT samples were centrally read and interpreted. Among PPI, 22 SIBO positive patients and 42 CH4 producers were treated with Rifaximin 1200mg/daily for 3 weeks and rechecked with ULBT after 1 month. The area under the curve (AUC) before and after treatment was also calculated for both SIBO positive patients and CH4 producers.

Results: In the PPI group, 38/125 (30.4%) had a positive ULBT for SIBO vs. 27/100 (27%) of the Control group (p < 0.05). Interestingly, 77/125 (61.6%) of PPI patients were found to be CH4 producers vs. 21/100 (21%) controls (p < 0.05). In particular, among SIBO patients in the PPI group, 34 (89.4%) were also CH4 producers vs. 17/27 (63%) controls (p < 0.05). After Rifaximin treatment, ULBT results were negative in 15/22 (68.2%) of treated patients vs. 23/42 CH4 producers (54.8%) (p < 0.05). At the AUC analysis, an overall reduction of 54.2% for H2 in SIBO patients and of 47.7% for CH4 in CH4 producers was assessed after Rifaximin treatment (p < 0.05).

Conclusion: Chronic use of PPI could be able to increase the prevalence of SIBO and to shift the intestinal microbial composition towards a CH4-producing flora. Rifaximin could represent a useful therapeutic option for PPI-induced SIBO and for modulating CH4-producing flora.

Further studies are underway to determine the exact implications that sustain these findings. Disclosure: Nothing to disclose

P9588 THE IMBALANCE OF THE HOMEOSTASIS SERINE PROTEASES-INHIBITORS IN INFLAMMATORY BOWEL DISEASE NAIVE PATIENTS: A HORIZON FOR NEW PERSPECTIVES THERAPIES?

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Introduction: The pathogenesis of chronic inflammatory bowel disease (IBD) suggests an inappropriate activation of the intestinal immune system against the intestinal host’s flora of genetically predisposed persons. The intestinal microbiota can be involved in different ways in this pathogenesis. Indeed, an excessive proteolytic activity of the intestinal microbiota of IBD subjects was one of the mechanisms demonstrated hypothesis.

Aims and Methods: A prospective comparative study was enrolled in our medical center from January 2015 to December 2015. Were included to the study all the hospitalized new cases of IBD and a second group of healthy voluntary people. All subjects (controls and patients) treated with an antibiotic, anti-inflammator, or pro-biotic in the 6 months prior to inclusion were excluded. All patients have benefited of a physical and biological examination and colonoscopy. Stool samples were collected for fecal water extraction. At the first step we measured the fecal proteolytic activity which was acting as a substrate in both groups. To highlight the nature of the proteins involved, we studied the inhibitory effect of specific serine protease inhibitors on fecal proteolytic activity. We used PMSF and SBTI as chemical serine protease inhibitors and Serpin ES expressed by a commensal bacterium of the intestinal microbiota. This Serpin was previously purified and optimized in the Ife laboratory, Metagenopolis at INRA Jouy-en-Josas in France using recombinant strain of E. coli (plasmid pDES717). The final step was to search a natural serpin deficient in

<table>
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<tr>
<th>Species</th>
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<th>Recovery</th>
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<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Dog</td>
<td>Small intestinal length</td>
<td>21/19</td>
<td>515/85</td>
<td>85/105</td>
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</tbody>
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Table 1: Percentage (%) increase relative to control group (males/females)

Conclusion: A significant dose-related intestino-protective effect was seen following 26 and 39 weeks of glepaglutide exposure in rats and dogs, respectively. This response was similar to findings after 7 days of dosing in rats. At all doses, increased length, weight and length as well as macroscopic thickening and villous hyper trophy were noted in all segments of the small intestine. These findings were still present following a 6-week recovery period, indicating prolonged intestino-protective effects of glepaglutide.

Disclosure: Nothing to disclose

P9586 INTESTINOTROPHIC EFFECTS OF GLEPAGLUTIDE FOLLOWING CHRONIC EXPOSURE IN RATS AND DOGS

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Introduction: Glepaglutide is a novel, long-acting GLP-2 analog being developed for the treatment of Short Bowel Syndrome. Nonclinical pharmacology studies have shown that glepaglutide is a potent and selective GLP-2 receptor agonist, with activity across the intestinal tract.

Aims and Methods: The objective of these studies was to assess the systemic chronic toxicology and toxicokinetic (Tk) profile of glepaglutide in the Wistar rat and the Beagle dog. In addition, pharmacodynamic effects were compared to sub-chronic effects.

In chronic studies, rats were dosed subcutaneously (SC) with vehicle, 1, 3 and 10 mg/kg glepaglutide on a daily basis for 26 weeks. Furthermore, sub-groups of control and high-dose animals were allowed a 6-week recovery period following completion of the dosing period. Dogs were dosed SC with vehicle, 0.25, 1 and 5 mg/kg glepaglutide on a daily basis for 39 weeks. Sub-groups of control and high-dose animals were allowed a 6-week recovery period following completion of the dosing period. Blood samples were taken at regular intervals during the studies for determination of Tk profile. In addition to standard toxicology parameters measured during the studies (data not presented), the length and the weight of the small and large intestines were measured at necropsy as indicators of intestino-protective effects and the intestinal tract was evaluated histologically. In sub-chronic studies, rats were dosed SC with vehicle, 1, 4 and 10 mg/kg glepaglutide on a daily basis for 7 days. The length and weight of the small and large intestines were measured at necropsy as indicators of intestino-protective effects.

Results: At steady state, Tk profiles of glepaglutide within the interval were relatively constant in rats and dogs, and therefore an accurate half-life could not be determined. In chronic studies, glepaglutide induced dose-related significant (p < 0.01) increases in length and weight of the small intestines in both rats and dogs (Table 1). Furthermore, the length and weight of the large intestine was also slightly increased in rats. At all dose levels, macroscopic thickening of the duodenum, jejunum and ileum was present. Histologically, glepaglutide produced a dose-related increase in macroulcer hyperplasia of the duodenum, jejunum and ileum. Interestingly, at the end of the recovery period significant intestino-protective effects were still present in the high-dose groups although partial recovery was seen. Sub-chronic treatment in the rat induced significant dose-related increases in small intestinal mass, similar to those observed after chronic dosing.

Disclosure: Nothing to disclose

P9589 THERAPIES? NAIVE PATIENTS: A HORIZON FOR NEW PERSPECTIVES
**IBD group** so we studied in both groups the proteolytic activity of the fecal water with which degraded all the proteins except serpins. For the statistical analysis we used Spss software (20.0) (significant difference for $p<0.05$).

**Results:** Were included in the first group of IB 28 patients vs. 15 in the second group of healthy controls. The middle age was 46 years vs. 48 years in the second group. The sex ratio [H/F] was 1.33 vs. 1.14. The IBD group were divided in 15 cases of Crohn disease and 13 cases of Ulcerative colitis (UC) disease. The activity of the disease was variable from minimal to severe. Proteolytic activity was greater in patients with Crohn’s disease. (294.3 U/ml vs. 22.9U/ml, $p<0.05$). Particularly high activity has been observed in the severe forms of both UC and Crohn’s disease. We found a significant decrease in protease activity in the presence of both inhibitors: PMSF (1mM) (294.3 ml vs 63.60 U/ml $p<0.01$) and SBTI (1mM) (294.3 U/ml vs 76 U/ml, $p<0.05$). Using the serpin ES (14 g/ml) non-significant decrease in the proteolytic activity was found (294.3 ml vs 242.2 U/ml, $p>0.05$). In reverse zymography only one band was found in the first group vs. three bands in the healthy groups.

**Conclusion:** This demonstrated a higher proteolytic activity of fecal water in IB group comparing to healthy people and this activity was concordant to the severity of the thirst. Serine inhibitors were able to decrease the proteolysis. Thus, majority were serine proteases. The lower concentration of serpin ES may explain the lesser inhibition. Finally, in IBD patients there is a natural deficiency in serpins therefore an imbalance in the homeostasis can be suggested as hypothesis to the pathophysiology of the IBD. Restoring this balance protease-inhibitors can lead to new therapeutic perspectives especially by manipulating the microbiota using genetically modified probiotics.

**Disclosure:** Nothing to disclose

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**P0580 TISSUE TRANSGLUTAMINASE DEPOSITS COMPARED TO THE SCORE 'COELIAC-LITE' IN THE DIAGNOSIS OF COELIAC DISEASE: genetics and proteomic analysis**

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**Introduction:** Recently, we have described a diagnosis scoring system (Score 'Coeliac-lite') that allows diagnosing the forms of coeliac disease (CD) without atrophy. The Score is based on the assessment of the intraepithelial lymphocyte count, the gammadelta+ cell count, coeliac serology, and HLA-DQ2/5.8 (UEG 2012). The Score has a good accuracy to predict GFD mucosal damage (ACE, 0.83). The ESPGHAN 2012 CD diagnostic criteria support the use of tTG mucosal deposits in doubtful cases.

**Aims and Methods:** To assess whether the determination of tTG deposits in the duodenal mucosa can improve the diagnostic accuracy of the Score 'coeliac-lite'. 119 patients with symptoms of the CD spectrum without villous atrophy were included (age, 39.6±1.5 years, 71% women), who were treated with a gluten-free diet (GFD) based on positive serology and/or compatible histology (lymphocytic enteritis) and/or a positive coeliac genetics and/or CD IEL cytometry pattern. In all of them, the Score coeliac-lite (cut-off $>$ 10) and the presence of subepithelial tTG IgA deposits (confocal immunofluorescence) were analysed. 28 patients (15%) with inconclusive results of the tTG deposits assay were excluded.

Response to GFD was defined as clinical plus histological (or serological when positive) remission. The diagnosis of CD was based on the rule of ‘4 of 5’ by Catsassi. The relationship between the presence of deposits and Score positivity and GFD response was analysed using a binary logistic regression analysis.

**Results:** The response to GFD was 86% in patients with a Score $>$ 10 and 29% for a Score $<$ 10 ($p<0.001$). The tTG deposits were positive in 55% of patients, being more frequently positive in patients with a Score $>$ 10 (40%, 38%; [10–16], 74%; [2–17], 87.5% vs. 80%). There was a non-significant trend to a higher response rate to GFD in patients with a Score $>$ 10 and positive tTG deposits (Score $>$ 10: tTG+ 23% vs. tTG- 33%, $p=0.39$; and Score $<$ 10: tTG+, 91% vs. tTG- 67%, $p=0.06$). This trend was likely due to that tTG deposits were positive in 35% of patients with positive serology (serum tTG $>$ 2 U/mL in 30% of patients, being those with a Score $>$ 17). The logistic regression analysis showed that only the Score ‘coeliac-lite’ (OR, 14; $p<0.001$) had an independent predictive value for GFD response (tTG deposits OR: 1,08, $p=0.9$).

**Conclusion:** The assay technique of tTG deposits was inconclusive in 15% of the patients, which limits its routine use. As well, a positive result does not seem to provide important additional information with respect to the Score ‘coeliac-lite’.

**Disclosure:** Nothing to disclose

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**P0589 FREQUENCY OF SERONEGATIVE VILLOUS ATROPHY IN FUNCTION OF THE DEFINITION USED: DIAGNOSTIC UTILITY OF TRANSGLUTAMINASE DEPOSITS AND GAMMADELTA+ CELLS COUNTING**

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**Introduction:** Seronegative villous atrophy (SNVA) can be caused by coeliac or non-coeliac causes. Despite several international consensus on coeliac disease (CD), there is no agreement on how to approach the diagnosis of subjects with SNVA.

**Aims and Methods:** Evaluate 1) The diagnostic accuracy for CD of different tTG cut-offs with or without EnaM and 2) The frequency of SNVA of coeliac cause in our geographical area. Between April 2010 and November 2017 all consecutive patients with villous atrophy (VA) were prospectively registered. Coeliac serology (tTG and EnaM), tTG subepithelial deposits, and gammadelta+ intraepithelial cells (by flow cytometry) were measured. This diagnosis was based on the Catatsi criteria (rule 4 of 5). Three definitions of positive serology were used: 1. Definition based on NICE guidelines (tTG+ or recom tTG+). 2. Definition based on manufacturer: Elia Celikey, Phadia plus EnaM+ for titres of tTG between 8 and 2 U/mL. 2. Given that $>$98% of the individuals in the general population of our health area have serum tTG $<$ 2 U/mL titres of tTG between 2 and 8 U/mL with EnaM+ were considered positive; 3. tTG $>$ 2 U/mL (even without EnaM). For each cut-off definition, sensitivity (S) and specificity (E) for the diagnosis of CD were calculated.

Receiver VA were diagnosed (225 CD, 13 non-CD) (age, 18±1.2 years, limits 0 to 84, 70% women). 24 of the 225 (11%) patients with CD presented serum titre of tTG $<$ 8 U/ml or between 8 and 20 U/ml with negative EnaM ($<$ 17 years, 5% vs. 17 years, 21%; $p<0.01$). All had positive tTG deposits (19/24) or gammadelta+ cells (22/24) and clinical response to a gluten-free diet confirming the diagnosis of CD. Using the NICE definition as a cut-off point, 37/238 patients had SNVA (24 CD, 13 non-CD) (S, 94%; E, 100%). Considering also as tTG+ (titre $>$ 8 U/ml) (recommended by the manufacturer: Elia Celikey, Phadia) plus EnaM+ for titres of tTG between 8 and 20 U/mL. 2. Given that $>$98% of the individuals in the general population of our health area have serum tTG $<$ 2 U/mL titres of tTG between 2 and 8 U/mL with EnaM+ were considered positive; 3. tTG $>$ 2 U/mL (even without EnaM). For each cut-off definition, sensitivity (S) and specificity (E) for the diagnosis of CD were calculated.

**Conclusion:** Sensitivity and SNVA in our area. Based on the definition of negative serology used, the frequency of seronegative CD varies from 2 to 11%. Both the tTG deposits and the gammadelta+ cells analysed by flow cytometry are complementary diagnostic tools of great value in these patients. The serum tTG cut-off in clinical practice should be recommended.

**Disclosure:** Nothing to disclose
P0593 PREDICTIVITY OF AUTOIMMUNE STIGMATA FOR GLUTEN SENSITIVITY IN SUBJECTS WITH MICROSCOPIC ENTERITIS: A RETROSPECTIVE STUDY

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Introduction: Non celiac gluten sensitivity (NCGS) is an emerging gluten-related disorder characterized by a selective involvement of innate immune system. Some reports suggested a possible association with other autoimmune diseases. We aimed to investigate whether the presence of autoimmune stigmata in a group of patients with both clinical suspicion of NCGS and histological picture of microscopic enteritis could be predictive factors of NCGS.

Aims and Methods: Patients with microscopic enteritis were followed up by means of periodical laboratory and clinical examinations. At baseline, we collected data about previous clinical history, including existence of autoimmune diseases, and patients with a gluten exposure or coeliac enteropathy were excluded from the study. Autoantibodies were searched for in all patients according to well-established protocols. Patients with celiac disease were excluded from the final analysis. Student’s t and chi-square test were applied in univariate analysis for continuous and binary variables, respectively. Kaplan-Meier curves were drawn and Cox regression was used to estimate hazard ratios (HR).

Results: 63 patients were included in our final analysis. 22 had a final diagnosis of NCGS, while the remaining 41 had non gluten-related causes of microscopic enteritis (irritable bowel syndrome was found in 34). The prevalence of autoimmune thyroiditis was higher among NCGS (40.1%) than in other microscopic enteritis (14.6%). Furthermore, the positivity rate for IgA anti-gliadin antibodies (AGA) (27.3% versus 2.5%, p = 0.006) and anti-nuclear autoantibodies (ANA) (45.4% versus 12.2%, p = 0.005). Autoimmune thyroiditis was associated to an increased risk of NCGS diagnosis (HR = 2.4, 95% CI 1.1-4.8, p = 0.02). Both ANA (HR = 2.4, p = 0.04) and AGA (HR = 2.7, p = 0.04) were directly associated to NCGS diagnosis.

Conclusion: NCGS may have a cohort of autoimmune stigmata that can precede its diagnosis and may have a predictive value.

Disclosure: Nothing to disclose

P0594 COGNITIVE IMPAIRMENT IN COELIAC DISEASE: NON-COMPLIANCE FOLLOWING GLUTEN-FREE DIET

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Introduction: Patients with coeliac disease commonly report symptoms of ‘brain fog’. The mechanisms are poorly understood, but disease-related cognitive deficits and psychological problems have been suggested.

Aims and Methods: The aim of the study was to register self-reported symptoms of inattention and concentration impairment in coeliac disease before and after treatment with gluten-free diet, compared to a healthy control group. Patients with newly diagnosed coeliac disease were included consecutively from 2 patient clinics (Ols University Hospital and Løvisenberg Diakonal Hospital). The patients completed the questionnaires Adult ADHD Self-Report Scale v1.1 Symptoms Checklist (ASRS) and Hospital Anxiety and Depression Scale (HADS) prior to start of a gluten-free diet and after at least 12 months on the diet. Health care personnel at Oslo University Hospital served as healthy controls.

Results: A total of 33 newly diagnosed coeliac patients (median age 38, range 19–72, 24 women, 9 men) were included in the study. Of these, 27 patients met for follow up after minimum 12 months and repeated the questionnaires. 60 healthy controls (median age 45, range 24–69, 41 women, 19 men) completed the same questionnaires.

Coeliac patients had significantly higher scores than healthy controls on ASRS (median 27.0, IQR 20.0–35.5 vs. median 22.5, IQR 19.0–26.0, p = 0.007) and HADS (median 8.0, IQR 5.0–13.0 vs. median 5.0, IQR 2.0–8.0, p = 0.0008). After minimum 12 months on a gluten-free diet, coeliac patients improved their results on both ASRS (median 23.0, IQR 17.0–28.0, p = 0.013) and HADS (median 6.0, IQR 2.0–10.0, p = 0.003). There was no difference between coeliac patients on a gluten-free diet and healthy controls.

Conclusion: Coeliac patients reported significantly more symptoms than healthy controls on ASRS and HADS. The difference in regard to healthy controls disappeared after introduction of a gluten-free diet.

Disclosure: Nothing to disclose

P0595 DO CLINICAL SYMPTOMS OR SEROLOGY CORRELATE WITH CAPSULE ENDOSCOPY FINDINGS IN COELIAC DISEASE?

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Introduction: Small bowel capsule endoscopy (SBCE) has a useful role in detecting macroscopic changes and identifying complications of coeliac disease (CD). Small bowel capsule endoscopy (SBCE) was more likely to be of Marsh 3B (28.6%) and 3C (37.1%) (p = 0.013). There was no significance in SBT, abnormal length and percentage SB affected across presenting symptoms.

Conclusion: SBCE findings in CD correlate with serology (anti-gliadin IgA, anti-gliadin IgG). We have shown that SBCE correlates with length of abnormal SB, thus confirming that SBCE is affected by abnormal SB. This is the first study confirming a longer SBT in CD patients by SBCE.

Disclosure: Nothing to disclose

P0596 WHAT IS THE ROLE OF CAPSULE ENDOSCOPY IN EVALUATING PATIENTS WITH REFRACTORY COELIAC DISEASE?

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Introduction: Small bowel capsule endoscopy (SBCE) is used in refractory coeliac disease (RCD) to assess the extent of disease and ensure there are no complications (lymphoma or ulcerative jejunitis). However there are no published reports on SBCE in RCD following therapy.

Aims and Methods: Patients with histologically confirmed refractory coeliac disease (RCD) who underwent a SBCE at baseline and after treatment were enrolled in this study. These were compared to a group of control CD patients with no underlying RCD.

Results: 19 patients (median 53 years) with RCD (12 patients; 63.2% - type 1) were compared to 28 patients with control CD (median 48 years). There was no statistically significant difference in duration of disease, gender, age at SBCE and serology between the two groups.

Patients with RCD were more likely to have worse histology (Marsh 3a-c) than SBCE control CD who had a higher percentage of normal histology at the time of SBCE (p = 0.002) Those with RCD had a longer abnormal small bowel (SB) mucosa (185 SD±16.7 vs 29.5 SD±7.3 minutes p = 0.0001) and longer percentage of abnormal SB (53.9 SD±38.0 vs 6.9 SD±15.2 minutes p = 0.0001) when compared to those with control CD.

Conclusion: SBCE was carried out after a mean of 9.63 SD±2.8 months in patients with RCD following treatment. There was no statistical significant difference in histology and serology at the time of the first and second SBCE. Patients received the following treatment: 36.8% steroids, 26.3% immunosuppressants, 36.1% coeliac diet. This is the first study that shows an improvement in SB mucosa (185 SD±16.7 vs 29.5 SD±7.3 minutes p = 0.0001) and longer percentage of abnormal SB (53.9 SD±38.0 vs 6.9 SD±15.2 minutes p = 0.0001) when compared to those with control CD.

Disclosure: Nothing to disclose
**P0597** FREQUENCY AND DIFFERENTIAL CHARACTERISTICS OF ULTRASHORT CELIAC DISEASE


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Introduction: Ultrashort celiac disease (USCD) is a novel CD subtype limited to the duodenal bulb (D1), with recently conflicting frequency rates (0.1% to 1%). Compared to conventional CD (CCD), a mild clinic and histologic phenotype with minimal laboratory abnormalities has been reported. However, we currently lack data on flow cytometry findings in these patients.

Aims and Methods: Unicenter prospective study conducted from February 2015 to February 2018, including patients with a new diagnosis of CD. A systematic biopsy protocol (separate biopsies for flow cytometry and histologic study from D1 (1–2) and D2 (2–4)) was performed in all patients undergoing duodenal biopsies to rule out CD. CD diagnosis was defined by Catassi and Fasano criteria plus compatible duodenal flow cytometry (CD103+ > 90, TCR gammadelta > 16, and NK-CD3 < 8), either in D1 or both D1+D2. Baseline characteristics were compared between CCD and USCD patients.

Results: A total of 66 patients (54% pediatric) with a new diagnosis of CD were included of whom 7 (10%) showed USCD. No significant differences were observed between CCD and USCD regarding demographic, clinic, laboratory or CD serology parameters. Of note, 71% of USCD showed immunitor positive CD serology titres within a 5yr period before diagnosis, and CD had been previously ruled out in 54% of them by means of normal D2 biopsies. Marsh I-II lesions on D1 histology were significantly higher in CCD compared to USCD patients (60% vs. 15%, p<0.04). As for flow cytometry, no relevant differences in typical NK-CD3 count was significantly less diminished in USCD patients (CCD 1.2±0.9 vs. USCD 7.5±5.5, p<0.001).

Conclusion: Up to 10% of pediatric and adult CD patients in our series showed USCD. No villous atrophy was documented in up to 57% of patients with USCD. Flow cytometry was instrumental for an adequate diagnosis. A immunophenotype with a minimal decrease in NK-CD3 cells, mimicking that of CD patients on a gluten-free diet, was observed in USCD patients.

Disclosure: Nothing to disclose

Reference

**P0598** MICRONRNA PROFILING AS A GUIDE TO PERSONALIZED MEDICINE IN ENTEROPATHY ASSOCIATED T-CELL LYMPHOMA AND REFRACTORY CELIAC DISEASE

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Introduction: Peripheral T-cell lymphomas (PTCLs) are considered orphan diseases and develop in the setting of chronic inflammation as celiac disease (CD). A small proportion of CD patients develops refractory celiac disease (RCD), associated with an increased risk of enteropathy associated T lymphoma (EATL). In this context our group has focused on EATL in CD patients with the aim to profile microRNA contents in CD, RCD and EATL patients to obtain molecular biomarkers useful to classify and stratify CD patients according to their ‘neoplastic risk’.

Aims and Methods: Clinical series were composed by 7 RCD, 24 EATL, 10 AITL, 16 PTCLs. EATL and lymphomatous infiltration of RCD (RCD-TIL) were obtained by Laser MicroDissection (LMDS600, Leica) from FFPE blocks. The miRNA profile of 301 miRNA was determined using TaqMan Array Microfluidic Cards (Thermo Fisher Scientific). Statistical analysis was performed using BRBArray Tools, GenePattern and R Software Packages.

Results: Our data show that miRNA profiling distinguished EATLs from other PTCLs, characterized by a subset of miRNAs significantly up- or down-modulated compared to PTCLs. When RCD patients were considered in the analysis, our data showed that RCD-TILs are more similar to EATLs than to other PTCLs (by PCA analysis). Therefore these results suggest that these two diseases are conserved for RCD and EATL. On the other hand, our results show that specific oncosuppressor miRNA families are lost in EATL compared to RCD patients, such as the mir-200, let-7 and mir-192-215 families.

Conclusion: These data suggest that the identification of such signatures could trace the evolution of the inflammatory response of CD into a carcinogenetic process. The availability of accurate biomarkers could implement surveillance and early EATL diagnosis. CD patients’ stratification according to their neoplastic risk could address follow-up and screening program, pursuing a ‘personalized medicine’ approach for CD patients.

Disclosure: Nothing to disclose

Reference

**P0599** PRIMARY GASTROINTESTINAL FOLLICULAR LYMPHOMA: A PROSPECTIVE, LONG TERM FOLLOW-UP CLINICAL STUDY OF 27 CASES

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Introduction: Primary gastrointestinal follicular lymphomas (PGFL) represent a rare entity whose clinical characteristics, management and prognosis after a long term follow-up, have not been well described.

Aims and Methods: Our aim was to prospectively analyse the clinical, biological, endoscopic and pathological features, as well as treatment outcome, of a series of consecutive patients with PGFL. All adult patients with PGFL, consecutively enrolled into the multicenter French national study between 1990 and 2014, were retrospectively reviewed and followed up prospectively. Diagnosis was based on histomorphological criteria according to the WHO classification (confirmed by a reference pathologist). Follow-up comprised at least annual clinical, biological and endoscopic evaluation for all patients.

Results: Among 27 patients with PGFL included in the study, there were 13 men and 14 women, median age at diagnosis was 61 years (extremes: 33–79). The median follow-up was 88 months (6–190). The most frequent circumstances of diagnosis were fortuitous diagnosis (n=11), followed by abdominal pain (n=6), weight loss (n=5), and dyspepsia (n=4). The duodenum was the most common site of involvement (n=13) and multifocal localizations were observed in 7 patients (26%). Endoscopic aspect was the most frequently micronodular or polyposis type or mixture of both. Surveillance was the most frequently adopted strategy (flow in immunostaining) (n=18, 66%), followed by chemotherapy (n=7, 26%). The overall 5-year survival rate was 93%. Out of 16 patients receiving only surveillance, 6 (22%) reached a spontaneous complete remission. On the other hand, in 3 patients a transformation into high-grade lymphoma was observed. Moreover, in 3 patients, an episode of carcinoid syndrome was observed.

Conclusion: This study is the biggest series of PGFL including clinical and endoscopic results with a long term follow-up, published so far. It shows that PGFL are frequently fortuitously diagnosed by gastroenterologist during endoscopy, most frequently localized in the duodenum, and usually of an indolent course and good prognosis. However, in rare cases, their transformation into more aggressive high-grade lymphoma may be observed. An appropriate characterization and follow-up of these lymphomas is mandatory.

Disclosure: Nothing to disclose

Reference

**P0600** NEUROENDOCRINE TUMORS OF THE GASTROINTESTINAL TRACT ARISING IN INFLAMMATORY BOWEL DISEASES: MORE THAN A COINCIDENCE?

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Introduction: The association between inflammatory bowel diseases (IBD) and neuroendocrine intestinal malignancies is higher in patients affected by inflammatory bowel diseases (IBD). Apart from colorectal cancer, associated with grade and duration of the active inflammation, there is a growing evidence of neuroendocrine tumors (NETs) development in IBD patients and a correlation between these two diseases has been postulated.

Enteroendocrine cells seem to be involved in the innate immune system machinery that is damaged in IBD: studies performed in IBD patients and experimental murine models proved that subtypes of interleukin-17 and Toll-like receptors (TLR) are expressed in neuroendocrine cells. In addition, defects of density, differentiation and hormonal production in enteroendocrine cells have been described in an experimental study and microcarcinoids have been detected in up to 10% of patients affected by long standing ulcerative colitis.

Aims and Methods: We report a series of 5 NETs developed in 4 IBD-affected patients. Histological parameters and immunophenotype of the neoplastic lesions were reviewed by an expert pathologist. The neoplastic lesion immunophenotype was assessed using A-choriomagenin (CgA), synaptophysin (Syn), serotonin and chromogranin A (CgA).

Results: We evaluated 4 patients (3 M, 1 F), aged between 32 and 63 years affected by Crohn’s disease (3 cases) and ulcerative colitis (1 case) with a diagnosis of gastro-intestinal NET. In 3 cases diagnosis was incidental after surgery for severe IBD relapse (1 was located in the appendix, 2 in the ileum), whereas in 1 case NET was discovered in the duodenum during an endoscopic examination. 4 G1 (ki67 < 3%), well differentiated, WHO 2017 NETs and a mixed epithelial - neuroendocrine tumor (MANEC) were detected in the resection specimens of the
four cases (Table 1). In 3 cases active IBD was found in specimens, with focal, superficially spread pseudomembrane, or in ISB, which were localized lesions, corresponding to the Lugano classification stage I-II. 2 of the 5 cases occurred post-treatment, and included 1 follicular lymphoma and 1 diffuse large B-cell lymphoma, which were advanced lesions corresponding to Lugano classification stage IV. A total of 13 DBEs were performed for these strictures. The diameter at the first dilation was limited to 10mm or less to avoid perforation before remission, and then gradually increased up to the largest possible size (12-18mm) to facilitate long-term patency. 4 of the 5 strictures required multiple DBE-assisted EBDs (2 lesions: 2 EBDs, 2 lesions: 4 EBDs). The median follow-up after the final DBE-assisted EBD was 22 months (9-49 months). 1 patient developed bowel obstruction during follow-up, due to adhesions (no recurrent stenosis). No adverse events associated with DBE-assisted EBD were observed.

Conclusions: DBE-assisted EBD provides favorable outcomes in patients with small intestinal strictures secondary to primary small intestinal lymphoma. DBE-assisted EBD for the strictures associated with primary small intestinal lymphoma has the potential to be a safe and effective treatment to avoid surgical interventions.

Disclosure: Hironori Yamamoto has patents for double-balloon endoscopy produced by Fujifilm Corporation. He also has a consultant relationship with the Fujifilm Corporation and has received honoraria, grants, and royalties from the company. Tomonori Yano, Yoshikazu Hayashi, and Keijiro Sunada have received honoraria from Fujifilm Corporation.
114 (54%), small bowel Crohns in 14 (6.7%), NSAID enteropathy in 11 (5.2%) and CD in 7 (3.4%). This results in a detection rate of 3.4% (7 out of 208) for neoplasia. The tumour detection rate of 3.4% in our series of 208 IDA patients with a mean age of 68 is compared with a rate 4.5% from a series of 220 IDA patients with a mean age of 40.5, 2.

Conclusion: In our series the diagnostic yield of CE for IDA is 76.0%. 3.4% were diagnosed with malignancy. Patients with malignancy were older than those without. While small bowel tumours are rare, our experience suggests that they are more common than previous data suggests. CE is a beneficial tool in the investigation of IDA with negative bi-directional endoscopies, particularly in the investigation for malignancy.

Disclosure: Nothing to disclose.

References

P0604 PROGRAMMED CELL DEATH LIGAND-1 EXPRESSION IS ASSOCIATED WITH MICROSATELLITE INSTABILITY IN NON-FAMILIAL SMALL BOWEL CARCINOMAS: RESULTS FROM THE SMALL BOWEL CANCER ITALIAN CONSORTIUM


Aims and Methods: To study PD-L1 expression in a large cohort of non-familiar SBC, either not associated with CD or CrD, and compared it with MSI status. We assessed PD-L1 immunohistochemistry (clone E1L3N, Cell Signaling) in a total of 82 non-familial SBC, i.e. 32 CrD-SBC, 23 CD-SBC and 27 spo-SBC. We correlated PD-L1 expression with MSI, which was evaluated using a pantepanel of monomorphic mononucleotide repeats.

Results: PD-L1 positivity (>5% of tumour or immune cells) was seen in 22 (27%) cases, including 8 CrD-SBC (25%, 3 MSI and 3 non-MSI cases), 8 CD-SBC (35%, 7 MSI and 1 non-MSI), and 6 spo-SBC (22%, 3 MSI and 3 non-MSI). In all positive cases, PD-L1 was essentially expressed on stromal immune cells, which were predominantly macrophages restricted to the tumour invasive margin, while PD-L1 reactivity on tumour cells was found only in two, both MSI cases, i.e. one CrD-SBC (tumour cell membrane) and one CD-SBC (tumour cell cytoplasm). The frequency of PD-L1 positivity did not differ significantly among the 3 groups. PD-L1 positivity was more frequently observed in MSI SBC (13/27, 48%) in comparison with non-MSI SBC (9/55, 16%). The association between PD-L1 immunoactivity and MSI status was statistically significant (p 0.0035). The single CrD-SBC case with PD-L1 positivity had a lymphoepithelioma-like morphology and was positive for Epstein-Barr virus latent phase markers.

Conclusion: Our study showed an association between PD-L1 immunoactivity and MSI status, similar to that reported in colorectal and gastric cancers. Interestingly, an Epstein-Barr virus positive case of CrD-SBC also expressed PD-L1 on tumour cells. These findings could be relevant in selecting patients affected by SBC in whom therapeutic PD-1/PD-L1 inhibition could be beneficial.

Disclosure: Nothing to disclose.

References


Microbiota composition was studied by sequencing of the V3-V4 variable regions of the 16S rRNA gene according to the recommended protocol of 16S metagenomic sequencing Library Preparation. Diet - by quantitative assessment. Statistical analysis was performed using the R3.1.0., generalized linear models (FDR, age, and sex adjusted).

Results: 104 participants were included (38 men). BMI obesity (O) was determined in 26%, abdominal obesity (AO) in 55%, O and AO were associated with high abundance of gram-negative opportunistic genera Serratia (FDR 0.003; 0.004) and Prevotella (FDR <0.001). Low Oscillospira abundance was strongly correlated with AO (FDR <0.001). This genus is a ‘central energy maturant’ of the gut microbiome, which reduce inflammation and associated with leanness and high physical activity level. The average caloric intake was 2156±545 kcal. Average daily intake of carbohydrates 210±91g; proteins 79±28 g; fat 107±32g. Bifidobacterium (FDR 0.008) representation was increased and Serratia decreased (FDR 0.008) in those who consumed more starch. High fat consumption was associated with high Serratia (FDR 0.014) and low Oscillospira (FDR 0.004) abundance. Thus, high representation of opportunistic bacteria was associated with O and AO. In addition, the bacteria were more presented among those who consumed smaller amounts of starch, and beneficial bacteria abundance was lower in those who consumed a lot of fat.

Conclusion: We conclude that GM composition is strongly associated with obesity and AO, modulating diet may be a relevant therapeutic avenue for obesity.

Disclosure: Nothing to disclose

References:

P0606 STRESS RESPONSE IN HIGH-FAT DIET-INDUCED OBESE MICE: FOCUS ON INTESTINAL PERMEABILITY

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Introduction: Obesity is a major public health issue; it may have different impacts depending on its grade. Indeed, grade I/II obese subjects seem to be protected from irritable bowel syndrome (IBS) while IBS prevalence is increased by a factor of six in morbid obesity patients than to the general population.

Aims and Methods: The aim of the present study was to evaluate the response of obese mice to a stress model, the water avoidance stress (WAS), which is frequently used to study the pathophysiology of IBS. Male C57Bl/6 mice fed a high fat diet (60% kcal as Fat; HFD) or non (standard diet; SD) for 12 weeks (W12). At W12, WAS (1h/day for 10 consecutive days) was performed (SD-WAS and HFD-WAS, n =15) and not (SD-CC and HFD-CC, n =15). Body composition was assessed by EchoMRI (at W0, W12 and after WAS). The intestinal permeability was evaluated in vivo by oral gavage with FITC-dextran. Colonic permeability was assessed ex vivo by using Ussing chambers. Expression of tight junction proteins and plasma corticosterone were evaluated by westernblot and ELISA, respectively.

Results: HFD mice had a higher body weight than SD mice, related to increased fat mass without altering lean mass. In response to WAS, only HFD mice lost weight. A strong increase in plasma corticosterone was observed among HFD-WAS mice compared to SD-CC and SD-WAS mice. HFD-WAS mice also showed an increase in intestinal permeability compared with the other groups. There was a positive correlation between intestinal permeability and corticosterone levels (r = 0.51, p = 0.021). Finally, in vivo colonic permeability was increased in SD-WAS, HFD-CC and HFD-WAS groups compared with SD-CC group but in a more pronounced manner in HFD-CC and HFD-WAS groups. Occludin expression was reduced in SD-WAS, HFD-CC and HFD-WAS compared with SD-CC.

Conclusion: High-fat diet obesity modifies the response to stress in mice with an increased sensitivity and enhanced intestinal permeability. The involved mechanism and the impact on the functional bowel disorders remain to be determined.

Disclosure: Nothing to disclose

References:

P0607 OVERNIGHT OR MORNING ONLY SPLIT DOSING WITH L POLYETHYLENE GLYCOL NER1006 CAN DELIVER 92% OR HIGHER RATES OF SUCCESSFUL OVERALL COLON CLEANSING IN NORMAL WEIGHT AND OBESE PATIENTS

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Introduction: Adequate bowel cleansing is essential for effective colonoscopy, but may be hard to achieve in overweight or obese patients. The ESGE minimum performance standard for colon cleansing is 90%, a measure which includes overweight or obese patients. NER1006 is a novel L polyethylene glycol (PEG)-based bowel preparation. It was evaluated in the two phase 3, randomized, treatment-blinded, central reader-assessed trials MORA1 and NOCT. This post hoc analysis of MORA and NOCT assessed the cleansing efficacy of 2 split dosing regimens of NER1006 in patients according to body mass index ranges (BMI).

Aims and Methods: Patients aged 18-85 years were randomized to receive a split-dosing regimen of either evening/night (PM/AM) NER1006, or same day morning only (AM/AM) NER1006. Overnight split dosing started at ~6:00 pm (~2 h) with dose 2 at ~6:00 am (~2 h). Morning only dosing started at ~5:00 am (~2 h) with dose 2 at ~7:00 am (~2 h). The percentage of patients with overall bowel cleansing success (Harefield Cleansing Scale (HCS) grades A and B) was analysed for normal weight patients (BMI 18.5-29.9) and obese patients (BMI 25.0-29.9) and obese patients (BMI ≥30.0), respectively. Data were analysed using the modified full analysis set 2 (mFAS2) population, which comprised all patients who received at least 1 dose of study drug and who had documented primary endpoint data from a central reader.

Results: The mFAS2 population had 787 patients. Data from 776 (227 normal weight, 310 overweight, 239 obese) were included in the analysis (Table 1). 11 patients were excluded for missing or low (< 18.5) BMI data (insufficient sample sizes). Among normal weight and obese patients, both dosing regimens NER1006 PM/AM and NER1006 AM/AM attained overall cleansing success rates of 92% or higher. For overweight patients, NER1006 PM/AM attained overall cleansing success rates of 90-98%.

Conclusion: Overnight or morning only split dosing with NER1006 delivered overall HCS cleansing success (e.g. adequate level cleansing) in at least 92% of normal weight or obese patients and for overweight patients, NER1006 overnight split dosing was successful in 90-98%. NER1006 therefore meets the ESGE minimum performance standard for colon cleansing in these weight groups.

Disclosure: Bharat Amlani and Lucy Clayton, employees of Norgine Ltd

References:

Table 1. Overall HCS colon cleansing success using split dosing with NER1006 in normal weight, overweight and obese patients

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>NER1006 PM/AM</th>
<th>NER1006 AM/AM</th>
<th>NER1006 PM/AM</th>
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<td>Overall HCS cleansing success, per BMI category</td>
<td>MORA</td>
<td>MORA</td>
<td>NOCT</td>
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<td>Patients (mFAS2), N</td>
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<td>270</td>
<td>255</td>
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<tr>
<td>Normal weight patients (BMI 18.5-24.9), n (%)</td>
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<td>84/91 (92%)</td>
<td>47/49 (96%)</td>
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<tr>
<td>Overweight patients (BMI 25.0-29.9), n (%)</td>
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<td>100/114 (88%)</td>
<td>89/99 (90%)</td>
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<tr>
<td>Obese patients (BMI ≥30.0), n (%)</td>
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<td>Patients with missing BMI data or BMI &lt; 18.5, n</td>
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<td>3/270</td>
<td>2/255</td>
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Abstract No: P0607
P0608 DUODENO-JEJUNAL BYPASS LINER FOR THE TREATMENT MELTITIS IN OBESIVE PATIENTS: COMPLETENESS OF DUODENO BLINDING AS THE KEY FACTOR FOR EFFICACY
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Abstract: Introduction: The global increase in obesity incidence results in an increase of type 2 diabetes mellitus (T2DM). Surgical treatment has proven to be effective, however it carries a high risk of complications. The duodenal-jejunal bypass liner (EndoBarrier®, GI Dynamics, EB) is an endoscopic implant that mimics the intestinal environment of the Roux-en-Y Gastric Bypass. It results in weight loss and improvements in glucose control in obese patients with T2 diabetes mellitus (T2DM).

Aims and Methods: This is a analysis of a prospective, controlled, multicentre study to verify factors associated with an outcome of EB for T2DM. Seventy subjects (45 with an implant, 25 controls) were included in the study. The groups were comparable with respect to age, gender, BMI (mean 41.7 vs. 39.5 kg/m2), T2DM duration (7.8 vs. 8.3 years), HBa1C level (88 vs 86 mmol/mol) and T2DM in the EB group. T2DM medication could be reduced in more device subjects than controls. There was no significant adverse effect. Deepness of anchor ingrow, lower initial BMI and lower body height were identified as positive factors for efficacy for EB for T2DM compensation.

Conclusion: The EB was safe when implanted for 10 months, and results in significant weight loss and %EWL (19% vs. 7% and 43 vs. 12) and significantly improved long term compensation of T2DM marker HBa1C (decreased by 25 vs. 10 mmol/mol) in the EB group. T2DM medical treatment could be reduced in more device subjects than controls. There was no significant adverse effect. Deepness of anchor ingrow, lower initial BMI and lower body height were identified as positive factors for efficacy for EB for T2DM compensation.

Disclosure: Nothing to disclose.

P0609 THE EFFECT OF THE DIETICIAN SUPPORT AND BEHAVIOURAL THERAPY IN PATIENTS UNDERGOING INTRAGASTRIC BALLOON TREATMENT FOR OBESITY
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Introduction: Obesity is an important public health problem that has reached epidemic proportions in the world. The placement of intragastric balloon (IGB) is nowadays widely accepted as a main endoscopic procedure to lose weight. Other than the endoscopist, the dietician is the only professional considered essential in the multidisciplinary team for IGB patient management. He is considered in the international guidelines and his role during the follow up when IGB is in situ has been investigated. The aim of this study is to evaluate the impact of dietician and behavioural therapy in patients treated with IGB while the device is in situ.

Aims and Methods: We retrospectively reviewed records of 170 obese patients in a single endoscopy unit. The follow up was 15 days during IGB in situ (p = 0.03). Mean pre-procedural weight and BMI were significantly lower in the group treated with IGB and dietician (p = 0.02, BMI: 0.01; T2DM duration (7.8 vs. 8.3 years), HbA1c level (88 vs 86 mmol/mol) and T2DM treatment. In the EB group, all devices were successfully implanted. Only 6 devices had to be explanted prior to the end of the 10 months study period (bleeding, dislocation and need for ERCP because of choledocholithiasis). At 10 months, there was significant greater weight loss and %EWL (19% vs. 7% and 43 vs. 12) and significantly improved long term compensation of T2DM marker HBa1C (decreased by 25 vs. 10 mmol/mol) in the EB group. T2DM medical treatment could be reduced in more device subjects than controls. There was no significant adverse effect. Deepness of anchor ingrow, lower initial BMI and lower body height were identified as positive factors for efficacy for EB for T2DM compensation.

Conclusion: The EB is safe when implanted for 10 months, and results in significant weight loss and %EWL (19% vs. 7% and 43 vs. 12) and significantly improved long term compensation of T2DM marker HBa1C (decreased by 25 vs. 10 mmol/mol) in the EB group. T2DM medical treatment could be reduced in more device subjects than controls. There was no significant adverse effect. Deepness of anchor ingrow, lower initial BMI and lower body height were identified as positive factors for efficacy for EB for T2DM compensation.

Disclosure: Nothing to disclose.

P0610 ADHERENCE TO VITAMIN SUPPLEMENTATION AND NEW LIFESTYLES AFTER BARIATRIC SURGERY
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Introduction: Over the past decades, several studies have demonstrated that bariatric surgery (BS) is the gold standard for the treatment of morbid obesity and weight-related comorbidities and is far more effective than nonsurgical interventions. However, it permanently alters the gastrointestinal anatomy and might induce long-term deficiencies and absorption issues. Adherence to treatment recommendations such as multivitamins, iron tablets, Vitamin B and D supplements is a crucial aspect in the management of patients submitted to bariatric surgery.

Aims and Methods: The aim of this study was to evaluate the adherence to treatment recommendations in a large population of obese patients submitted to BS using a new validated web-based instrument. An anonymous web survey was used to assess adherence. A new validated questionnaire consisting of 23 items evaluating: A. Bariatric procedures performed; B. Individual reasons underlying BS; C. Lack of time since last BS, d. the frequency of follow-up (FU) visits post BS; e. Perception of well-being post BS; f. Adherence to recommendations post BS; g. Changes in lifestyles, was launched through e-methods. Participants have been invited among patients who underwent BS from 1996 to 2016. A single surgeon (L.A.) performed all procedures.

Results: We received an automatic notification of delivery from 1100 out of 1600 obesity patients and 290 (18.4 % female, mean age 49.3 yrs) filled in the questionnaire. 59% underwent Sleeve gastrectomy (SG), 31% Roux-en-Y gastric bypass (RYGB), 7.2 % adjustable gastric banding (AGB). 28% other procedures such as mini gastric-one anastomosis gastric bypass (MGB-OAGB) and duodenal switch (DS). 6.2% had a revisional procedure and only one underwent three bariatric operations. The time interval from surgical procedures was < 1 yrs in 20.9%, 1 to 3 yrs in 25.1%, 4 to 6 yrs in 29.6% and 7 to 10 yrs in 24.4%. The last FU visit was < 1 yrs in 51%, < 2 yrs in 18%, < 3 yrs in 6.9%, < 4 yrs in 7%, 5 yrs in 4.5% and > 5 yrs in 11.7% of obese subjects. Only 31.4% adhere to treatment recommendations. The risk of non-adherence to treatment recommendations was around two times higher in malabsorative (RYGB, DS, MGB-OAGB) than restrictive procedures (AGB and SG) and decreases with age and strict follow-up. (OR = 1.96, 95%CI: 1.26-3.05). It is also independent of sex, the time interval from BS and basal BMI. Moreover, 72% of subjects showed an improvement of their quality of life (QoL) due to a significantly stronger self-identity.

Conclusion: Adherence to treatment recommendations in our obese patients is low especially after malabsorative bariatric procedures possibly since in Italy, vitamin supplementation and micronutrient blood tests are not reimbursed by the national health insurance. Conversely, QoL strongly improved.

Disclosure: Nothing to disclose.

P0611 THE EFFECTS OF OAT β-GLUCAN CONSUMPTION AT BREAKFAST ON APPETITE AND FOOD INTAKE, AS WELL AS BLOOD GLUCOSE, PLASMA INSULIN AND PLASMA GLP-1 CONCENTRATIONS IN HEALTHY SUBJECTS
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Introduction: High fibre consumption is associated with lower body weight (1), and improved postprandial glycaemia (2). There is evidence that oat β-glucan lowers appetite and exerts an inhibitory effect on eating; however, not all studies have observed this effect (3). In the present study the Kruskal-Wallis test was used to analyse the results.

Aims and Methods: We investigated the effects of 4 g high molecular weight (MW; 2,213 x 106 g mol−1) oat β-glucan on ad libitum eating, subjective glycaemia, insulinaemia and plasma GLP-1 responses in 33 normal-weight subjects (23 female:10 male, mean age 26.9±1.0 yrs). The study followed a double-blind, cross-over design with subjects fed two different test breakfasts with and without oat β-glucan on two different days in random order, followed by an ad libitum test meal. Blood samples and ratings for subjective appetite were collected postprandially at regular time intervals. Viscosity of test meals were measured using a constant shear rheometer. Body Rheometer C-VOR 150 (Malvern Bohin Instruments) at a shear rate of 50 s−1.

Results: Oat β-glucan increased feelings of fullness (p = 0.046) and satiety (p = 0.021), but did not affect energy intake or amount eaten at the ad libitum test meal. There was a treatment by time interaction for plasma GLP-1.
insulin and blood glucose. GLP-1 was significantly reduced at 90 min (p = 0.021), blood glucose at 30 min (p = 0.008) and plasma insulin at 30 and 60 min (p = 0.002 and 0.017, respectively) following the oat β-glucan breakfast when compared with the control breakfast. Viscosity of test breakfast containing oat β-glucan was significantly greater compared to control (p < 0.05).

Conclusion: Four grams of high MW oat β-glucan lowers appetite but not ad libitum eating and beneficially modulates postprandial glycaemia and insulinemia, however, it does not increase plasma GLP-1 secretion.

Disclosure: Robert. E. Steiner is an employee of DSM Nutritional Products, Basel, Switzerland.

References

P0612 VARIABILITY IN THE NIGHT PROFILE OF TOTAL GHRELIN IN OBESE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA
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Introduction: Ghrelin is a hormone produced in the gastrointestinal tract. The main functions of ghrelin are the initiation of food intake and the stimulation of growth hormone secretion. Obstructive sleep apnea is the most common sleep breathing disorder in which occurs repetitive upper airway obstruction causing fragmentation of sleep and decreasing sleep quality. The most important cause of sleep apnea is overweight. In the literature, we find reports that both inefficient sleep and obesity affect ghrelin but the results concerning their impact, especially on the night ghrelin profile, still require research1,2.

Aims and Methods: Patients evaluated for sleep breathing disorders were divided into the study group with diagnosed obstructive sleep apnea and into control group. During sleep, blood samples were collected at 23, 1, 3, 5, 7. Total serum ghrelin was measured with a radioimmunoassay test, according to the manufacturer’s instructions. Statistical analyses were performed to find correlations between total ghrelin levels and sleep parameters from polysomnography – apnea hypopnea index (AHI) and % snoring time during sleep were chosen. Moreover, the correlations between total ghrelin levels and parameters of obesity (BMI, abdominal circumference) were assessed.

Results: The study included 59 patients (49 men and 10 women), 46 patients were diagnosed with sleep apnea (OSA group). Most of the patients included in the study were overweight (20.3%) or obese (74.6%). After analysis of results in both groups we observed a tendency towards lower ghrelin values in OSA group. However, only for values measured at 5 am this correlation was statistically significant, the trend in the other assays were close to statistical significance. However, only for values measured at 5 am this correlation was statistically significant, the trend in the other assays were close to statistical significance. Therefore, the research should focus on understanding the clinical significance of these results.

Disclosure: Nothing to disclose.
and integrated relaxation pressure reductions were achieved in both groups. No perioperative mortality or major postoperative complications occurred.

Conclusion: POEM is a minimally invasive, incisionless operation. POEM is a safe and effective operation for both paediatric and adult patients. POEM may be a useful treatment method for both paediatric and adult patients with achalasia. Long-term follow-up studies would be helpful to determine whether POEM could become an appropriate therapy for paediatric patients with achalasia in the near future.

Disclosure: Nothing to disclose

P0616 CHANGES OF MORPHOLOGICAL DISORDERS OF GASTRIC MUCOSA IN CHILDREN WITH CHRONIC GASTRITIS CO-INFECTED WITH HELICOBACTER PYLORI AND EPSTEIN-BARR VIRUS AFTER A COURSE OF ANTIHELICOBACTER THERAPY
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Introduction: The persistence of Epstein-Barr virus in the gastric mucosa in Hp-associated chronic gastritis increases the prevalence, severity and activity of inflammation.

Aims and Methods: The aim of the work is to estimate the dynamics of morphological disorders of the gastric mucosa in children with chronic gastritis co-infected with Helicobacter pylori and Epstein-Barr virus after course of anti Helicobacter therapy. 69 children aged 7-17 with chronic Hp-associated gastritis were observed. According to the study of gastrobiopsy there was a chronic inflammatory process in the body of the stomach in 62.5% and in Helicobacter pylori in the gastric mucosa was detected in 46 out of 69 patients (66.7%), highly in all cases. Via polymerase chain reaction Epstein-Barr virus (EBV) persistence in the gastric mucosa in Hp-infected children was determined. EBV - negative patients their number did not change, there was a significant decrease in severity of the process in the body of the stomach (62.5%) and in Helicobacter pylori in the gastric mucosa was detected in 31 patients (45.5%), highly in all cases. The persistence of Epstein-Barr virus in the gastric mucosa in Hp-infected children was determined.

Results: Altogether 284 (34%) patients had partial, 332 (40%) subtotal and 219 (26%) total violet atrophy. Those with more severe lesion were born (1996 vs 1996 vs 1991, p < 0.001) and diagnosed (2007 vs 2006 vs 1999, p < 0.001) during earlier years and had higher median endoscopy antibody titers (1:200 vs 1:500 vs 1:500, p < 0.001), and lower haemoglobin (126 vs 124 vs 121, p = 0.005) and body mass index (16.6 vs 16.1 vs 16.1, p = 0.005). They were also less often screen-detected (33% vs 25% vs 17%, p < 0.001) and had more anemia (16% vs 22% vs 25%, p < 0.003) and growth disturbances (20% vs 38% vs 54%, p < 0.001), whereas there was no difference in gender distribution or the overall frequency of symptoms at diagnosis. Differences between the groups at diagnosis persisted after adjustment with birth and diagnosis year. The groups had similar short-term (6-24 months) dietary adherence and treatment response. At total, 237 (42%) adults responded the questionnaires median of 18.5 years after the diagnosis. After adjustment of the groups, there were no differences in working full-time, presence of children or coeliac disease in the family, smoking or frequency of physical exercise, adherence to gluten-free diet, experience of dietary treatment, self-perceived health, presence of associated diseases, quality of life or gastrointestinal symptoms in adulthood.

Conclusion: Severe violet atrophy at childhood diagnosis was associated to more difficult clinical presentation. However, the degree of mucosal damage did not affect the long-term treatment outcomes in adulthood.

Disclosure: Nothing to disclose

P0617 SEVERITY OF HISTOLOGICAL DAMAGE IN COELIAC DISEASE: ASSOCIATED FACTORS AND LONG-TERM SIGNIFICANCE
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3Hospital District of Kanta-Häme, Department of Pediatrics, Hämeenlinna, Finland
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5Tampere University Hospital, Department of Internal Medicine, Tampere, Finland
6University of Tampere, Celiac Disease Research Center, Tampere, Finland

Introduction: Recent paediatric guidelines allow non-invasive diagnosis of coeliac disease in selected patients. However, besides diagnostic purposes, there might be other reasons for the duodenal biopsy. For example, it is unclear whether patients with severe villous atrophy have higher risk to develop long-term complications and should therefore be followed up more closely. We investigated if the severity of intestinal lesion affects other disease features and long-term prognosis.

Aims and Methods: Comprehensive medical data of 835 children diagnosed with coeliac disease in 1966-2014 were collected. Furthermore, questionnaires evaluating overall health, coeliac disease-related symptoms (GSRS questionnaire), quality of life (PGWB questionnaire), lifestyle and gluten-free diet were sent to 559 currently adult patients. All study variables were compared between patients divided to three groups based on the severity of diagnostic histopathology.

Results: There were 246 patients with mild, 300 with moderate and 113 with severe histopathology. Patients with severe villous atrophy had more symptoms, similar dietary adherence to adulthood, but more severe coeliac disease-related symptoms (GSRS questionnaire) at diagnosis. After adjustment with diagnosis year, the groups had similar short-term (6-24 months) dietary adherence and treatment response. At total, 237 (42%) adults responded the questionnaires median of 18.5 years after the diagnosis. After adjustment of the groups, there were no differences in working full-time, presence of children or coeliac disease in the family, smoking or frequency of physical exercise, adherence to gluten-free diet, experience of dietary treatment, self-perceived health, presence of associated diseases, quality of life or gastrointestinal symptoms in adulthood.

Conclusion: Severe villous atrophy at childhood diagnosis was associated to more difficult clinical presentation. However, the degree of mucosal damage did not affect the long-term treatment outcomes in adulthood.

Disclosure: Nothing to disclose

P0618 DIAGNOSTIC DELAYS IN CHILDREN WITH COELIAC DISEASE IN THE CENTRAL EUROPEAN REGION IN 2016
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Disclosure: Nothing to disclose

Abstract No: P0618: Table 1. Diagnostic delays in children with Coeliac disease in Central Europe

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<td>6</td>
<td>43</td>
<td>10y</td>
<td>3m (0-4y)</td>
<td>2m (0-7y)</td>
</tr>
<tr>
<td>Germany</td>
<td>5</td>
<td>39</td>
<td>6.5y</td>
<td>6m (0-5y)</td>
<td>0m (0-8m)</td>
</tr>
<tr>
<td>Hungary</td>
<td>21</td>
<td>283</td>
<td>7y</td>
<td>6m (0-14y)</td>
<td>1m (0-8y)</td>
</tr>
<tr>
<td>Italy</td>
<td>2</td>
<td>59</td>
<td>5y</td>
<td>6m (0-5.5y)</td>
<td>1m (0-8m)</td>
</tr>
<tr>
<td>Slovenia</td>
<td>7</td>
<td>35</td>
<td>7.5y</td>
<td>6m (0-7y)</td>
<td>1m (0-5y)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>41</td>
<td>459</td>
<td>7y</td>
<td>6m (0-14y)</td>
<td>1m (0-8y)</td>
</tr>
</tbody>
</table>
**Abstract No: P0621: Table 1. Clinical presentation of CD in different regions of Central Europe.**

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>TOTAL</th>
<th>CROATIA</th>
<th>GERMANY</th>
<th>HUNGARY</th>
<th>ITALY</th>
<th>SLOVENIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N = 652)</td>
<td>(N = 66)</td>
<td>(N = 69)</td>
<td>(N = 381)</td>
<td>(N = 82)</td>
<td>(N = 54)</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>20.2%</td>
<td>12.1%</td>
<td>23.2%</td>
<td>20.7%</td>
<td>24.4%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>33.1%</td>
<td>51.5%</td>
<td>36.4% (47.0%)</td>
<td>36.2% (56.5%)</td>
<td>24.4% (41.2%)</td>
<td>16.4% (23.2%)</td>
</tr>
<tr>
<td>Growth retardation</td>
<td>13.8%</td>
<td>21.9%</td>
<td>9.1% (16.7%)</td>
<td>17.4% (18.8%)</td>
<td>10.5% (17.8%)</td>
<td>13.4% (19.5%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>12.9%</td>
<td>30.6%</td>
<td>15.2% (25.8%)</td>
<td>4.3% (27.5%)</td>
<td>10.2% (23.9%)</td>
<td>12.2% (24.4%)</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>10.2%</td>
<td>24.0%</td>
<td>7.6% (15.2%)</td>
<td>2.9% (4.3%)</td>
<td>9.4% (24.9%)</td>
<td>6.1% (11.0%)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>7.1%</td>
<td>32.1%</td>
<td>3.0% (9.7%)</td>
<td>5.8% (20.3%)</td>
<td>6.6% (31.5%)</td>
<td>3.7% (11.0%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>5.4%</td>
<td>13.8%</td>
<td>3.0% (9.1%)</td>
<td>1.4% (5.8%)</td>
<td>3.9% (9.4%)</td>
<td>7.3% (19.5%)</td>
</tr>
<tr>
<td>Unexplained fatigue</td>
<td>3.3%</td>
<td>11.7%</td>
<td>1.5% (9.1%)</td>
<td>4.3% (14.5%)</td>
<td>2.4% (6.8%)</td>
<td>4.9% (14.6%)</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>4.0%</td>
<td>4.2%</td>
<td>0.0% (0.0%)</td>
<td>0.0% (0.0%)</td>
<td>4.7% (5.0%)</td>
<td>3.7% (3.7%)</td>
</tr>
</tbody>
</table>

**P0619 NATURAL HISTORY OF POTENTIAL CELIAC DISEASE: FACTORS PRECIPITATING EVOLUTION TO VILLOUS ATROPHY**

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**Introduction:** Potential celiac disease (PCD) is still a controversial clinical condition: there is not yet agreement on prognosis and treatment.

**Aims and Methods:** Aim of our study was to investigate the natural history of the disease and to identify risk factors associated with possible development of villous atrophy.

We prospectively enrolled 340 PCD children (twice positive anti-tTG IgA and anti-endoamylase antibodies + duodenal mucosa Marsh 0 or 1): 67.1% females, most asymptomatic (86.7%). They were followed till 144 months (median 76.1) without significant regional difference.

**Results:** During FU 88/340 (25.8%) became anti-tTG negative. 42 (20.2%) children developed villous atrophy: cumulative survival at 12 years was 42% and 61% for males and females, respectively. A cluster of events (children developing villous atrophy) observed in the first year of FU with no differences between sex. The best predictors of evolution to villous atrophy at the time of enrollment were: intraepithelial lymphocyte infiltration (p = 0.001), age > 10 years (p = 0.001), HLA homozygosity (p = 0.023), intensity of anti-tTG2 intestinal deposits (p = 0.049). Familiarity for CD and other autoimmune disease did not impact the natural history of this condition.

**Conclusion:** PCD is confirmed to be an heterogeneous condition, but it seems possible to identify risk factors at the time of diagnosis and in first years of follow-up to discriminate children who will develop eventually villous atrophy.

**Disclosure:** Nothing to disclose

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**P0621 CLINICAL PRESENTATION OF COELIAC DISEASE IN CHILDREN AND ADOLESCENTS FROM CENTRAL EUROPEAN REGION IN 2016**

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9Department of Paediatrics, University Medical Centre Maribor, Slovenia

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**Introduction:** Coeliac disease (CD) is a lifelong immune-mediated systemic disorder, affecting genetically susceptible individuals after ingestion of gluten. It occurs approximately in 1% of the population and has a diverse clinical presentation, ranging from classical gastrointestinal manifestation of malabsorption to subclinical and asymptomatic forms.

**Aims and Methods:** The aim of our study was to present clinical manifestations of CD among the children and adolescents in Central European (CE) region.

41 centres from five CE countries (Croatia (CRO) - 6, Germany (GER) - 5, Hungary (HUN) - 21, Italy (ITA) - 2 and Slovenia (SLO) - 7) provided data as part of a multi-centre web-based survey. We retrospectively analysed medical records of children and adolescents diagnosed with CD in 2016, focusing on a single leading symptom indicative of CD and other associated symptoms. We compared clinical presentation at the time of diagnosis of preschool (< 6y) and school-age children and analysed regional differences in clinical picture. Statistical analysis was performed using SPSS for Windows.

**Results:** Data from 652 children and adolescents (64.0% female, 37.0% preschool) from CRO (N = 66), GER (N = 69), HUN (N = 381), ITA (N = 82) and SLO (N = 54) with the diagnosis of CD, confirmed in 2016, were available for further analysis.

Median age at the time of diagnosis was 7 years (range 7m-18.5y). 20.2% of children were asymptomatic, out of which 64.4% belonged to a known risk group (73% with positive family history of CD).

The most common leading symptom at the time of diagnosis was abdominal pain (33.1%), followed by growth retardation (13.8%) and diarrhoea (12.9%). We did not find any regional differences regarding the most common leading symptom. Abdominal pain was also found to be the most common leading symptom in both, preschool (20.9%) and school-age (41.1%) children.

In preschool children, the second most common leading symptom was diarrhoea (17.0%), followed by growth retardation (16.0%) and in school-age children the opposite was found (growth retardation + 12.4%, diarrhoea - 10.2%).

**Conclusion:** Our data showed that clinical presentation of CD is diverse in children in CE. Although classical clinical presentation is not so frequent, gastrointestinal symptoms, especially abdominal pain, remain the leading symptom in all compared groups of children and adolescents. In school-age children, abdominal pain was twice as common in comparison to preschool children. In Germany it was a leading complaint in almost half of the included children.

Also becoming increasingly common is for CD to present as an asymptomatic disease. Our data showed that one fifth of included children had no symptoms before the diagnosis was confirmed with asymptomatic group being the largest in Italy and Germany compared to other regions.
P0622 UTILISATION OF DIAGNOSTIC TOOLS FOR COELIAC DISEASE IN CHILDREN IN 2016-2017 - A NATION-WIDE SURVEY


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12University of Pécs, First Dept. of Internal Medicine, Pécs, Hungary
13Szent Borbala Hospital, Free Municipal Hospital, Tatabánya, Hungary
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15Municipality of Maribor, Maribor, Slovenia

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Introduction: ESPGHAN allowed in 2012 to confirm the diagnosis of coeliac disease (CeD) without biopsy in children with CeD-relevant symptoms (as defined in Husby, JPGN 2012) and serum anti-transglutaminase antibody levels exceeding 10 times the upper limit of normal (High TGA+) in whom endomysial antibodies (EMA) are positive and who carry HLA-DQ2 or DQ8. In this study we explored how these criteria are followed in clinical practice.

Aims and Methods: Paediatric gastroenterologists in Hungary were asked to upload medical data of their patients diagnosed with CeD between January 2016-April 2017 concerning disease presentation, antibody, histology and DQ typing for the whole groups.

Results: 27 gastroenterology services representing all counties in Hungary uploaded altogether 654 patients’ data diagnosed in the last year with CeD, of whom 566 were children and adolescents below 18 years of age (median 8 years [range 1-18]). Biopsy was performed in 435 children (76.8%), which showed Marsh 2–3 lesions or villous atrophy by other grading in 413 (95%), Marsh 0–1 in 20 (4.6%). Biopsy was performed in 435 children (76.8%), which showedMarsh 2–3 lesions or villous atrophy by other grading in 413 (95%), Marsh 0-1 in 20 (4.6%).

Conclusion: The presence of antibodies reacting with the p53 tumor suppressor protein has been described in patients with some autoimmune disorders. Anemia is a common finding in untreated celiac disease, but the mechanisms behind this association are obscure. Abnormal expression of small intestine iron transport proteins could provide a possible explanation but the existing research is scarce and contradictory. We investigated whether aberrant expression of the transporter proteins is associated with anemia in pediatric celiac disease.

Aims and Methods: Duodenal cytokerochrome B (DecyB), divalent metal transporter 1 (DMT1), ferroportin, hephaestin and transferrin receptor 1 (TIR1) were stained immunohistochemically in duodenal biopsies of 27 celiac disease patients with villus atrophy and 16 children with normal mucosal morphology. Twenty of these 43 individuals had anemia. The expressions of the proteins were investigated as regards to intensity (negative/weak, strong) and the results were compared between the groups.

Results: In celiac disease patients, no differences in protein expressions between anemic and non-anemic patients were seen. The expressions of DecyB (p = 0.036) and hephaestin (p = 0.040) were significantly lower in celiac disease patients than individuals with normal mucosal morphology (Table 1), and there was a similar but non-significant trend in the expression of DMT1 (p = 0.060). In the subgroup analysis of the morphologically normal patients, there were no differences between seropositive or seronegative patients.

Disclosure: Nothing to disclose.

Table 1. The intensity of the iron transporter proteins in duodenal biopsies 43 children.

<table>
<thead>
<tr>
<th>Description</th>
<th>Celiac disease</th>
<th>No villous atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-value</td>
<td>N=27</td>
<td>N=16</td>
</tr>
<tr>
<td>Dcy</td>
<td>Negative/Weak 82.5</td>
<td>56.3</td>
</tr>
<tr>
<td></td>
<td>Strong 14.8</td>
<td>43.8</td>
</tr>
<tr>
<td>DMT1</td>
<td>Negative/Weak 77.8</td>
<td>50.0</td>
</tr>
<tr>
<td></td>
<td>Strong 22.2</td>
<td>50.0</td>
</tr>
<tr>
<td>Hph</td>
<td>Negative/Weak 74.1</td>
<td>75.0</td>
</tr>
<tr>
<td></td>
<td>Strong 25.9</td>
<td>25.0</td>
</tr>
<tr>
<td>TIR1</td>
<td>Negative/Weak 88.9</td>
<td>63.5</td>
</tr>
<tr>
<td></td>
<td>Strong 11.1</td>
<td>37.5</td>
</tr>
</tbody>
</table>

[The intensity of the iron transporter proteins in duodenal biopsies 43 children.]

Conclusion: We conclude that anemia in celiac disease is not associated with abnormal expression of iron transporters. Instead, the expressions of DcyB and hephaestin, enzymes catalyzing the reduction and oxidation of iron, respectively, decreased in patients with villus atrophy. These changes might lead to insufficient absorption of iron in the small intestine and thus predispose to the development of anemia in untreated celiac disease.

Disclosure: Nothing to disclose.

P0623 EXPRESSION OF IRON TRANSPORTER PROTEINS IN THE SMALL BOWEL MUCOSA OF CHILDREN WITH CELIAC DISEASE

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Introduction: The presence of antibodies reacting with the p53 tumor suppressor protein has been described in patients with some autoimmune disorders.

Aims and Methods: Our purpose was to explore the relationship between the level of vitamin D and the content of p53 proteins in the mucous membrane of the
duodenum in children with celiac disease (CD). In 42 children with CD at the age from 7 to 15 years in the biopsy samples of the duodenum was determined the level of p53 protein expression by monoclonal mouse antibodies to human pro-
teins (clone DO-7) Dakopatts, (Denmark). Level of 25 D (OH) was determined in serum by ELISA (Elecsys-2010).

Results: Vitamin D deficiency was diagnosed in 33 children with CD (13.3 ± 3.9 ng / ml), 9 patients have vitamin D insufficiency (24 ± 4 ng / ml). In the group of children with vitamin D deficiency, the amount of p53 protein in the mucous membrane of the duodenum was 6.5 ± 0.3%, and in the case of vitamin D defi-
cency it was 1.9 vs 0.22% (p < 0.001). The number of mitotically active cells of the small intestinal mucosa was 83.3 ± 5.4% in cases of vitamin D deficiency, at vitamin D insufficiency it was 38.0 ± 3.9%.

An inverse strong correlation was found between the values of vitamin D and the values of tissue protein p53 in over 50% of subjects. This could be an indirect confirmation of the delay in the regeneration of the small intestine at vitamin D deficiency.

Disclosure: Nothing to disclose

P0625 H. PYLORI INFECTION MAY EXACERBATE SMALL INTESTINAL MUCOSAL INJURY IN CONCOMITANT NON-SELECTIVE NSAIDS AND PPI TREATMENT

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Introduction: Helicobacter pylori (HP) infection is a primary cause of gastric and duodenal ulcers. Most HP uninfected gastric duodenal ulcers are caused by NSAIDs. Many capsule endoscopic studies of healthy volunteers revealed that concomitant administration of non-selective NSAIDs and PPI can induce small intestinal mucosal injuries in over 50% of subjects.

Aims and Methods: As HP infection is the main cause of duodenal ulcers, the impact on small intestinal mucosa is clear. Therefore, the aim of the study was to investigate any association between HP infection and small intestinal mucosal injury.

Results: Of the 48 children aged 14.6 ± 3.3 y, 8 did not satisfy all the SBOS criteria. Another 5 were excluded as they had a specific disease later at follow-

up (celiac disease, n = 2; giardiasis, n = 2; combined variable immunodeficiency, n = 1). SBOS as per the above criteria was present in 16/35 (46%) cases. The jejunal cultures (n = 16) yielded Pseudomonas (n = 8), Escherichia coli (n = 7) and Klebsiella (n = 4) and Streptococcus (n = 3). 7/16 cultures grew > 1 organism. 2/4 Klebsiella were resistant to all antibiotics and treated with empirical choice of antibiotics. Of the positive glucose (n = 12) and lactulose (n = 7) hydrogen breath tests, dual positivity was seen in three. In the first therapy phase, primary anti-
biotics administered as per sensitivity pattern were cefixime (n = 10), norfloxacin (n = 6) and co-trimoxazole (n = 2). 5/10 of cefixime group did not show response after 2 weeks. In the second therapy phase after wash out period, secondary antibiotics administered were co-trimoxazole (n = 8), norfloxacin (n = 4), cefe-
time (n = 2) and nitrafurantoin (n = 2). Cefixime resistant organisms (n = 5) and multi-antibiotic resistant Klebsiella (n = 2) responded clinically to co-trimoxa-
zole. Of the positive hydrogen breath tests, over a follow-up period of 3 (2–9) months, 5 patients (31%) had recurrence of symptoms. All 5 were primary antibiotic responsive and responded (clinical and breath test) to the same antibiotics during recurrence.

Conclusion: SBOS (jejunal mucosal injury and breath test positivity) is seen in 46% of chronic diarrhea with no discernable etiology. Gram negative organisms are the commonest flora in 80%; multibacterial in 43%. Primary antibiotic response is seen in two-thirds. Co-trimoxazole is a favourable drug for primary antibiotic failure and antibiotic resistant groups. One-third have relapse of SBOS and are respond to primary antibiotics.

Disclosure: Nothing to disclose

P0627 A FIRST APPROACH FOR AN EVIDENCE-BASED METHOD TO ADJUST PANCREATIC ENZYME REPLACEMENT THERAPY IN CYSTIC FIBROSIS

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Introduction: The aim of this project was to assess the effectiveness of a method to adjust pancreatic enzyme replacement therapy (PERT) in Cystic Fibrosis (CF). The method is based on the prediction of the optimal dose according to food properties, by means of modelling of results of in vitro digestion studies.

Aims and Methods: Prospective interventional study with 43 patients from 5 European centres. During 24h they followed a fixed diet (5 meals), along with the optimal dose of enzymes for each meal previously characterised or deter-
mined by in vitro digestion. Fat in stools was determined after samples collection, which was carried out using colorimetric markers for a precise identification of stools corresponding to the study meals. Beta regression models were applied to evaluate the relationship of study variables with coefficient of fat absorption (CFA).

Results: Median CFA was 90% (95% CI 84, 95%) with no differences among centres. Patients’ compliance with protocol was 99% and median Bristol stool scale was 3-4. No association of CFA with age, mutation or BMI score, but a significant effect was found with transit time (p < 0.05). Findings suggest that these variables do not play as an important role as food characteristics do on lipids digestion (on the basis of which the study doses were established).

Conclusion: Applying the in vitro predicted recommended PERT dose for each meal, the clinical target of CFA is reached with low variability among patients. The proposed approach can be considered a first step towards an evidence-based method to adjust PERT in CF.

Disclosure: Nothing to disclose
P0628 IMPACT OF CYP2R1, CYP27A1 AND CYP27B1 GENETIC POLYMORPHISMS CONTROLLING VITAMIN D METABOLISM ON SUSCEPTIBILITY TO HCV INFECTION IN A HIGH-RISK CHINESE POPULATION

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Introduction: CYP2R1 and CYP27A1 hydroxylases involve in the hydroxylisation from vitamin D3 to 25-hydroxyvitamin D3 (25[OH]D3), and CYP27B1 hydroxylase catalyzes the conversion of 25(OH)D3 to 1,25(OH)2D3, the most active Vitamin D metabolite, which plays a role in the immune regulation and pathogenesis of hepatitis C virus (HCV) infection. The present study aims to investigate the relationship between the polymorphisms of vitamin D pathway genes (CYP2R1, CYP27A1 and CYP27B1) and HCV infection outcomes in Chinese population.

Aims and Methods: Nine single nucleotide polymorphisms (SNPs) from CYP2R1, CYP27A1 and CYP27B1 were genotyped in a Chinese population with high risk of HCV infection. The distributions of these SNPs were compared among groups with different HCV outcomes, including 863 HCV persistent infection cases, 524 spontaneous clearance subjects and 1079 uninfected controls.

Results: Logistic regression analyses showed that CYP2R1 rs12794714-G, rs10741657-A, rs1582902-C, and rs1076197-G alleles were significantly associated with increased susceptibility to establishment of HCV infection (all p<0.05 in additive/dominant models), and the combined effect of the four unfavorable alleles was related to an elevated risk of HCV infection in a locus-dosage manner (p-trend=0.008). The risk effects of the four unfavorable alleles were more obvious among drug users and subjects aged ≥50 years. Moreover, haplotype analyses suggested that compared with the most frequent A>G>T>G, G>A>T>G, T>G>A>T, and G>A>T>G>SNPs haplotype, the haplotype containing the four unfavorable alleles GACG indicated a risk effect of HCV infection (adjusted OR=1.243, p=0.006). However, no links were found between these SNPs and viral clearance, and also no associations of the other two genes with infection outcomes were found.

Conclusion: Our study implicated that genetic variants in CYP2R1 may be involved in HCV infection susceptibility in Chinese population.

Disclosure: Nothing to disclose.

P0629 INHIBITION OF CYCLOOXYGENASE-2 AMELIORATES LIVER CIRRHOSIS BY TARGETING SPLENIC ABNORMALITIES

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Introduction: Spleen plays an important role in the immune regulation and pathogenesis of liver cirrhosis. The immune cells and cytokines derived from spleen may be affected by the progression of liver cirrhosis. However, the abnormalities of splenic portal circulation. The immune cells and cytokines derived from spleen may play a role in the immune regulation and pathogenesis of hepatitis C virus (HCV) infection. The present study aims to investigate the relationship between the polymorphisms of vitamin D pathway genes (CYP2R1, CYP27A1 and CYP27B1) and HCV infection outcomes in Chinese population.

Aims and Methods: Nine single nucleotide polymorphisms (SNPs) from CYP2R1, CYP27A1 and CYP27B1 were genotyped in a Chinese population with high risk of HCV infection. The distributions of these SNPs were compared among groups with different HCV outcomes, including 863 HCV persistent infection cases, 524 spontaneous clearance subjects and 1079 uninfected controls.

Results: Logistic regression analyses showed that CYP2R1 rs12794714-G, rs10741657-A, rs1582902-C, and rs1076197-G alleles were significantly associated with increased susceptibility to establishment of HCV infection (all p<0.05 in additive/dominant models), and the combined effect of the four unfavorable alleles was related to an elevated risk of HCV infection in a locus-dosage manner (p-trend=0.008). The risk effects of the four unfavorable alleles were more obvious among drug users and subjects aged ≥50 years. Moreover, haplotype analyses suggested that compared with the most frequent A>G>T>G, G>A>T>G, T>G>A>T, and G>A>T>G>SNPs haplotype, the haplotype containing the four unfavorable alleles GACG indicated a risk effect of HCV infection (adjusted OR=1.243, p=0.006). However, no links were found between these SNPs and viral clearance, and also no associations of the other two genes with infection outcomes were found.

Conclusion: Our study implicated that genetic variants in CYP2R1 may be involved in HCV infection susceptibility in Chinese population.

Disclosure: Nothing to disclose.

P0630 CELECOXIB ATTENUATES HEPATOCELLULAR APOTOPSIS THROUGH INHIBITION OF ENDOPLASMIC RETICULUM STRESS IN CIRRHOTIC RATS

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Introduction: Endoplasmic Reticulum Stress (ERS) is an important mechanism in the process of liver disease and chronic progression. ERS is involved in the progression of liver fibrosis and its recovery. Excessive and prolonged ER stress triggers apoptosis to eliminate dysfunctional cells. Apoptosis induced by ER stress is is considered to be important way on the origin and development of liver fibrosis. Cox-2 induction is closely related to endoplasmic reticulum stress. Our previous studies have found that the Cox-2 inhibitor, Celecoxib, can improve hepatic fibrosis and portal hypertension. But the role of Celecoxib in alleviating liver fibrosis is related to alleviating ERS, and there is no research report.

Aims and Methods: To investigate whether celecoxib could alleviate the development of liver fibrosis by reducing hepatocyte apoptosis via inhibition of endoplasmic reticulum stress (ERS) response. Methods: Peritoneal injection of thioacetamide (TAA) was employed to induce liver cirrhosis for 16 weeks (200 mg/kg/3 days before weeks, 100 mg/kg/3 days after weeks). 45 male Sprague-Dawley rats were randomly assigned to the control, TAA, and TAA-celecoxib groups. TAA-cirrhotic rats received celecoxib (20 mg/kg/day) or its vehicle by gastric gavage for last 8 weeks. rats were put to death after 16 weeks, and serum AST, ALT and ALB content in rats were detected. The degree of fibrosis was assessed by fibrous hepatic fibroblasts (Sirius red) and hydroxyproline contents. The stress level of endoplasmic reticulum was evaluated by detecting its marker protein GRP78 and CHOP. Apoptosis level was evaluated by the detection of Caspase-12 and Caspase-3, hepatic expression of PERK, IRE1 and ATF6 was related to ERS.

Results: Celecoxib administration significantly decreased serum AST and ALT levels in the liver, without significant changes in ALB. The degree of fibrosis in liver fibrosis and hydroxyproline was significantly reduced to celecoxib (~38% and ~25.7%, p<0.01). Compared with the TAA group, celecoxib ameliorated endoplasmic reticulum stress by lowering the level of GRP78 (p<0.05). Consistently, the up-regulation of hepatic apoptosis-level (Caspase-12, Caspase-3) and CCAAT/enhancer binding protein (CHOP)inhibited by TAA was significantly inhibited after celecoxib administration. Furthermore, the expressions of critical molecules in ERS (PERK, IRE1, ATF6) was reduced after celecoxib management (p<0.05).

Conclusion: Therapeutic administration of celecoxib can efficiently reduce hepatic apoptosis in TAA-cirrhotic rats. These effects may be due to the suppression of CCAAT / enhancer binding protein homologous protein (CHOP) expression, which are subsequent to the inhibition of endoplasmic reticulum stress.

Disclosure: Nothing to disclose.

SMA increased significantly by 2.3-fold compared with that in the control group. While hepatic a-smooth muscle actin (α-SMA) protein expression decreased significantly in TAA-celecoxib group. Elevated protein expression of COX-2 was detected in the spleen of the TAA group compared with that in the control group. But celecoxib significantly reduced the expression of COX-2 in spleen of the TAA-celecoxib group. Besides, compared with the control group, the protein expression of IgM and IgG in spleen and serum were found to be greatly increased in the TAA group. While they were significantly reduced in TAA-celecoxib group compared with that in TAA group. Moreover, the number of splenic total T cell, CD8+ T-cell, Treg, total B cell and the activated B cell (B220+CD38+) were all increased in TAA group compared with the control group, while dramatically reduced in TAA-celecoxib group. Interestingly, compared with the control group, the number of splenic marginal B cell (B220+CD21+CD23-) were decreased in TAA group, while increased in TAA-celecoxib group. And no obvious changes of splenic CD4+ T-cell and follicular B cell (B20+CD21+CD23+) were observed in each group.

Conclusion: The present study indicates that COX-2 may be involved in regulating the development and differentiation of immune cell subsets in spleen of liver cirrhosis. And the inhibition of COX-2 by celecoxib could attenuate the liver cirrhosis and the relevant immune dysfunction. Furthermore, the study shed light on the fact that Celecoxib may ameliorate liver cirrhosis partly through the targeting spleenic abnormalities.

Disclosure: Nothing to disclose.
P0631 THE PREDICTIVE ABILITY OF LABORATORY INDICES IN ASSESSING ADVANCED HEPATIC FIBROSIS AMONG CHRONIC HEPATITIS C PATIENTS WITH DIFFERENT STATUSES OF ANTI-VIRAL TREATMENT AND BODY MASS INDEX

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Introduction: Histological staging is essential for prognostication and treatment decision among patients with chronic hepatitis C. Liver biopsy is the gold standard in assessing liver fibrosis but is invasive with potential complications. Therefore, many non-invasive methods to predict liver fibrosis have been reported. Aspartate aminotransferase (AST)/platelet ratio index (APRI) and fibrosis-4 (FIB-4) are well-known serum markers and have been widely used to predict histological results. However, in clinical settings, serum biomarkers might rapidly fluctuate over time and be influenced by many factors, such as anti-viral treatment, steatohepatitis status, and other comorbidities. It is not well established how these factors influence the diagnostic accuracy of APRI and FIB-4 in evaluating liver fibrosis. Therefore, this study aimed to investigate the predictive ability of two laboratory indices for liver fibrosis in patients with different statuses of anti-viral treatment, body mass index (BMI), and other comorbidities.

Aims and Methods: A total of 96 patients (men, 53.1%) with chronic hepatitis C infection who underwent liver biopsy between September 2015 and December 2017 at Taichung Mackay Memorial Hospital, Taiwan were retrospectively reviewed. The histological appearance of fibrosis was assessed using the Ishak scoring system (range, 0–6) and several laboratory values were evaluated. The APRI was calculated as AST [IU/L] / upper limit of normal AST [IU/L] × 100 / platelet count [109/L]. The FIB-4 index was calculated as AST [IU/L] / upper limit of normal ALT [IU/L] × 100 / platelet count [109/L] × alanine aminotransferase (ALT) [IU/L] / 2.

The predictive performance of two indices was assessed using receiver operating characteristic (ROC) analysis, and the area under the ROC curve (AUROC) was evaluated.

Results: The mean age was 59.3 (range, 35–83) years. The proportion of diabetes, hyperlipidemia, and hypertension was 27.1%, 69.8%, and 47.9%, respectively. A total of 29 (30.2%) patients were hepatitis C treatment naïve, 18 (18.8%) had virological breakthrough during interferon-based anti-viral treatment, and the remaining patients completed anti-viral treatment. The APRI and FIB-4 AUROCs were both higher in patients who completed the treatment than those who did not. Furthermore, patients with BMI ≥ 25 kg/m² had higher predictive ability of the two laboratory indices than those with BMI < 25 kg/m². The diabetes status in patients with hepatitis C, BMI, and the treatment status had a significant influence on the predictive ability of the two indices.

The laboratory indices, APRI and FIB-4, can predict advanced fibrosis (Ishak ≥ 4) with high sensitivity and specificity. BMI could be an important factor that affects the predictive ability of the two indices.

<table>
<thead>
<tr>
<th>AUROC</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
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<tbody>
<tr>
<td>Total 96 patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APRI 0.747</td>
<td>0.66</td>
<td>64.9%</td>
<td>71.2%</td>
<td>58.5%</td>
<td>76.4%</td>
</tr>
<tr>
<td>FIB-4 0.739</td>
<td>2.63</td>
<td>62.2%</td>
<td>78.0%</td>
<td>63.9%</td>
<td>76.7%</td>
</tr>
<tr>
<td>Treatment naïve or virological breakthrough (n=47)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APRI 0.691</td>
<td>1.26</td>
<td>60.0%</td>
<td>77.3%</td>
<td>75.0%</td>
<td>63.0%</td>
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<tr>
<td>FIB-4 0.635</td>
<td>4.18</td>
<td>48.0%</td>
<td>81.8%</td>
<td>75.0%</td>
<td>58.1%</td>
</tr>
<tr>
<td>Treatment completion (n=49)</td>
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<td></td>
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<tr>
<td>APRI 0.757</td>
<td>0.52</td>
<td>58.3%</td>
<td>83.8%</td>
<td>53.9%</td>
<td>86.1%</td>
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<tr>
<td>FIB-4 0.784</td>
<td>1.91</td>
<td>75.0%</td>
<td>78.4%</td>
<td>53.0%</td>
<td>90.6%</td>
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<tr>
<td>BMI ≤ 25 (n=43)</td>
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<tr>
<td>APRI 0.890</td>
<td>1.11</td>
<td>83.3%</td>
<td>80.6%</td>
<td>62.4%</td>
<td>92.6%</td>
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<tr>
<td>FIB-4 0.796</td>
<td>2.69</td>
<td>75.0%</td>
<td>74.2%</td>
<td>53.0%</td>
<td>88.5%</td>
</tr>
<tr>
<td>BMI &gt; 25 (n=53)</td>
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<td></td>
<td></td>
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<tr>
<td>APRI 0.699</td>
<td>0.44</td>
<td>76.0%</td>
<td>60.7%</td>
<td>42.8%</td>
<td>86.7%</td>
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<td>FIB-4 0.740</td>
<td>1.78</td>
<td>80.0%</td>
<td>64.3%</td>
<td>46.5%</td>
<td>89.3%</td>
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</tbody>
</table>

Conclusion: The laboratory indices, APRI and FIB-4, can predict advanced fibrosis in patients with hepatitis C. BMI is an important factor that affects the predictive ability of the two indices. BMI could be an important factor that affects the predictive ability of the two indices.

Disclosure: Nothing to disclose.

P0632 DENDRITIC CELL CONTRIBUTES TO AUTOIMMUNE HEPATITIS VIA AUTOPHAGY INHIBITION

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Introduction: Dendritic cells (DC) is a pivotal cell participating in various kinds of autoimmune diseases and plays an important role in autoimmune hepatitis (AIH). However, the mechanism used by DCs to take part in the development of AIH in vivo and vitro remains unclear.

Aims and Methods: The study was aimed to investigate the functions of DCs and mechanisms of DCs alteration in AIH. Peripheral blood samples were collected from 12 patients with biopsy-proven AIH and 6 healthy controls (HC). Mature DCs (CD11C+HLA-DR+) and activated T lymphocytes (CD4+CD3+ and CD8+CD3+) were detected by flow cytometry (FCM). In conca-

navalin A (Con A, 20 μg/kg for 12h) induced AIH mice, the percentage of mature DCs (CD11C+CD80+) and activated T lymphocytes (CD4+CD69+) were detected in the blood, spleen and liver were detected by FCM. Circulating TNF-α, IFN-γ, and IL-6 were assessed by ELISA. In vitro, immature DCs were generated from mouse bone marrow (BMDCs) cultured with GM-CSF (100ng/ml) and IL-4 (10ng/ml). We then treated the immature BMDCs with Con A (10, 20, 40μg/ml) and LPS (1μg/ml) for 24 hours respectively. The expression of major histocompatibility complex II (MHC-II), CD80 and CD86 was determined by FCM. The expression of autophagy related proteins were determined by western blot.

Results: The percentage of mature DCs in the peripheral blood of AIH patients was obviously higher than that in HCs, accompanied by the elevation of activated T lymphocytes. Similarly, the percentage of mature DCs and activated T lymphocytes in blood, spleen and liver were also increased in the Con A-induced hepatitis mice. Moreover, the inflammatory cytokines, such as TNF-α, IFN-γ, and IL-6 were significantly up-regulated in the Con A-treated group. Further study showed that the percentage of LPS-induced mature BMDCs from AIH mice was increased than that from control mice. In vitro, Con A stimulation promoted the maturation of BMDCs as evidenced by higher levels of MHC-II, CD80 and CD86 as compared with control cells. Interestingly, Con A markedly decreased autophagy level (decreased LC3 protein expression) in BMDCs.

Conclusion: We provided a strong evidence that abnormal maturation of DCs mediated the progression of AIH. Furthermore, the impaired autophagy activity could be an important mechanism for DCs to promote the development of AIH.

Disclosure: Nothing to disclose.

P0633 ROLE OF ADIPOCYTE Fatty acid BINDING PROTEIN (AFABP) IN THE DIAGNOSIS OF NAFLD

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Introduction: NASH diagnosis and the need for reliable noninvasive methods to distinguish it from simple steatosis and allow for grading and staging of disease are of high necessity. Adipocyte fatty acid binding protein (AFABP) is adipokine involved in the inflammation and insulin resistance.

Aims and Methods: We aimed to evaluate efficiency of AFABP in diagnosis and quantification of histopathological status of NAFLD in Egyptian patients. A total of 90 subjects (45 male and 45 female) were included in the study and were divided into 3 groups; NASH, steatosis and control. All participants were subjected to calculation of HOMA-IR, NAFLD score, BARD score, complete blood counts, lipid profile, fasting and post-prandial blood glucose level, liver function tests, HCV-Ab, HbsAg, serum AFABP, liver biopsy and abdominal ultrasound.

Results: A significant increase was detected in fasting insulin, HOMA-IR, serum AFABP level and NAFLD score in NASH group (p<0.01) and there was significant increase in BMI in both NASH and steatosis groups compared to control (p<0.05).

The AUROC cut off level (pg/ml), sensitivity, specificity and accuracy of AFABP in diagnosis of fibrosis according to Brunt score in NASH were (0.838, 10.6, 75, 72.7 and 83.8 respectively) (p=0.005 and 95% CI: 0.686-0.991). Also, AUROCs of non invasive markers for diagnosis of NASH have been showed highly significant value of BARD score, NAFLD score and HOMA-IR. Highly significant value of AFABP in diagnosis of significant histological grade (A2-A3) according to Brunt score in NASH was found (p=0.001).

While in steatosis, AUROCs showed highly significant value of BARD score, NAFLD score, HOMA-IR and AFABP. As regards AFABP, the AUROCs, cut off level (pg/ml), sensitivity, specificity and accuracy were (0.928, 9.36, 100, 80 and 92.8 respectively) (p=0.003 and CI: 0.880-1).

Conclusion: AFABP proved to be a promising marker in predicting fibrosis stages, histological grades and activity.

Disclosure: Nothing to disclose.
Disclosure:
liver regeneration after PHx in mice. Hepatic angiocrine HGF signaling is not
Conclusion:
Angiocrine HGF signaling plays a crucial role in the early stage of
KO mice.
of hepatocytes was significantly impaired at 48 hours after PHx in HGF-LSEC-
PHx. HGF-LSEC-KO mice had a higher mortality after PHx and the proliferation
HGF is specifically knocked out in LSEC, were used. 70% PHx was performed
M Ohara
P0635 EXTRACELLULAR VESICLES FROM AMNION-DERIVED
O Maehara4, G Suda1, N Sakamoto1
(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay). The effects of AMSC-EVs on

Aims and Methods: To investigate the effects of angiocrine HGF signaling on
liver regeneration. Stab-2CreERT2(HGF+)/(HGF-/-LSEC-KO) mice, where
HGF is specifically knocked out in LSEC, were used. 70% PHx was performed
on these mice and the kinetics of liver to body weight ratio, hepatocyte prolifera-
tion, HGF/c-MET signaling pathways, and cell-cycle-associated genes were ana-
lyzed at different time points after PHx.

Results: We observed that HGF-LSEC-KO mice have a significantly reduced liver to body weight ratio compared to the control group at 72 hours after PHx. HGF-LSEC-KO mice had a higher mortality after PHxs and the proliferation of hepatocytes was significantly impaired at 48 hours after PHx in HGF-LSEC-KO mice.

Conclusion: Angiocrine HGF signaling plays a crucial role in the early stage of
liver regeneration in mice. Hepatic angiocrine HGF signaling is not only essential for liver regeneration after injury but also for the growth of the liver and even the whole organism.

Disclosure: Nothing to disclose

P0635 EXTRACELLULAR VESICLES FROM AMNION-DERIVED MESENCHYMAL STEM CELLS AMELIORATE HEPATIC INFLAMMATION AND FIBROSIS IN RATS
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Introduction: There are no approved drug treatments for liver fibrosis and non-
alcoholic steatohepatitis (NASH), an advanced stage of fibrosis which has rapidly
become a major cause of cirrhosis. Therefore, development of anti-
inflammatory and anti-fibrotic therapies are desired. Mesenchymal stem cell (MSC)-based cell therapy which has been extensively investigated in the pub-
lished medicine for various organs, can reportedly achieve therapeutic effect in
NASH via paracrine action. Extracellular vesicles (EVs) encompass a variety
of vesicles released by cells that fulfill functions similar to those of MSCs includ-
ing induction of cell proliferation as well as anti-inflammatory, immunomodu-
ulatory, anti-fibrotic, and anti-apoptotic effects.

Aims and Methods: We herein investigated the therapeutic effects of EVs from amnion-derived MSCs (AMSCs) in rats with NASH and liver fibrosis. AMSC-EVs were collected from supernatant of AMSCs with ultracentrifugation. NASH was induced by a 4-week high-fat diet (HFD), and liver fibrosis was induced by intraperitoneal injection of 2 mL/kg 50% carbon tetrachloride (CCL4) twice a week for six weeks. AMSC-EVs were intravenously injected at week 4 after NASH (15 μg/kg) and at week 3 in rats with liver fibrosis (20 μg/kg). The extent of inflammation and fibrosis were evaluated with quantitative reverse transcription polymerase chain reaction (qRT-PCR) and immunohistochemistry. The in vitro effect of AMSC-EVs on inflammatory and fibrogenic response was investigated using hepatic stellate cells (HSCs) and Kupffer cells (KCs). In addition, the effect of AMSC-EVs on lipopolysaccharide (LPS)-tolllike receptor (TLR) 4 signaling pathway was investigated in HEK293 and 293TLR4-MD2-CD14 cells.

Results: Our results demonstrated that the diameter distribution of AMSC-EVs ranged from 50 to 150 nm, with a single peak at approximately 100 nm. Additionally, the expression of the EV marker CD81 was observed by western blotting of AMSC-EVs. Animal experiments demonstrated that AMSC-EVs significantly decreased the number of KCs, reduced the extent of cell infiltration, and the mRNA expression levels of inflammatory cytokines such as tumor necrosis factor (TNF-α), interleukin (IL)-1β, IL-6, and transforming growth factor (TGF-β). Furthermore, AMSC-EVs significantly decreased fibrosis accumulation, KC number, and HSC activation in rats with liver fibrosis. In vitro, AMSC-EVs significantly inhibited KC and HSC activation. AMSC-EVs dose-dependently suppressed the expression of TNF-α. In addition, the increase in LPS-induced NF-κB transcriptional activity was significantly suppressed by AMSC-EVs.

Furthermore, LPS-induced phosphorylation of IκBα and p65 was inhibited by AMSC-EVs. AMSC-EVs suppressed the LPS/TLR4 signaling pathway.

Conclusion: AMSC-EVs ameliorated inflammation and fibrogenesis in a rat model of NASH and liver fibrosis, potentially by attenuating HSC and KC activation. AMSC-EV administration should be considered as a new therapeutic strategy for chronic liver disease.

Disclosure: Nothing to disclose

P0636 INTRODUCTION OF CRYOPRECIPITATE INTO THE LIVER LEADS TO IMPROVEMENT OF PORTAL BLOOD FLOW
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Introduction: Liver cirrhosis is a very common pathology in the structure of gastrointestinal diseases. The amount of five-year survival rate is 62% in the compensation stage of cirrhosis whereas it decreases to 19% in the decompensa-
tion stage. However, the long-term cirrhosis is characterized by hypertrophy and hyperplasia of ultrastructure of hepatocytes. In this respect, we give preference to minimally invasive techniques with the use of agents influ-
encing an inflammation process and liver regeneration such as cryoprecipitate. The cryoprecipitate is a highly concentrated solution of fibrinogen derived from donor plasma by cryoprecipitation, which consist of growth factors to decrease macrophage activity and cirrhosis progress.

Aims and Methods: To study the effects of portal blood flow in patients with liver cirrhosis after introduction of cryoprecipitate into cirrhotic liver tissue. 40 patients (28 men and 12 women) aged from 25 to 60 (the mean age 45 years) with liver cirrhosis were supervised from 2000 to 2017 in Faculty Surgery Clinic No1. 27 patients had alcoholic cirrhosis and 13 patients had mixed (viral and toxic) cirrhosis. Cirrhosis of Class A according to Child-Pugh was diagnosed in 8 patients, Class B in 13 patients, Class C in 19 patients. Cryoprecipitate was injected into liver tissue (1.5–2 ml in each segment) by percutaneous puncture under ultrasonic guidance. The portal blood flow study was carried out before and 6 and 12 months after the procedure using duplex ultrasound examination.

Results: Statistically significant changes were observed after 6 months in 92% of patients.
Serum albumin index (ratio of the linear velocity of flow to the diameter of the vessel) became normal in 6 months in all patients, which correlates with the risk of bleeding from esophageal veins. In patients with long-term cirrhosis of the liver class A, B and C, the circulation in the portal system was normalized, and the risk of bleeding from esophageal veins was minimal in 6 months. The results obtained 12 months after the procedure did not change.

Conclusion: Stimulation of liver regeneration with cryoprecipitate in patients with long-term cirrhosis reduces portal hypertension after 6 months in 92% of patients.

Disclosure: Nothing to disclose

P0637 TOLL-LIKE RECEPTOR 3 PROMOTES LIVER REGENERATION AFTER PARTIAL HEPATECTOMY
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Introduction: Following two-thirds partial hepatectomy (PHx), the liver restores its organ mass due to compensatory growth of the remnant liver. Inflammation plays a crucial role inducing regeneration by stimulating adult G0 hepatocytes to enter G1 phase.1 The endosomal Toll-like receptor 3 (TLR3) detects double-
stranded RNA and activates signaling pathways that can either lead to cell
survival or cell death. Further, it promotes inflammation via inducing the expres-
sion of pro-inflammatory cytokines (e.g. TNFα, IL-6).2 Previous work has shown that TLR3 supports tissue regeneration during dermal wound repair, but seems to have either host-protective or detrimental effects in the intestine.3 In contrast, the exact role of TLR3 in the process of liver regeneration needs further clarification.

Aims and Methods: The present study aims to evaluate the role of TLR3 in liver regeneration. Therefore, we examine TLR3-deficient mice (TLR3−/−) and wild
type (WT) controls by applying a standardized PHx. With regard to distinct
cell cycle phases, we demonstrate the biomolecular characteristics of both
mouse strains. Male TLR3−/− on C57BL/6 background and C57BL/6 WT control
mice were subjected to surgery. PHxs in mice was performed according standard
procedures.4 Animal experiments were performed in accordance with Federal
Animal Regulations and were institutionally approved by the District
Government of Upper Bavaria. The assessment of liver regeneration was conducted by calculating the liver/body weight ratio. Hepatocyte proliferation was analyzed via IHC applying anti-BrdU monoclonal antibody. For cell cycle analyses Western blotting with following primary antibodies was applied: p-STAT3 (Ty705), p-ERK1/2 (Thr202/Thr204), p-JNK (Thr183/Tyr185), p-CAMKII, p-c-Jun, p-FOXO3A, p-p38, p-ERK2, p-JNK, p-c-Jun, and p-FOXO3A. The cell cycle inhibitor p21 was examined by quantitative real-time PCR and IL-6 concentrations in serum were measured by an ELISA assay. P values < 0.05 were considered significant.

Results: Liver regeneration was significantly reduced in TLR3−/− according to liver/body weight measurement at 72 hours, 168 hours and 336 hours. Further, TLR3−/− did not reach the WT ratio level after the end of the regeneration process. 4 hours after PHx serum levels of IL-6 were higher in TLR3−/− but no difference in
the protein levels of pSTAT3 was detectable. Cell cycle examinations via Western blotting using antibodies to Rb protein and p-CDK2 at 32 hours and 40 hours, respectively. In line with G1/S transition block, less BrdU-positive hepatocyte nuclei in S phase at 32 hours and 40 hours were detectable in TLR3−/− compared to controls. Supporting this finding, also CDK1 in G2 phase was significantly diminished in TLR3−/−. The cell cycle inhibitor p21 showed a significant increase at 32 hours after PHx in TLR3−/−.

Conclusion: According to our results, TLR3 appears to have a tissue growth promoting effect on the liver after PHx. This was shown by a diminished liver-to-body weight ratio in TLR3−/− deficient mice. Supporting this finding, the level of proliferation promoting effector proteins such as CDK2 or Rb protein were reduced. Finally, these results were confirmed by IHC where less BrdU-positive hepatocyte nuclei were found in TLR3−/−. The elevated fold induction of cell cycle inhibitor p21 on mRNA level at 32 hours after PHx could explain the delay of cell cycle progression in our TLR3−/−. However, further investigation of TLR3 influencing liver regeneration is warranted. In this respect, the main objective continue to be the revelation of TLR3-associated signalling pathways inducing cell proliferation and arrest of differentiation. After 7 days the medium was changed in TLR3−/−.

Disclosure: Nothing to disclose

References

P0638 DEVELOPMENT OF SELF-RENEWING 3D ORGANOIDS CULTURE FROM HUMAN FETAL BILIARY TREE STEM CELLS (HBTSCS): A NEW STRATEGY FOR REGENERATIVE MEDICINE AND DISEASE MODELLING
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Introduction: 3D organoids represent an advanced culture technology in the field of regenerative medicine, recapitulating embryonic organ development. Adult or fetal biliary tree represent ideal cell sources of stem/progenitor cells to be used for the regenerative medicine of liver and pancreas. The aim of our study was to generate 3D organoid cultures of HBTSCs and differentiate them toward hepatocyte cells which are suitable for cell therapy and regenerative medicine of liver.

Aims and Methods: The fetal biliary tree (N = 3, obtained from elective pregnancy termination) was digested, mechanically and enzymatically, to isolate them toward hepatocyte cells which are suitable for cell therapy and regenerative medicine of liver.

Results: An average of 85 ± 7 million (N = 3) EpCAM/LGR5 enriched fetal hBTSCs were obtained. The cells isolated from fetal biliary tree showed a high tendency to generate organoids with high colony formation efficiency (> 60%). Cell proliferation and population doubling in organoids was significantly higher compared to 2D conditions (p < 0.05). Fetal biliary tree organoids were composed of single layered cuboidal epithelium and inner cell masses. RT-qPCR analysis demonstrated that organoids in expansion condition expressed multiple markers of enteric epithelium: SOX2, NANGA (nose hair), endoderm-specific, organizer cell markers (LGR5, EpCAM, PDX1, SOX17), hepatic progenitors and ductal markers (CK19, CK7) and stem/progenitor surface genes (NCAM, CD133, CD44), recapitulating major processes of embryonic development, whereas the differentiated organoids expressed high level of mature hepatocyte marker like CYP3A and ALB. Interestingly, LGR5 Expression reduced notably in organoids in differentiation condition compared to organoids in expansion condition (p < 0.01). Moreover differentiated organoids acquired a hepatocyte morphology, including polygonal cell shape and secreted significant high level of Albumin in medium respect to the same cells in 2D culture.

Conclusion: We have demonstrated that organoids expand clonogenically stable human hepatic stem cells and they can differentiate toward mature functional hepatocyte. This system has potential applications in regenerative medicine of liver and pancreas and in disease modeling.

Disclosure: Nothing to disclose

P0639 ORAL BRANCHED CHAIN AMINO ACID SUPPLEMENTATION INCREASES LIVER PROTEIN SYNTHESIS AND REGENERATION VIA mTOR/4E-BP1 AND AKT IN HEPATITIC HEPATOCITOMIZED MICE
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Introduction: Branched chain amino acid (BCAA) supplementation may benefit patients with liver cirrhosis and hepatocellular carcinoma. In this study, we attempt to elucidate the effects of BCAA on protein synthesis and hepatocyte regeneration in mice after hepatectomy. Aims and Methods: Mice were subjected to hepatectomy and then supplemented with or without BCAA. The expression and activity of various proteins were evaluated to determine the mechanistic effects of BCAA supplementation. In addition, the effects of various doses of BCAs on HepG2 cells were evaluated. Results: BCAA supplementation for 1 day significantly increased the body weight, liver/body weight ratio, and epididymal fat weight of hepatomized mice. BCAA intake for 7 days significantly increased serum albumin levels and increased the expression of phosphorylated mammalian target of rapamycin (p-mTOR) and p-eukaryotic translation initiation factor 4E binding protein 1 (4E-BP1), thereby promoting liver protein synthesis. BCAA supplementation for 1, 3, and 7 days increased DNA synthesis in mouse hepatocytes after liver hepatocyte and activated p-protein kinase B (Akt). In HepG2 cells, 1×, 2×, and 5× concentrations of BCAs increased cell proliferation. All doses of BCAs activated mTOR and p-Akt, while 2×, 5×, and 10× doses of BCAs increased the protein expression of p-4E-BP1 and only 1× BCAA increased cyclin D1 protein levels.

Conclusion: These results suggest that BCAA supplementation may play a therapeutic strategy for patients undergoing liver operation by increasing liver protein synthesis and may play a role in hepatocyte regeneration. The beneficial effects of oral BCAA supplementation may involve the mTOR/4E-BP1 and Akt pathways.

Disclosure: Nothing to disclose

P0640 NEW OPPORTUNITIES OF COMBINED DIAGNOSTICS OF HEPATIC FIBROSIS AND STEATOSIS IN CLINICAL PRACTICE
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Introduction: Non-invasive diagnoses of hepatic fibrosis (HF) have become a part of clinical practice over the past 10 years. Non-invasive techniques for quantification of hepatic steatosis (HS) remains not always available. Meanwhile, the clinical importance of steatosis determination is great, since HS is a non-invasive, histological marker of alcoholic (ALD) and non-alcoholic liver disease (NAFLD), metabolic and drug-induced liver injury (DILI), HS accompanies chronic viral hepatitis (CVH) and aggravates the progression of HF. Transient elastography using the FibroScan® 502 Touch with XL probe and CAP technology allows to reliably define HF and HS in obese patients.

Aims and Methods: We aimed to evaluate the capabilities of the FibroScan 502 TOUCH with XL probe and CAP technology in non-invasive diagnostics of the combined determination of HF and HS. 1265 participants with first grade relatives’ appointment were included in the study. Men 728 (59%), mean age 36.4 ± 5.7 years, duration of the disease 1–10 ± 1.9 years, BMI ≥ 30–407 (33%), hepatic steatosis according to ultrasound in 456 (37%). Patients were divided into 3 groups: 1) with cytosis more than 1.5 norms, 2) with the presence of steatosis by ultrasound, 3) patients with CVH. All participants underwent general examination to find out the etiology and activity of the disease.

Results: Patients from group 1 have had the following diseases: NAFLD (35%), ALD (26%), spinocerebellar hypertrophy (5%), autoimmune hepatitis and autoimmune thyroiditis (4%), primary biliary cholangitis (3%), DILI (25%). According to FibroScan 502 TOUCH with XL probe and CAP evaluation the HS was identified in 88% of cases (ALD, NAFLD, DILI) in group 1, NAFLD (55%), DILI (28%), DILI (17%), all patients had HS. In group 3: CHC (100%), HS - in 75%, in half of cases HS was not associated with BMI ≥ 25. 82% of patients had genotype 3.

Conclusion: Transient elastography using the FibroScan® 502 Touch with XL probe and CAP technology reliably define HF and HS in normal weight and overweight patients. It helps to prescribe the patients correct medications.

Disclosure: Nothing to disclose
Aims and Methods: We included 153 patients with NAFLD and we divided them into 2 groups: 73 patients NASH group and 80 non-NASH group, age and sex-matched. The diagnostic criteria for NASH was fatty liver accompanied by the presence of steatohepatitis in biopsy samples. Severity of NAFLD was diagnosed by activity (grade) and fibrosis (stage). In all patients we determined BMI, aminotransferases, insulin level, HOMA -IR, leptin level and DHEA-s level.

Results: In NASH group BMI was 32.5 ± 3 and in non-NASH group BMI was 30.3 ± 3, without statistic significance. In NASH group DHEA-s level was lower than normal value adjusted with age and gender and also lower compared with non-NASH group where the DHEA-s level was normal. In NASH group DHEA-s correlated with leptin level (p = 0.028), aminotransferases level (ASAT p = 0.143 and ALAT p = 0.119). If we selected from NASH-group only 21 patients with low degree of fibrosis (0-2) based on Brunt’s C score we observed that DHEA-s level correlated with fibrosis progression, in the others 21 patients with high degree of fibrosis or cirrhosis DHEA-s didn’t correlate with progression of the disease. In non-NASH group DHEA-s didn’t correlate with any parameters (aminotransferases, leptin, insulin or HOMA-IR).

Conclusion: In our study, decreased level of DHEA-s was associated with inflammation and progression of fibrosis in early stages of disease and, also, correlated with leptin and insulin resistance. In patients with simple steatosis or high degree of fibrosis the DHEA-s level didn’t prove to be a marker for disease’s evolution.

Disclosure: Nothing to disclose.
Aims and Methods: We selected patients from the International PLD registry from 1996 to 2009. Patients were identified who were treated with octreotide or lanreotide, during two cycles (On-1 and On-2) separated by a drug holiday (Off-1). Each separate period lasted at least 3 months. For our primary outcome we compared the effect of SA between On-1 and Off-2, expressed as percentage change in liver volume (LTV) assessed by computerized tomography or magnetic resonance imaging. For our secondary outcomes we compared natural liver growth before SA treatment (Off-0) with liver volume change during drug holiday (Off-1).

Results: Out of 741 patients in the PLD registry, 45 patients were treated at least twice with SA. In 34 patients, the initial liver volume reducing effect was similar to that after rechallenge (−2.5% per 6 months [IQR -3.8-0.8] vs. −1.6% per 6 months [IQR -3.0-0.9], p = 0.521). In patients who responded in On-1, defined as a liver volume decrease of ≥4.6% from randomization to On-2. In 25 patients, the increase in LTV in 6 months was significant higher during the drug holiday (Off-1) compared with the natural growth (Off-0) before initial SA exposure (4.5% vs 1.6%, p = 0.009) suggesting a rebound effect. In the group of patients with the natural treatment (On-1), LTV decreased with 0.1% per 6 months in the total observation period (On-1, Off-1 and Off-2) in which patients were treated for 53.1% of the time (−0.6% after 46.5 months).

Conclusion: These results postulate that a drug holiday reneseates the liver to the beneficial pharmacological effects of SA. Our results suggest the concept of rechallenge after a drug holiday as a strategy for selected patients with PLD. This strategy avoids needless continuous therapy and reduces medical costs.

Disclosure: Nothing to disclose.

P0647 EVALUATING CIRCULATING HORMONES IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE AS POTENTIAL BIOMARKERS
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Introduction: Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of liver disease from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH), which may potentially progress to liver cirrhosis and hepatocellular carcinoma. Liver biopsy remains the gold standard method to distinguish steatosis from NASH and to identify the extent of liver injury and fibrosis despite its invasive nature and serious complications.

Aims and Methods: We aimed to evaluate the performance of circulating levels of hormones relevant for the pathogenesis of NAFLD/NASH as potential biomarkers. Serum levels of adiponectin, leptin and insulin-like growth factor-I (IGF-I) were evaluated in a cohort of morbidly obese patients with a clinical and biospy-proven diagnosis of steatosis (n=26) or NASH (n=13), using enzyme-linked immunosorbent assays (ELISA) recently developed and produced by Mediagrost. Hormone levels were correlated with fasting serum glucose and insulin, hepatic transaminases, gamma-glutamyltransferase (GGT), direct bilirubin, free fatty acids, triglycerides, apolipoprotein A1, cytokerin 18, high-density lipoprotein (HDL) and low-density lipoprotein cholesterol, and total cholesterol. Serum of liver disease-free healthy controls was also analyzed.

Results: Leptin levels were significantly augmented in steatosis and NASH patients, compared with healthy controls (p<0.05). The area under the receiver-operating characteristic (AUROC) related to NAFLD versus healthy control was 0.88 (95% CI: 0.77-0.99; p<0.0001). In turn, IGF-I concentrations were significantly diminished in steatosis and NASH patients. Compared with controls (p=0.05), showing an AUROC of 0.81 (95% CI: 0.68-0.94; p<0.05). Finally, adiponectin levels were significantly decreased in patients with NASH compared with controls (p=0.05) and healthy individuals (p<0.01), and the AUROC of adiponectin were negatively correlated with serum levels of glucose, insulin, GGT, alanine aminotransferase and bilirubin in the cohort of NAFLD patients (r=0.6, p<0.05).

Conclusion: Overall, these parameters are potentially valuable tools for non-invasive stratification of patients with NAFLD. Particularly, adiponectin might discriminate the presence of NASH in morbidly obese patients. Future studies should validate these biomarkers in independent larger cohorts, as well as the impact of confounding factors such as obesity.

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Disclosure: Nothing to disclose.

P0648 HIGH PREVALENCE OF DYSPLASIA BUT INSUFFICIENT STATIN USE IN PATIENTS WITH NON-CIRRHOTIC CHRONIC LIVER DISEASE
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Introduction: Dysplasia increases cardiovascular risk in the general population. Chronic liver disease (CLD) affects lipoprotein synthesis, but prevalence/relevance of dysplasia in CLD is controversial. Interestingly, statins and fibric acids have hepatoprotective effects. Therefore, we investigated lipid profiles in patients with non-cirrhotic and cirrhotic CLD of different etiologies, as well as the utilization of statins in these patients.

Aims and Methods: Patients with alcoholic liver disease (ALD; n=121), hepatitis B (HBV, n=438), hepatitis C (HCV, n=384), NAFLD (n=532), cholestatic liver disease (n=119), or autoimmune hepatitis (AIH, n=114) were included. Liver stiffness values ≥15kPa defined cirrhosis. Dysplasia was diagnosed by either (i) total cholesterol >200mg/dL, (ii) LDL >130mg/dL or (iii) triglycerides >200mg/dL.

Results: Across all etiologies, total cholesterol levels was lower in patients with cirrhosis as compared to non-cirrhotic patients. Similarly, LDL levels were lower in cirrhotic HCV, HBV, NAFLD and AIH. HDL decreased in HCV and autoimmune hepatitis. Dysplasia did not differ between non-cirrhotic and cirrhotic patients. Comorbidities (arterial hypertension, NIDDM and IDDM) were more prevalent in patients with cirrhosis, while in general, the prevalence of dysplasia was lower in cirrhotic than non-cirrhotic patients (33.9% vs. 25.4%, p<0.01). Lipid lowering therapy was underutilized in patients with liver disease as 27.9% did not receive indicated therapy (29.9% in patients with and 20.0% in patients with cirrhosis, respectively).

Conclusion: Dysplasia and cardiovascular comorbidities are common in patients with CLD. Progression to cirrhosis affects total cholesterol and HDL LDL levels. Lipid-lowering therapy is highly underutilized in patients with CLD.

Disclosure: Nothing to disclose.
P0649 COMPARISON BETWEEN M AND XL PROBES OF TRANSIENT ELASTOGRAPHY FOR THE ASSESSMENT OF HEPATIC STEATOSIS WITH CONTROLLED ATTENUATION PARAMETER (CAP)

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Introduction: Controlled attenuation parameter (CAP) is a new method for the non-invasive diagnosis of hepatic steatosis (HS) acquired by transient elastography. The aims of this study were to assess the concordance of HS measurements with the M and XL probes of FibroScan® as well as to determine the concordance of classification of the grade of steatosis using the cut-off values determined by de Ledinghen et al [1].

Aims and Methods: In a cross-sectional prospective study, transient elastography acquisitions were performed using the M probe then the XL probe. The interobserver concordance for CAP measurements was assessed using the intra-class correlation coefficient and the concordance of the steatosis grade classification was characterized using the k index. Cutoffs were (M and XL probes respectively) 246/242 for the presence of HS and 285/286 dB/m for the presence of severe HS.

Results: A total of 136 patients were included. Women accounted for 51.5%. Fifty (36.8%) patients were hepatitis C virus (HCV) mono-infected, 46 (33.8%) were hepatitis B virus (HBV) mono-infected, 17 (12.5%) had NAFLD, 5 (3.7%) were HIV/HCV coinfected and 2 were HIV/HCV coinfected (1.5%). Thirty one percent of our patients were obese (BMI >30 kg/m2) and 32.6% were overweight (BMI ≥ 25 kg/m2). The mean CAP value using the M probe was significantly higher than the mean CAP value using the XL probe (255.5 ± 19 dB/m vs 234.5 ± 19 dB/m, respectively). The corresponding median liver stiffness measurements were 6.5 kPA and 5.9 kPA respectively. The overall intra-class correlation coefficient for the single measures was 0.738 (95% confidence interval: 0.645–0.808). Hepatic steatosis was present in 51.9% and 55.6% of patients with the M and XL probes respectively. Severe HS was noted in 28.9% and 25.2% of patients with the M and XL probes respectively. The k indexes for the concordance of classification for the presence of significant HS and severe HS were 0.581 and 0.605, respectively.

The rates of CAP examinations with IQR > 50 using the M probe was 7.4% whereas it reached 46.7% using the XL probe.

Conclusion: Single CAP values with the M and XL probes are well correlated however the use of cutoff values leads to a suboptimal concordance of grade classification. The rate of examinations with an IQR > 50 is much higher using the XL probe.

Disclosure: Nothing to disclose

Reference

P0651 NEUTROPHIL-TO-LYMPHOCYTE RATIO: AN ACCURATE METHOD FOR PREDICTING INFECTION IN CIRRHOSIS

P0652 HOSPITAL READMISSION RATES IN HEPATIC CIRRHOSIS: WHICH PATIENTS PRESENT HIGHER RISK?

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Introduction: Patients with hepatic cirrhosis (HC) are at high risk of hospital readmission (HR).

Aims and Methods: We aimed to determine the HR rate at 30 and 90 days after admission (AI) for decompen-sation (IH) for decompensation, as well as the reasons and possible predictors.

Retrospective and uniconfined study involving patients with HC who were hospitalized within 9 years.

Results: Included 177 patients, 85.3% with alcoholic HC.

At IH, 73.4% of the patients presented with ascites, 47.5% with variceal bleeding, 22.6% hepatic encephalopathy (HE), 7.9% hepatocellular carcinoma and 1.1% hepatorenal syndrome (IRS). Regarding intra-hospital complications, 11.9% had Spontaneous Bacterial Peritonitis (SBP), 20.9% acute kidney injury (AKI) and 20.3% other types of infections (respiratory, urinary, cutaneous).

The HR rate at 30 and 90 days was 40.1% and 28.2% respectively.

In the univariate analysis we found that patients with HE (60% vs 34.3%, p = 0.004), SBP (66.7% vs 35.6%, p = 0.008) and AKI (56.8% vs 35.7%; p = 0.02) were more frequently readmitted at 30 days. Patients with HE (45% vs 23.4%, p = 0.007) and AKI (43.2% vs 24.3%; p = 0.023) in IH were more frequently readmitted at 90 days.

In the multivariate analysis, the presence of HE (OR 2.485 CI 95% 1.166–5.298; p = 0.018) and SBP (OR 3.599 IC95% 1.333–9.721; p = 0.012) were predictors of HR at 30 days.

In the multivariate analysis HE was the only predictor for HR at 90 days (OR 3.245 ±95% 1.097–5.014; p = 0.028).

Conclusion: In a population of cirrhotic patients, a high rate of hospital readmission of 40.1% and 28.2% was observed at 30 and 90 days respectively. HE was a common predictor of readmission at 30 and 90 days.

Disclosure: Nothing to disclose

P0653 CEREBRAL VASCULAR RESISTANCE IS INCREASED IN CIRRHOTIC PATIENTS WITH MINIMAL HEPATIC ENCEPHALOPATHY: ENEPHALOPATHY AND REMAINS UNCHANGED AFTER MEDICAL TREATMENT

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Introduction: In cirrhotic patients, cerebral vascular resistance indices (resistivity index, RI and pulsatility index, PI) are good indicators of cerebral hemodynamic abnormalities and are commonly correlated with the severity of cirrhosis, hepatic encephalopathy (HE) and ascites. However there are still poor data about cerebral vascular indices in patients with minimal hepatic encephalopathy (MHE) or with minimal WMH.

Aims and Methods: The aim of this study was to correlate cerebral arteries resistance indices with the presence of MHE and to evaluate their modification after treatment with rifaximin.

38 consecutive cirrhotic patients were enrolled in this study. Exclusion criteria were overt HE (West Haven ≥1), age < 18 years, active alcohol consumption, sepsis, cerebrovascular diseases, cerebral neoplasms, cardiac diseases, peripheral vascular diseases, treatment with rifaximin in the previous 30 days. Patients with two or more signs of MHE at the psychometric evaluation (TMT-A, TMT-B and DST) received rifaximin 1200 mg daily for 10 days. All patients underwent TCD for the measurement of RI and PI of the mean cerebral artery (MCA) and of posterior cerebral artery (PCA) at baseline and within 2 weeks after rifaximin treatment. Median value of the right and left side arteries have been used for the analysis. Subdural and intracerebral vessels (renal arteries, mesenteric artery, portal vein) flow parameters were also assessed, and the Child-Pugh score was calculated.

Results: Among the patients enrolled in the study 17 had MHE (44.7%). MCA-PI, PCA-PI and RI were significantly increased in patients with MHE compared to those without (MCA-PI 1.04 vs 1.05, p = 0.05; PCA-PI 1.12 vs 0.9, p = 0.02; PCA-RI 0.64 vs 0.56, p = 0.01) while MCA-RI showed a trend towards the increase (0.65 vs 0.61, p = 0.07). No significant difference was found in the intra-abdominal vessels flow parameters between the two groups. Furthermore, cerebral arteries resistance indices were not associated with the Child-Pugh score. After treatment with rifaximin, TMT-A and B and DST showed a significant
that a low lymphocyte count was an independent risk factor for mortality (OR: 0.76 [95% CI 0.609–0.955]; p = 0.018), as well as for mortality (OR: 0.69 [95% CI 0.503–0.957]; p = 0.026). The AUC value was 0.758 ± 0.015 (p < 0.025), with a cut-off value ≤0.8 and 70% (95% CI 34.8–93.3) of sensitivity and 81.8% of specificity (95% CI 54.8–97.9), PPV - 77.8% (95% CI 48.1–93.0), NPV - 76.9 (95% CI 55.6–89.9) for SIRS outcome. In multivariate analysis, the lymphocyte AUC was 0.864 ± 0.09 (p < 0.001), with a cut-off value ≤1.3 and 90% (95% CI 58.7–99.8) of sensitivity and 81.8% of specificity (95% CI 48.2–97.7), PPV - 83.3% (95% CI 58.5–94.7), NPV - 90% (95% CI 57.6–93.3) of specific positive and negative predictive values.

Conclusion: According to these results NLR and lymphocyte count can be regarded as independent prognostic factors for the development of SIRS with proven infection and for mortality during hospitalization in patients with decompensated liver cirrhosis. Nevertheless, further research is essential to confirm these findings.

Disclosure: Nothing to disclose

P0654 ACUTE OCCLUSION OF EXPANDED POLYETRAFLUROETHYLENE-COVERED TRANSGULULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT: INCIDENT, CLINICAL OUTCOMES, AND PROGNOSTIC FACTORS

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Introduction: The expanded polytetrafluoroethylene (ePTFE)-covered stent has been widely used in the transjugular intrahepatic portosystemic shunt (TIPS) procedure. The purpose of this study was to evaluate the incidence, clinical outcomes, and independent risk factors of acute occlusion (AT0) in TIPS recipients using ePTFE-covered stents.

Aims and Methods: A retrospective study, including 222 TIPSs created with ePTFE-covered stents between June 2015 and June 2017 was performed. Medical records were reviewed to identify demographics, underlying liver disease, and TIPS procedure data, and the influence of these variables on AT0 was assessed by multivariate logistic regression analysis.

Results: TIPS technical success was achieved in 219 patients (98.6%). Two patients were excluded due to missing data, leaving 217 patients for final analysis. AT0 occurred in nine patients (4.1%). In all series, parameters that were significantly different between patients with and without AT0 were platelets levels, previous splenectomy, portal vein thrombosis, portal cavernoma, shortage of stent in the hepatic vein, structure on the shunt, and residual thrombosis below the shunt. On multivariable logistic regression, structure on the stent (hazard ratio = 36.09; 95% confidence interval [CI]: 2.93–443.96; p = 0.005), and previous splenectomy (hazard ratio = 22.99; 95% CI: 1.29–408.39; p = 0.033) demonstrated as independent, significant risk factors for AT0.

Conclusion: AT0 is uncommon in the era of ePTFE-covered stents. The structure on the shunt and previous splenectomy are vital prognostic factors for AT0 in TIPS recipients.

Disclosure: Nothing to disclose

P0655 NEUTROPHIL TO LYMPHOCYTE RATIO AS PREDICTOR OF SERIODING INFECTIONARY SYNDROME AND MORTALITY IN PATIENTS WITH DECOMPENSATED LIVER CIRRHOSIS

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Introduction: Fatal infections with signs of systemic inflammatory response syndrome (SIRS) are often seen in patients with decompensated liver cirrhosis. SIRS in these patients is associated with progressive organ dysfunction. Simple prognostic factors to predict mortality in such patients are needed.

Aims and Methods: The aim of the study was to evaluate the role of the neutrophil-to-lymphocyte ratio (NLR) to predict SIRS and mortality in patients with decompensated liver cirrhosis during hospitalization.

In this retrospective observational cohort study were enrolled 36 patients with decompensated liver cirrhosis between January 2009 and December 2016. The primary end points of the study were survival during hospitalization and presence of SIRS. NLR along with Child-Pugh score, MELD score, leukocyte, lymphocyte, neutrophil, and neutrophil lymphocyte counts were assessed for the prediction of mortality and SIRS.

Results: A strong correlation was found between mortality and the following parameters: the level of neutrophils (r = 0.720; p < 0.001), lymphocytes (r = 0.68; p = 0.001), neutrophil count on the 2nd day of admission (r = 0.705; p < 0.001). The median NLRs were 2.4 (IQR: 1.9–3.9) and 21.6 (IQR: 9.3–30.6) in surviving and decompensated liver cirrhosis patients, respectively, with 62.5% (95% CI 44.4–77.7) positive and 90% (95% CI 73.6–97.3) negative predictive values. A multivariable analysis showed that a value of NLR < 3.0 was an independent risk factor for mortality (OR: 4.033 were 100% (95% CI 73.5–98.3) positive and 90% (95% CI 73.6–97.3) negative predictive values.

Discussion: As independent, significant risk factors for the development of SIRS with proven infection and mortality during hospitalization in patients with decompensated liver cirrhosis.

Disclosure: Nothing to disclose

P0656 HEPATIC OSTEODYSTROPHY - IS THERE CLINICAL RELEVANCE?

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Introduction: Hepatic osteodystrophy, including osteoporosis, is an abnormal bone metabolism related with chronic liver disease. Osteoporosis is associated with increased morbidity and mortality, with a significant impact on morbidity, quality of life and mortality. Several factors may contribute to reduced bone mineral density (BMD) in liver cirrhosis, such as malnutrition, cholestasis, alcohol and tobacco abuse and low vitamin D levels.

Aims and Methods: We aimed to assess the prevalence of osteopenia and osteoporosis in patients with liver cirrhosis. We conducted a prospective study between September/2017 and March/2018 including patients with liver cirrhosis. BMD was determined by dual energy X-ray absorptiometry at L1-L4 and femoral neck. As defined by the World Health Organization criteria, osteoporosis was present when a t-score lied between −1 and −2.5 standard deviations (SD), and osteopenia when a t-score was −2.5 ≤SD. Results: 60 patients were included (87% male, mean age of 63.6±9 years; 91.7% alcoholic etiology; Child-Pugh A-65%, B-28.3%, C-6.7%). 55.5% had history of falls and 21.7% prior fragility fracture (mainly long bones). Osteoporosis was diagnosed in 73% and osteopenia in 22% in cases. Femoral neck was more frequently affected. Patients with osteoporosis or osteopenia had lower weight and body mass index (p < 0.05) and higher Child-Pugh score (p < 0.01). There was a correlation between osteoporosis and prior fragility fracture (p = 0.015, R = 0.313), esophageal varices (p = 0.04; R = 0.278), concomitant chronic pancreatitis (p = 0.002; R = 0.389) and proton-pump inhibitors (p = 0.037, R = 0.27). There was also a correlation between low vitamin D levels and the t-score at the femoral neck (p = 0.025; R = 0.296).

Conclusion: This study demonstrates a high prevalence of metabolic bone disease in patients with chronic liver disease. The prevalence of prior bone fracture is also concerning. Osteoporosis and bone fractures have a harmful effect on quality of life and are particularly relevant in patients with liver cirrhosis, allowing the detection of bone disorders and the institution of prophylactic measures to optimize bone health.

Disclosure: Nothing to disclose

P0657 ROYAL FREE HOSPITAL CIRRHOSIS GLOMERULAR FILTRATION RATE (RFHC-GFR): APPLICATION AND IMPLICATIONS FOR LIVER CIRRHOSIS IN CLINICAL PRACTICE

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Introduction: Both serum creatinine and current creatinine-based equations for GFR estimation have been proven to be inaccurate in cirrhotic patients. A more accurate formula has been proposed1 - the RFHC-GFR that warrants further validation.

Aims and Methods: To compare different creatinine-based equations for GFR estimation in patients with liver cirrhosis.

We determined to compare the conventional and corrected Model For End Stage Liver Disease (MELD-Na) as predictors of 12-month mortality. Clinical and laboratory data of 123 consecutive outpatients with cirrhosis between January and December 2016 were retrospectively collected. Patients with acute kidney failure, extra-hepatic neoplasms and history of kidney or liver transplantation were excluded. GFR rates were calculated using RFHC, Modification of Diet Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. A ‘corrected creatinine value’ was obtained through backward application of MDRD equation using RFHC-GFR values. “Corrected MELD-Na” was then calculated.
Introduction: Liver cirrhosis is characterized by chronic hepatic parenchymal damage, hepatocyte loss, fibrosis formation causing progressive hepatic dysfunc-
tion and hepatic failure. Liver cirrhosis causes significant morbidity and mortal-
ity and accounts for 2% of all annual death worldwide. The epidemiology of liver cirrhosis is different in different geographical areas of the world.

Aims and Methods: This study is the first registered data on epidemiology of liver cirrhosis in Iran focusing on underlying liver diseases and complications. This registry has been established at Gastroenterology Research Center, Shiraz, Iran. The data has been started from March 2015. All patients with confirmed liver cirrhosis by biopsy and/or transient elastography plus clinical clues were included. Patients with liver cirrhosis that had been admitted in hospitals due to various complications of cirrhosis were also included. Data of patients were recorded in a web-based software designed and produced based on data gather-
ing forms and questionnaires of the registry. Demographic data, laboratory data, anthropometric indices, drug history, social history including alcohol consump-
tion, cigarette and water pipe smoking, opium consumption, co-morbid diseases were recorded. Complications of liver cirrhosis including hepatocellular carcino-
noma (HCC), esophageal or gastric varices, spontaneous bacterial peritonitis (SBP), ascites, hepatorenal syndrome, portal vein thrombosis (PVT) and hepatic encephalopathy were recorded.

Results: Of the 123 patients included in the study 78.9% were male and the mean age was 58.2 (range 23.8–95.9) years. 86.9% had chronic active (CAF) and/or chronic hepatitis (CHC) and 13.1% had significant comorbidities and 8.9% had hepatocellular carcinoma. The percen-
tage of patients in the Child-Pugh Score A, B and C was 53.7%, 35.8% and 10.6% respectively. Median MELD score was 13 (±12). There was a statistically signific-
ant difference between male and female (p < 0.05). The RFH-GFR was significantly lower when compared to CAF to EKI or MRDR (p < .001). When RFH-GFR was used a significantly larger proportion of patients were considered to have moderate-to-severe GFR reduction than with CHF, with 82.3% vs. 98% respectively and p < 0.001. The median value of corrected MELD-Na was 2 points higher than conventional MELD-Na (p < .001) and had a higher AUC (0.788 vs. 0.775 p = 0.56) for 12-
month mortality prediction.

Conclusion: Lower uncorrected GFR can potentially increase the risk of adverse outcomes such as renal toxicity and more importantly increase conventional calculated MELD-Na scores which could alter liver transplant priority.

Disclosure: Nothing to disclose

References

P0659 RESULTS OF LIVER CIRRHOSIS REGISTRY IN IRAN: EPIDEMIOLOGY, UNDERLYING CAUSES AND COMPLICATIONS
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Introduction: Liver cirrhosis is characterized by chronic hepatic parenchymal damage, hepatocyte loss, fibrosis formation causing progressive hepatic dysfunc-
tion and hepatic failure. Liver cirrhosis causes significant morbidity and mortal-
ity and accounts for 2% of all annual death worldwide. The epidemiology of liver cirrhosis is different in different geographical areas of the world.

Aims and Methods: This study is the first registered data on epidemiology of liver cirrhosis in Iran focusing on underlying liver diseases and complications. This registry has been established at Gastroenterology Health Research Center, Shiraz, Iran. The data has been started from March 2015. All patients with confirmed liver cirrhosis by biopsy and/or transient elastography plus clinical clues were included. Patients with liver cirrhosis that had been admitted in hospitals due to various complications of cirrhosis were also included. Data of patients were recorded in a web-based software designed and produced based on data gather-
ing forms and questionnaires of the registry. Demographic data, laboratory data, anthropometric indices, drug history, social history including alcohol consump-
tion, cigarette and water pipe smoking, opium consumption, co-morbid diseases were recorded. Complications of liver cirrhosis including hepatocellular carcino-
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tage of patients in the Child-Pugh Score A, B and C was 53.7%, 35.8% and 10.6% respectively. Median MELD score was 13 (±12). There was a statistically signific-
ant difference between male and female (p < 0.05). The RFH-GFR was significantly lower when compared to CAF to EKI or MRDR (p < .001). When RFH-GFR was used a significantly larger proportion of patients were considered to have moderate-to-severe GFR reduction than with CHF, with 82.3% vs. 98% respectively and p < 0.001. The median value of corrected MELD-Na was 2 points higher than conventional MELD-Na (p < .001) and had a higher AUC (0.788 vs. 0.775 p = 0.56) for 12-
month mortality prediction.

Conclusion: Lower uncorrected GFR can potentially increase the risk of adverse outcomes such as renal toxicity and more importantly increase conventional calculated MELD-Na scores which could alter liver transplant priority.

Disclosure: Nothing to disclose

References

P0660 SPONTANEOUS BACTERIAL PERITONITIS: ARE WE FOLLOWING GUIDELINES?
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Introduction: Spontaneous bacterial peritonitis (SBP) is the most common serious infection in patients with cirrhosis, occurring in 25% of those who develop ascites. It is associated with significant morbidity and mortality rates of 20–
40%.1,2

British Society of Gastroenterology (BSG) and National Institute of Clinical Excellence (NICE) guidelines recommend long-term prophylaxis (LTP) with Ciprofloxacin or Norfloxacin in patients with cirrhosis who have low ascitic fluid protein concentration (<1 g/L) or without prior episode of SBP (primary LTP) or who have had an episode of spontaneous bacterial peritonitis (secondary LTP).3-2

Aims and Methods: We carried out a retrospective observational study using our electronic system for admissions with a diagnosis of ascites and cirrhosis across the East Kent Hospitals NHS Foundation Trust from April 2014 to April 2017. Ascitic fluid analysis results were reviewed against discharge summaries to audit whether LTP was started according to national guidelines.

Results: Of the 123 patients with cirrhosis and ascites were reviewed against discharge summaries to audit whether LTP was started according to national guidelines.

Conclusion: East Kent Trusts followed national guidelines in starting secondary LTP for SBP in 18% (10 out of possible 56) of cases and 0% of cases requiring primary LTP for SBP. This study serves as a reminder to clinicians to carefully consider LTP in patients with ascites secondary to cirrhosis on each admission. We also recom-
mend that trusts review local microbiology guidelines to ensure it adheres to national guidelines.

Disclosure: Nothing to disclose

References
3. Britsoc Gastroenterology (BSG) and National Institute of Clinical Excellence (NICE) guidelines recommend long-term prophylaxis (LTP) with Ciprofloxacin or Norfloxacin in patients with cirrhosis who have low ascitic fluid protein concentration (<1 g/L) or without prior episode of SBP (primary LTP) or who have had an episode of spontaneous bacterial peritonitis (secondary LTP).3-2

Aims and Methods: We carried out a retrospective observational study using our electronic system for admissions with a diagnosis of ascites and cirrhosis across the East Kent Hospitals NHS Foundation Trust from April 2014 to April 2017. Ascitic fluid analysis results were reviewed against discharge summaries to audit whether LTP was started according to national guidelines.

Results: 337 cases of ascites with cirrhosis were identified (93 female: 244 male) with a median age of 58 (range 30–92 years).

Frequency 664/1 619/1 443/1 427/1 154/1 83/1 54/1
Percent (%) 20.20 18.83 13.47 12.9 4.68 2.52 1.64
Male/female (%) 81/19 59/1 70/2/ 50/4.9 5/6.3 48/2 61/39

[ Frequencies and proportions of major causes of liver cirrhosis in the registry ]
References

P0661 STAGE 1 OF ACUTE KIDNEY INJURY IN CIRRHOSIS - THE SUBCLASS REALLY MATTERS?
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Disclosure: Nothing to disclose

Introduction: Recent studies propose a subclassification of stage 1 of acute kidney injury (AKI) in patients with cirrhosis, according to the serum creatinine value (sCr) at the time of diagnosis.1-3

Aims and Methods: The aim was to evaluate the association of subclassification stage 1 of AKI in patients with cirrhosis with the presence of acute-on-chronic liver failure (ACLF), progression of AKI and 30-day mortality. A retrospective assessment of patients with cirrhosis admitted for acute decompensation with AKI stage 1 was performed. AKI stages were determined based on the time of enrollment and according to criteria defined by the International Ascites Club. Stage 1 was subclassified in 1A if sCr < 1.5 mg/dL and 1B if sCr ≥ 1.5 mg/dL.

Results: Ninety patients were included, 45 in stage 1A (45%) and 45 (50%) in stage 1B. The mean differences between sCr at diagnosis and baseline were higher at stage 1B compared to 1A, 0.7 ± 0.23 vs 0.43 ± 0.11, p < 0.001. Progression of AKI occurred more frequently in patients with stage 1B (40%) compared to stage 1A (14%), p < 0.001. Hepatorenal syndrome occurred more frequently in stage 1B than in 1A, 20% vs 2.2%, p = 0.007. ACLF was more frequent in patients with stage 1B (42.2%) compared to patients with stage 1A (4.4%), p < 0.001. There was a higher mortality at 30 days in 1B patients compared to patients with 1A, 40% vs 8.9%, p = 0.001.

Conclusion: Stage 1B patients are at higher risk for progression of AKI, higher mortality, and more frequently present ACLF, thus requiring more attention in identifying, monitoring and treating them early.

Disclosure: Nothing to disclose

References

P0662 THE POLYMORPHIC VARIANT OF SERPINB3 (SCCA-PD) IS A RISK FACTOR WITH THE SEVERITY OF PORTAL HYPERTENSION AND COMPLICATIONS ONSET IN PATIENTS WITH ADVANCED LIVER DISEASE
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Introduction: Hepatic fibrosis and portal hypertension are major determinants of clinical outcome in advanced chronic liver disease. Liver fibrosis is driven by persistent activation of hepatic stellate cells, with TGF-β being the key fibrogenic cytokine. SerpinB3 (or SCCA1) has been reported to activate hepatic stellate cells and SerpinB3 transfected cells up-regulate TGF-β production, an effect shown to rely on the integrity of the reactive site loop of this serpin. The polymorphic variant SerpinB3 (A350) is a substitution in the reactive center loop of the protein (Gly351Ala), determining an improved anti-protease activity of this isoform. Aims and Methods: To assess the effect of SCCA-PD polymorphic variant on TGF-β expression by using in vitro models and to disclose the clinical characteristics and the course in a cohort of cirrhotic patients carrying or not this polymorphic variant. TGF-β transcripts and protein levels were determined in HepG2 and in Huh7 cells transfected with either wild-type SerpinB3 (SCCA-WT) or with SCCA-PD polymorphic variant. Cells transfected with the plasmid alone were used as control. TGF-β1 expression was also evaluated in the human stellate cell line LX2 in response to recombinant SCCA-WT or SCCA-PD proteins. In addition, SCCA polymorphism was assessed in 59 cirrhotic patients (72.9% male; mean age±SD: 53.9±9.1 years), prospectively followed up at our outpatient Clinic for a median period of 14 months (range 6-14). The results were related in relation to clinical data, hemodynamic features at baseline and the onset of new complications during follow up.

Results: Transfected cell lines showed increased TGF-β1 expression, compared to control. This finding was more evident in cells transfected with SCCA-PD, both at transcript and protein levels (SCCA-WT vs SCCA-PD, mRNA: p = 0.027, protein: p = 0.009). Accordingly, the addition of recombinant SCCA-PD to human LX2 cells induced higher TGF-β1 production, compared to human SCCA-WT protein (p < 0.01). SCCA-PD polymorphism was detected in 27% of the enrolled patients that at baseline, despite they had similar age than patients carrying SCCA-WT (52±8 vs 54±9 years), presented signs of more advanced portal hypertension, including portal vein dilatation (portal vein > 14 mm: 50% vs 5% in patients carrying SCCA-WT p < 0.001). The variant was moderately predictive of fibrosis regression (AUROC = 0.594, p = 0.001), while the optimal cut-off values were different between non-cirrhosis and cirrhosis patients (38% vs. 45%). Fibrosis regression could be predicted with a high positive predictive value (96%) in non-cirrhosis patients and could be excluded with a high negative predictive value (94%) in cirrhosis patients.

Conclusion: The polymorphic variant SCCA-PD is able to increase TGF-β production in vitro more efficiently than the corresponding wild type protein. Patients with advanced liver disease carrying the SCCA-PD polymorphism present signs of more severe portal hypertension and develop more frequently cirrhosis complications during follow up, supporting a role of this polymorphic variant in liver disease progression.

Disclosure: Nothing to disclose

P0663 LONGITUDINAL MONITORING OF LIVER FIBROSIS STATUS BY TRANSIENT ELASTOGRAPHY IN CHRONIC HEPATITIS B PATIENTS DURING LONG-TERM ENTECAVIR TREATMENT
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Introduction: There has been a marked increase in studies revealing that oral antiviral treatment can suppress the replication of hepatitis B virus (HBV) and induce the regression of liver fibrosis, in which the degree of liver fibrosis is of great significance. In addition to liver biopsy, the gold standard, liver stiffness measurement (LSM) by non-invasive transient elastography has shown its out-standing value in monitoring the progression and regression of fibrosis and chronic hepatitis B (CHB)-related complications. In this study, we aim to evaluate the prognosis performance of LSM in predicting the subsequent regression of liver fibrosis in patients receiving long-term entecavir (ETV) treatment.

Aims and Methods: The study was designed to explore the correlation between improvement in longitudinal liver stiffness and fibrosis regression during long-term antiviral therapy in CHB patients. We prospectively recruited a total of 120 consecutive adult patients with CHB, which received oral antiviral therapy with ETV for 114 months. Five patients were excluded because of non-cirrhosis group and 65 CHB patients were enrolled in the cirrhosis group. In study, liver stiffness was serially performed by Fibroscan apparatus (Echosens pavis, France) every 12-weeks. At baseline and term of week 26, week 52 and week 78 of ETV therapy, liver biopsy was performed for every patients. The liver tissue was obtained by ultrasonography-guided percutaneous biopsy (Bard 16G Magnum®16G;USA). Serum fibro-sus markers, Fibrosis-4 (FIB-4) and aspartate aminotransferase (AST) to platelet ratio index (APRI) scores were assessed at baseline and every 2-months. Continuous variables were summarized as mean±standard deviation or median and interquartile range (IQR) and categorical variable as frequency and percentage. Analyses of unpaired data were evaluated by the Mann-Whitney U-test, Categorical data and Fish’s exact test. Statistical analyses were performed using SPSS software version 22.0 (SPSS INC Chicago, USA).

Results: Compared with non-cirrhosis group, gamma-glutamyltransferase, international normalized ratio (INR), APRI, FIB-4 and LSM were significantly higher in cirrhosis group at baseline. On the other hand, LSM values at point of week 26, week 52 and week 78 during antiviral treatment. The serum levels of ALT, AST and INR gradually decreased after antiviral therapy. While albumin and cholesterol levels were significantly increased after initiating ETV treatment. The serum fibro-sus scores (APRI and FIB-4) also declined gradually during the antiviral treatment. Dynamic changes of LSM and serum biomarkers also show the association of LSM improvement with fibrosis regression at 78 weeks after ETV treatment. Moreover, percentage decline of 78-week liver stiffness was more prominent in patients who carried the polymorphism in comparison with those not carrying the polymorphism (38% vs. 45%). Fibrosis regression could be predicted with a high positive predictive value (96%) in non-cirrhosis patients and could be excluded with a high negative predictive value (94%) in cirrhosis patients.

Conclusion: Serial liver stiffness measurement could be applied for longitudinal monitoring of fibrosis status in CHB patients. Continuous decline of liver stiffness after effective antiviral treatment could partially reflect fibrosis regression at an optimal cut-off value.

Disclosure: Nothing to disclose
P0664 RESOLUTION OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION AFTER SUSTAINED VIREOLOGY INFECTION-RELATED参数PREVENTS HEPATIC DECOMPENSATION
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Introduction: Sustained virologic response (SVR) to interferon (IFN)-free therapies ameliorates portal hypertension (1–4). However, the impact of the hemodynamic response on hepatic decompensation has yet to be investigated in this setting.

Aims and Methods: Seventy-seven patients with portal hypertension (HVPG ≥10 mmHg) who underwent hepatic venous pressure gradient (HVPG) and liver stiffness (LS) measurement before (baseline [BL]) and after (follow-up [FU]) IFN-free therapy were retrospectively studied.


P0665 NUTRITIONAL PARAMETERS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS, THEIR INFLUENCE IN EARLY READMISSION AND 1-YEAR MORTALITY
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Introduction: The prevalence of malnutrition among patients with cirrhosis is particularly concerning due to its association with mortality and inherent complications. Multiple studies described a rate of protein-calorie malnutrition around 50–100% in patients with decompensated cirrhosis, and at least 20% with compensated cirrhosis. Early hospital readmissions (within the next 30 days after discharge) among patients with decompensated cirrhosis predict a poor outcome and increase the 1-year mortality. We consider that early rehospitalization could be predictable and therefore, potentially preventable. This study aims to recognize an association between the nutritional status of the patients with decompensated cirrhosis and early readmissions.

Aims and Methods: This is a prospective study performed in a tertiary referral hospital of Spain. This study included 136 patients admitted to the Hepatology Unit with decompensated cirrhosis. Before the discharge, we collected clinical and laboratory data from the medical chart. We evaluated the following nutritional parameters: weight, height, body mass index (BMI), albumin at income, brachial perimeter, tricipital skinfold, and scapular skinfold. We also calculated the “dry body weight” known as the weight adjusted to the total weight lost (subtracting from the total weight: 2.2 kg. in grade I, 6 kg. in grade II, and 14 kg. in grade III). The follow up was performed 30 days, 6 months and 1-year after the discharge, via telephone or in the clinic if the dates matched with the visits.

Results: The median of BMI in patients with early readmissions was 26.0 kg/m² (p = 0.01). Nutritional parameters with statistic significance in the univariate analysis related with early readmission were: BMI < 18.5 (0.0 vs 10.8%; p = 0.001) BMI 25–29 (47.5% vs 21.6%; p = 0.02), Dry BMI < 18.5 (0.0 vs 13.5%; p < 0.01), brachial perimeter in mm. (270 vs 250 mm; p = 0.03) and albumin (32 vs 29 g/L; p = 0.02). The early readmission rate was 27.2%. The 1-year overall mortality was increased in those patients who had early readmission (56.8% vs 20.2%). In the multivariate model two nutritional parameters showed association with early readmission: Dry BMI < 18.5 (HR 4.23, 95% CI: 1.14–15.74; p = 0.03) and albumin as a protector factor (HR 0.89, 95% CI: 0.82–0.96; p = 0.004). None of the nutritional factors presented an association with 1-year mortality.

Conclusion: Dry BMI < 18.5 and albumin are the nutritional parameters that influence in 30-day readmission. Therefore, nutritional status should be a target of preventive actions of early readmissions. As these variables are also related to progression of liver failure, more studies with advanced nutritional measurements are needed in this population.

Disclosure: Nothing to disclose

P0666 SEROLOGICAL INDICES OF LIVER FIBROSIS IN THE COURSE OF ALCOHOLIC LIVER CIRRHOSIS - A PILOT STUDY
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Introduction: Liver biopsy has been described as a gold standard in the assessment of the severity of liver fibrosis so far. However, due to its limitations, it is crucial to look for noninvasive laboratory parameters, which make it possible to monitor liver stiffness.

Aims and Methods: The aim of our investigation was to determine the usefulness of selected serological indices in the assessment of liver fibrosis in the course of alcoholic liver cirrhosis (ALC). We enrolled 55 participants in the survey and among them 22 patients with ALC in research group together with 33 persons in control group. The diagnosis of ALC was based on commonly known criteria.

We measured concentration of direct indicators of liver fibrosis in serum of all participants: platelet-derived growth factor AB (PDGF-AB), transforming growth factor-β1 (TGF-β1), soluble receptor of type III collagen (PIIINP), procollagen I carboxyterminal propeptide (PICP) and laminin. Several indirect parameters of liver fibrosis were obtained too: aspartate aminotransferase (AST) to alanine aminotransferase ratio (APRI), fibrosis-4 (FIB-4) score and red cell volume distribution width (RDW) to PLT ratio (RPR). To evaluate a clinical outcome of patients, we assessed Model for End-Stage Liver Disease (MELD) score and neutrophil to lymphocyte ratio (NLR).

Results: ALC patients (n = 22) Controls (n = 33) p value

<table>
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<th>PLT (10^9/L)</th>
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<td>RPR</td>
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<td>MPV (fL)</td>
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<td>PCT (%)</td>
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<td>PDW (%)</td>
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<td>APRI</td>
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<td>MELD</td>
<td>6.04±6.14</td>
<td>1.01±0.48</td>
<td>&lt;0.01</td>
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</table>
Ledipasvir (n = 99), 98% of HCV patients with HBV or past HBV infection were male, with a mean age of 59 years (range: 20–85), 357 (98%) out of 365 HCV patients with HBV or past HBV serology before treatment; 293 (21.9%) had negative HBsAg and 204 (14.9%) had positive HBsAg. Two hundred and twenty five (61%) out of 365 HCV patients with HBV or past HBV infection were male, with a mean age of 59 years (range: 20–85), 357 (98%) out of 365 HCV patients with HBV or past HBV serology before treatment; 293 (21.9%) had negative HBsAg and 204 (14.9%) had positive HBsAg. Two hundred and twenty five (61%) out of 365 HCV patients with HBV or past HBV infection were male, with a mean age of 59 years (range: 20–85), 357 (98%) out of 365 HCV patients with HBV or past HBV serology before treatment; 293 (21.9%) had negative HBsAg and 204 (14.9%) had positive HBsAg. Two hundred and twenty five (61%) out of 365 HCV patients with HBV or past HBV infection were male, with a mean age of 59 years (range: 20–85), 357 (98%) out of 365 HCV patients with HBV or past HBV serology before treatment; 293 (21.9%) had negative HBsAg and 204 (14.9%) had positive HBsAg. The prevalence of HBV infection (positive HBsAg) in chronic HCV patients in the southern region of Madrid was low. HBV reactivation in HCV/HBV coinfected patients receiving AAD is frequent, but without clinical relevance. Disclosure: Nothing to disclose.

References

P0669 ASSOCIATION BETWEEN LOW VITAMIN D SERUM CONCENTRATION WITH HIGH LEVELS OF HEPATITIS B VIRUS REPLICATION IN CHRONIC HEPATITIS B PATIENTS FROM ALGERIA

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Introduction: Vitamin D is an important immunomodulator that plays an emerging role in inflammatory and metabolic liver diseases, including infection with hepatitis C virus (HCV), which has been intensively studied. However, studies on the potential interaction between vitamin D level and chronic hepatitis B are still limited.

Aims and Methods: This study aimed to explore whether any association existed between serum vitamin D level and clinical determinants in patients with chronic hepatitis B infection. Therefore, we quantified 25(OH)D3 serum levels in a cohort of 187 treatment naïve patients with chronic hepatitis B virus (HBV) infection and tested for their association with clinical parameters of CHB.

Results: Mean 25-hydroxyvitamin D value was 21.90ng/mL. The percentage of patients with different concentration of 25-hydroxyvitamin D (adequate ≥20ng/mL, insufficient/10-20ng/mL, deficiency <10ng/mL) were 29.5%, 43.2% and 27.3%, respectively. In both uni- and multivariate analyses, HBV DNA viral load (log10 IU/mL) was a strong predictor of low 25(OH)D, serum levels (PS0.0008 and PS0.000038, respectively) and vice versa. Mean 25(OH)D3 serum concentrations in patients with HBeAg-positive HBV DNA <2,000 versus 2,000 IU/mL were 18 versus 12ng/mL, respectively (P <0.0001). In addition, hepatitis B early antigen (HBeAg)-positive patients had lower 25(OH)D3 serum levels than HBcAg-negative patients (PS0.013). 25-hydroxyvitamin D serum level is not associated with viral load or fibrosis stage in chronic hepatitis B patients. Finally, 25(OH)D3 and HBV DNA serum levels showed inverse seasonal fluctuations.

Conclusion: We demonstrate a significant association between low 25(OH)D3 serum levels and high levels of HBV replication in chronically infected patients. Future studies to evaluate a therapeutic value of vitamin D and its analogs in HBV infection may be justified.

Disclosure: Nothing to disclose.

Reference
1. FARNIK ET AL. HEPATOLOGY, Vol. 58, No. 4, 2013. Low Vitamin D Serum Concentration Is Associated With High Levels of Hepatitis B Virus Replication in Chronically Infected Patients.

P0670 EFFICACY OF ANTI CHRONIC B HEPATITIS VACCINATION IN CHRONIC HEMODIALYSIS PATIENTS

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Introduction: Hepatitis B virus (HBV) is a public health problem in the world and in Tunisia. Hemodialysis (HD) patients are at high risk of infection and vaccination against HBV remains the best prevention option for these patients. However, the immune deficiency of chronic renal failure (CRF) patients leads to a low seroconversion rate after vaccination and a faster decrease in antibody levels compared to healthy subjects.

Aims and Methods: To evaluate the efficacy of the vaccine protocol in chronic renal failure patients at the hemodialysis stage and to identify the factors that may influence the immune response.

This was a descriptive and cross-sectional retrospective study conducted in six hemodialysis centers in the southern suburbs of Tunis, in patients who had received a standardized accelerated vaccination protocol with HBV vaccine, in single dose and deltoid intramuscular protocol by a recombinant vaccine of 2nd generation without pre-S2. The endpoint is the titer of anti-HBs antibodies. The response was described as non response, low response and good response for an anti-HBs antibody titer of less than 10 IU/L, between 10 and 100 IU/L and greater than 100 IU/L, respectively. Age, sex, diabetes, high blood pressure and the notion of active smoking were tested according to an analytical scheme in univariate and multivariate studies. The Chi-square test was used. A threshold of 5% was considered significant.

Results: In total, 61 patients were included in our study. The mean age of patients was 56.9 ± 17.3 years with a sex ratio of 1. The notion of active smoking was found in 47.5% (n = 29) of patients. Comorbidity was noted in all patients of...
which 70.5% (n = 43) were diabetic and 72.1% (n = 44) were hypertensive. C. Viral Hepatitis infections in only one patient: an HDV serology was positive in all cases. Vaccine seroprotection was obtained in 54% of patients after a primary vaccination. The patients were low responders in 33.3% (n = 11) of cases and good responders in 66.7% (n = 22) of patients. In univariate and multivariate studies, the risk of non-response and low response to the B virus vaccine were advanced age, female gender, active smoking, and the presence of diabetes.

Conclusion: In our series, anti-viral B vaccination in hemodialysis patients is less effective compared to literature data. Smoking control and a review of the legislation governing the modalities of vaccination for hemodialysis may improve immunization coverage.

Disclosure: Nothing to disclose

P0671 COMPARISON BETWEEN TWO POPULATION-BASED SEROSURVEYS, SIXTEEN YEARS AFTER THE IMPLEMENTATION OF UNIVERSAL HEPATITIS B VACCINATION IN A HEPATITIS DELTA ENDEMIC AREA IN GREECE

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Introduction: The prevalence of hepatitis B virus (HBV) and hepatitis delta virus (HDV) infections has declined significantly in Greece, particularly after the introduction of universal HBV vaccination (1997). A rural area in Greece (Archangeli, Rhodes, Greece) was reported to be highly endemic for HBV/HDV during the 1980s, with 10.5% of the local population testing positive for hepatitis B surface antigen (HBsAg) and 27.3% of the HBsAg carriers testing positive for anti-HDV.

Aims and Methods: To compare between two population-based HBV/HDV serosurveys performed with a 16-year interval (1997–2013) in a highly-endemic area in Greece. Two population-based cross-sectional serosurveys were performed among the population in the same sample area (Archangeli, Rhodes, Greece), in 1997 (n = 1938; M/F = 900/1038; children: 29.5%; immigrants: 0%); and in 2013 (n = 1076; M/F = 505/571; children: 21%; immigrants: 17.4%), respectively. From each individual, a blood sample was obtained and tested for HBsAg; all HBsAg-positive individuals were tested for anti-HDV. The demographic and ethnic origin data were recorded.

Results: A total of 1302 patients were included in the study. The immunosuppressive treatment distribution of the patients was as follows: 648 cytotoxic chemotherapy (356 combined with steroids), 325 long-term high-dose steroids, 218 biological agents, 111 rituximab. Six hundred and fifty two (50.1%) of the patients had screened for HBsAg and/or anti-HBclg. HBsAg positivity was found in 162 (23.4%) and anti-HBclg positivity in 29.7% (113/380) of patients. The rates of HBsAg and/or anti-HBclg screening were 94% (205/218) in group 1 and 42.7% (447/1048) in group 2. There was a statistically significant difference between the two groups (p < 0.001). The rates of HBsAg and/or anti-HBclg screening according to the immunosuppressive treatment were as follows: in patients receiving cytotoxic chemotherapy the HBsAg was 53% (348/648), in rituximab patients the HBsAg was 51% (57/111) and in patients with long-term high-dose steroid treatments the HBsAg was 13% (42/325). There was a statistically significant difference in the patients receiving biological agent treatment compared to other treatment groups (biological agent vs cytotoxic chemotherapy p < 0.05, biological agent vs rituximab p < 0.05, biological agent vs long-term high-dose steroid p < 0.05).

Conclusion: The screening rates are very low in patients receiving cytotoxic chemotherapy, rituximab and long-term high-dose steroids and it was found that only half of risky patients received antiviral treatment. Interestingly, almost all of the patients screened were positive using the biological agent had screened and starting HBV prophylaxis. We suggested that the patient safety form, which is mandatory in patients receiving biologic therapy, is effective at this end. We also believe that the use of the patient safety form application in patients receiving immunosuppressive therapy can improve the low rates of HBV screening and antiviral prophylaxis in real life.

Disclosure: Nothing to disclose

Reference

P0673 REACTIVATION OF HEPATITIS B VIRUS INFECTION DURING TREATMENT OF HEPATITIS C WITH DIRECT-ACTING ANTIVIRALS

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Introduction: Reactivation of hepatitis B virus (HBV) can occur during treatment of hepatitis C with direct-acting antivirals (DDAs). It has been almost exclusively described in the cases of positive AgHBs and in no case of positive antiHBs. The risk in cases of isolated anti-HBc positive (anti-HBcPI) is minimal and its surveillance is not well defined.

Aims and Methods: The aim of this study was to investigate the risk of reactivation of HBV during treatment with DDAs in anti-HBcPI patients. A prospective study was conducted in a cohort of 329 chronic hepatitis C patients treated with DDAs from February 2015 to March 2017. Virolological reassessment of HBV infection was performed in the 12 and 24 week posttreatment period. Definitions of HBV reactivation: DNA detectable HBV with or without elevated transaminases and increased HBV DNA > 1 log10 in cases of positive DNA initially.

Results: At baseline, HBV infection was identified in 125 patients (77% men, 53 years on average). 37 patients (29%) were positive AgHBs and 96 patients (77%) were positive antiHBs. 60 patients (48%) were positive AgHBc and 65 patients (52%) were positive antiHBc. 39 patients (31%) were positive HBeAg and 86 patients (69%) were positive antiHBe.

Conclusion: In this cohort, HBV reactivation was prevalent (21%). However, none of these patients had biochemical or virological reactivation at standard short-term follow-up. The frequency of surveillance of these patients remains to be defined.

Disclosure: Nothing to disclose
P0074 ROLE OF BIOLOGICAL NON-INVASIVE TESTS IN PREDICTING FIBROSIS IN CHRONIC HEPATITIS B
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Introduction: The evaluation of fibrosis has been based on liver biopsy. The use of non-invasive tests is more and more common, despite they are still not recommended in hepatitis B due to lack of data.

Aims and Methods: The aim of this study was to compare the results of some biological non-invasive tests with those of liver biopsy in chronic hepatitis B (CHB).

We investigated all the CHB patients admitted in our department in the period between January 2009 and December 2015. Only patients who underwent a liver biopsy were enrolled. The following scores were calculated: ratio aspartate aminotransferase (AST)/alanine aminotransferase (RAA), APRI, FIB-4 and Pohl's score. The results of these scores and liver biopsy were compared.

A significant fibrosis (SF) was defined by a fibrosis score ≥ 2 and an advanced fibrosis (AF) by a fibrosis score ≥ F3 on liver biopsy.

Results: Eighty eight patients were included in our study. Their mean age was 38.5 years [18-83] and the sex ratio was 3.4 (M:F). The mean CTP scores in all the participants who were positive for IgM anti-HDV and 24 (13.3%) were positive for IgG anti-HDV. Six (3.3%) were positive for both IgM and IgG anti-HDV. The prevalence rate of IgG anti-HDV was higher than those with uncomplicated CHB (26.7%) than those with uncomplicated CHB (10.7%) (p = 0.025). However, within the different diagnostic groups, the CTP scores were not significantly different in the patients with uncomplicated CHB due to lack of data.

Conclusion: The CTP scores in all the patients with complicated CHB irrespective of their anti-HDV sero-status. The mean CTP scores in the anti-HDV positive and anti-HDV negative subjects were 6.1 ± 2.1 and 5.5 ± 1.2 respectively (p = 0.025). However, within the different diagnostic groups, the CTP scores were not significantly different in the anti-HDV positive compared to the anti-HDV negative subjects.

Disclosure: Nothing to disclose

P0075 SERO-PREVALENCE OF DELTA HEPATITIS ANTIBODIES, LIVER FUNCTION TEST PROFILE AND SEVERITY OF LIVER DISEASE AMONG INDIVIDUALS WITH CHRONIC HEPATITIS B INFECTION SEEN IN A TERTIARY HOSPITAL IN ABUJA, NIGERIA
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Introduction: Hepatitis D virus (HDV) is a defective RNA virus that requires the helper function of hepatitis B virus (HBV) to be infectious. About 5% of the 350 million HBV carriers worldwide are estimated to have HDV infection. There is paucity of studies in Nigeria on the contribution of HDV to the burden of HBV infection.

Aims and Methods: The study aimed at determining the prevalence rate of delta hepatitis virus (HBV) to be infectious. About 5% of the 350 million HBV carriers worldwide are estimated to have HDV infection. There is paucity of studies in Nigeria on the contribution of HDV to the burden of HBV infection.

The study was a cross-sectional study of 180 consecutive chronic hepatitis B (CHB) infection. The other objectives were to compare the liver function test (LFT) profile and disease severity, using the Child-Turcotte-Pugh (CTP) score, among the anti-HDV positive and anti-HDV negative subjects.

Results: The mean levels of AST and ALT were 1.6 times ULN [0.5 - 36.6] and 1.9 times ULN [0.4 - 40] each. Mean Platelet count was 196 × 10^12 L^-1 (37%). On liver biopsy, 29.5% of patients had a SF and 11.4% had an AF. The mean values of RAA, APRI and FIB-4 were respectively estimated to 0.99 [0.38 - 1.89], 0.8 [0.15 - 18.48] and 1.36 [0 - 7.1]. Pohl's score was positive in 91.3% of cases. SF was determined to APRI and FIB-4 scores with AUC calculated to 0.766 and 0.668 each, and inversely correlated to platelet count with an AUC estimated to 0.692. This correlation wasn't found with RAA (AUC = 0.457). AF was also correlated to APRI and FIB-4 scores with inversely estimated to 0.454 and 0.821, and inversely correlated to platelet count with an AUC of 0.756, however, this correlation was not significant with RAA (AUC = 0.482). In addition, Pohl's score was comparable to AF (p = 0.014) but not to SF (p = 0.18).

Conclusion: In our study, APRI, FIB-4 and Pohl's scores in addition to platelet count were useful in predicting advanced fibrosis. These simple tests could in some cases be sufficient, without need to a liver biopsy.

Disclosure: Nothing to disclose

P0076 DIFFUSION-WEIGHTED MR IMAGING AND MICRO-RNA IN DIAGNOSIS AND STAGING OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS C
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Introduction: Non-invasive tests for the evaluation of the severity of chronic liver diseases seem to be an alternative option designed to replace liver biopsy. These new non-invasive methods are including radiological techniques or biochemical markers like Diffusion weighted MRI and microRNAs.

Aims and Methods: To assess diffusion-weighted MR imaging (DWI) and micro-RNAs (miR) (200b, 21 and 29b) in diagnosis and staging of hepatic fibrosis in patients with chronic hepatitis C. Comparative cross-sectional study was conducted upon 208 patients and 82 age and sex-matched controls underwent DWI of the abdomen, miR and liver biopsy. The pathological score was classified according to META VIR scoring system. The ADC and miR were calculated and correlated with pathological scoring.

Results: The ADC was decreased significantly from controls (F0), patients with early fibrosis (F1 and F2) and those with late fibrosis (F3 and F4), (median 1.92, 1.53 and 1.25 × 10^-3 mm²/s) respectively (p = 0.001). The cutoff ADC value used to differentiate patients from controls was (1.83 × 10^-3 mm²/s) with area under curve (AUC) of 0.992. Combined ADC and miR-200b revealed highest AUC (0.993) for differentiating patients from controls with accuracy (96.9%). The cutoff ADC to differentiate early fibrosis from late fibrosis was 1.61 × 10^-3 mm²/s with AUC of 0.866. Combined ADC and miR-200b revealed best AUC (0.925) for differentiating early fibrosis from late fibrosis with accuracy (80.2%). The ADC correlated with miR-200b (r = -0.61, p = 0.001), miR-21 (r = -0.67, p = 0.001) and miR-29b (r = -0.52, p = 0.001).

Conclusion: Combined ADC and miR (200b, 21 and 29b) offer an alternative surrogate noninvasive diagnostic tool for diagnosis and staging of hepatic fibrosis in CHC patients.

Disclosure: Nothing to disclose

References:

P0078 IMPROVEMENT OF LIVER STIFFNESS, INDIRECT PARAMETERS OF PORTAL HYPERTENSION IN CHRONIC HEPATITIS C VIRUS PATIENTS ONE YEAR AFTER SUSTAINED VIROLOGICAL RESPONSE TO DIRECT ACTING ANTIVIRALS
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Introduction: The outcome of patients with chronic hepatitis C virus infection (HCV) and advanced, compensated liver disease who have obtained a sustained virological response (SVR) to treatment with direct-acting antivirals (DAAs) has not yet been completely defined. In particular, previous studies included heterogeneous populations, or patients with advanced, decompensated liver disease.

Aims and Methods: In this prospective study, our aim was to assess the clinical and instrumental outcome of patients with advanced, compensated chronic HCV-related liver disease who had obtained a SVR to DAAs treatment, and who had at least 1-year follow-up following the end of treatment. We included 52 patients with cirrhosis (n = 27) and a META VIR fibrosis stage F3 (n = 25) who
were followed-up for a median of 60 weeks (95% CI, 52–68 weeks) following the end of treatment. Clinical assessment of liver transient elastography, and measurement of the spleen bi–polar diameter were carried out before treatment and at the end of follow-up. The transient elastography results compatible with the presence (i.e., ≥21.0 kPa) or absence (i.e., <13.6 kPa) of clinically significant portal hypertension were obtained from the current literature.

Results: We observed that liver stiffness decreased (p < 0.0001) from a median baseline of 15.2 kPa (12.0–20.0 kPa) to 9.3 kPa (7.5–12.0 kPa) at follow-up. Overall, absolute liver stiffness values decreased in 45 patients (86.6%), were unchanged in 2 patients (3.8%), and increased in 5 patients (9.8%). The end of follow-up liver stiffness values were compatible with a METAVIR stage F4 in 17 patients (32.6%), F3 in 8 patients (15.4%), F2 in 7 patients (13.5%), F1 in 13 patients (25.0%), and F0 in 7 patients (13.5%). Moreover, we observed that a liver stiffness value suggestive of the presence (>21.0 kPa) of clinically significant portal hypertension was found in 13 patients (25.0%) at baseline of 15.2 kPa (12.0–20.0 kPa) to 9.3 kPa (7.5–12.0 kPa) at follow-up.

Conclusion: We observed that liver stiffness decreased (p < 0.0001) from a median baseline of 15.2 kPa (12.0–20.0 kPa) to 9.3 kPa (7.5–12.0 kPa) at follow-up. Overall, absolute liver stiffness values decreased in 45 patients (86.6%), were unchanged in 2 patients (3.8%), and increased in 5 patients (9.8%). The end of follow-up liver stiffness values were compatible with a METAVIR stage F4 in 17 patients (32.6%), F3 in 8 patients (15.4%), F2 in 7 patients (13.5%), F1 in 13 patients (25.0%), and F0 in 7 patients (13.5%). Moreover, we observed that a liver stiffness value suggestive of the presence (>21.0 kPa) of clinically significant portal hypertension was found in 13 patients (25.0%) at baseline and in 7 patients (13.5%) at follow-up (p = 0.037). Platelet count significantly increased [143 ± 107/117–176 ± 107] to 153 ± 107/139–186 ± 107/107, p < 0.001), while spleen bi–polar diameter significantly decreased [120 mm (112–123 mm) to 110 mm (102–116 mm), p = 0.0009] from baseline to the end of follow-up.

Disclosure: Nothing to disclose

P0679 FROM ALFA-INTERFERON TO DAAS: IMPACT ON HOSPITALIZATION RATE FOR HCV LIVER-RELATED DISEASES FROM 2000 TO 2016 IN NORTH EAST ITALY

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Aims and Methods: This is a retrospective cohort study based on Veneto Region anonymous computerised database of hospital discharges between 2000 and 2017. All Veneto residents discharge records with principal diagnosis of hepatitis C (ICD-9-CM: 070.41, 070.44, 070.51, 070.54, 070.70, 071.01, 571.5, 571.9) were included in the study. The Standardised Hospitalisation Ratio (SHR) per five-year age group (ref. pop. Venice 2008) was calculated and expressed per 10,000 population.

Results: In the period considered 37046 hospital admissions diagnosed with HCV have been recorded. Approximately half of patients were males (56%). Despite their lower age (56.2±7.2 vs. 65.2±8.3), they had the greatest hospitalisation rate (48.0 vs. 36.5; OR: 1.36; 95% CI: 1.19–1.59; p < 0.001). The analysis of the hospitalisation trend shows a 14% increase in the average age of patients (from 57.3±9.5 to 65.9±9.9) and a substantial decrease in hospital admissions (X2 per trend: 9315.644; p < 0.001). Between 2000 and 2017, there has been a trend in hospital admissions (i.e. from 78.9 to 17.3), with a comparable decrease in both genders/sexes ratio (M:F 1.3-1.5) and in the last year considered (2017) SHR were respectively 20.3 and 14.3. It can be observed that the introduction of new therapies has been followed by several reductions in SHR, all with a significantly low decline of hospitalization rate from 2000 (73.6) to 2006-2012 (73.6 to 35.5; OR: 0.48; 95% CI: 0.47–0.49; p < 0.05) reflects the efficacy of Interferon standard and the subsequent improvement of the cure due the use of Peg Interferon Plus Ribavirin. Then with new therapies SHR fell from 21.3 of triple therapy 2013-2014 (OR: 0.29; 95% CI: 0.28–0.30; p < 0.05) to 18 of DAAs 2015-2017 (OR: 0.24; 95% CI: 0.24–0.26; p < 0.05).

Conclusion: HCV liver-related disease as cause of hospital admission is in progressive and constant decline. The slope of the curve representing the decline of hospitalization rate is significantly related to the treatment schedules available in each period and care setting.

Disclosure: Nothing to disclose

Reference
Introduction: analyze DAA treatment impact on post-transplant survival. For this purpose, we undertook OLT recipients who were treated between 7/2014 and 5/2017 and that failed, or as an immediate therapy in 26 patients at an average time of 6 months after OLT. SVR was achieved in 97.4% and in 88.5% patients in the salvage and immediate therapy groups, respectively (p = 0.018). The median follow-up period was only 1. This translated into significantly better 3-year survival, when compared to a historical cohort of 152 patients with HCV graft recurrence from pre-DAA era (97% vs. 78%, p < 0.001). After DAA introduction, none of the patients died of fibrosing cholestatic hepatitis and none underwent re-OLT owing to chronic HCV graft failure, as compared to pre-DAA era patients out of whom 6.7% died of fibrosing cholestatic hepatitis and 5.7% required re-OLT. Disclosure: Nothing to disclose.

Aims and Methods: We retrospectively analyzed 195 (14.2% of 1373 total OLT) patients who underwent OLT between 7/1995 and 5/2017. There were 271 males and 68 females, average age 54.7 ± 8.2 years. 97% of patients were infected with genotype 1b. In Czech Republic, DAA became available in 5/2014 (DAA era, N = 43). Until that time, patients were treated with peginterferon-α and ribavirin (PEG-α/RBV) (pre-DAA era, N = 152). Treatment efficacy (sustained virological response, SVR) in individual groups was assessed by Fisher’s exact test, patient survival 3 years post-transplant by log-rank test.

Results: In the DAA era, we treated 64 patients with biopsy-proven recurrent HCV. SVR at 12 weeks (SVR12) was 100%. A total of 11 patients with SOF/daclatasvir, 12 patients with SOF/simeprevir, 26 with SOF/ledipasvir and 13 with paraprevir/ritonavir/ombitasvir/dasabuvir. DAA were administered at an average of 6.8 months post-transplant as a salvage therapy to 38 patients with graft cirrhosis in whom previous PEG-α/RBV treatment had failed, or as an immediate therapy in 26 patients at an average time of 6 months after OLT. SVR was achieved in 97.4% and in 88.5% patients in the salvage and immediate therapy groups, respectively (p = 0.018). The median follow-up period was only 1. This translated into significantly better 3-year survival, when compared to a historical cohort of 152 patients with HCV graft recurrence from pre-DAA era (97% vs. 78%, p < 0.001). After DAA introduction, none of the patients died of fibrosing cholestatic hepatitis and none underwent re-OLT owing to chronic HCV graft failure, as compared to pre-DAA era patients out of whom 6.7% died of fibrosing cholestatic hepatitis and 5.7% required re-OLT. Disclosure: Nothing to disclose.

Aims and Methods: We assessed the results of DOPR in the end of the treatment (EOT). This prospective study included patients with hepatitis C treated with DOPR for 12 weeks, in the Infectious Disease Clinic Galati, Romania. The eligibility criteria were limited to advanced fibrosis (FibroMax F3/F4; Child-Pugh score ≥5). The demographic data, hepatitis C Virus - Ribonucleic Acid (HCV-RNA), co-morbidities and the rate of EOT were statistically analyzed.

Results: Demographic characteristics of 103 eligible patients are the old age (median age: 61±10.8 years) and 100 months of post-transplantation (62%). The base-line data are: HCV-RNA average 202624±3742998 IU/ml; F3/D4 ratio 0.98, Alamine Aminotransferase (ALT) 98,1±6.3 IU/L, Aspartate Aminotransferase (AST) 53.2±8.5 IU/L, total bilirubin 0.8±0.3 mg/dl, albumin 4.9±0.3 mg/dl, prothrombin concentration 80.8±17.2%. Alpha Fetoprotein 11.3±15 IU/ml, degree of esophageal varices 0: 79.6% patients, 1: 15.5% patients, 2: 3.8% patients, 3: 0.9% patients. As minimum one co-morbidity was counted (15.4%), most frequent hypertension (26%), diabetes (18%), depression (10.6%), oncologic history (8%), ischemic cardiopathy (5.8%), hepatitis B co-infection (4.8%). The rate of the complete 12 weeks treatment was 97%. All patients achieved viral suppression (HCV-RNA < 15 IU/ml) in EOT and had normal transaminases. The interruption of DOPR was decided for 3 patients, due to adverse events (nausea, vomiting, renal failure, acute pancreatitis, increase over 5 times the initial transaminases), but these events were not serious and there were not any deaths. The follow-up on 24 weeks is available to 35% patients, all of them with sustained virologic response.

Conclusion: The antiviral regimen with Dasabuvir, Ombitasvir, Paritaprevir and Ritonavir (DOPR) is effective and safe in the treatment of hepatitis C patients, all of them with sustain virologic response. The antiviral regimen with Dasabuvir, Ombitasvir, Paritaprevir and Ritonavir (DOPR) is effective and safe in the treatment of hepatitis C patients, all of them with sustain virologic response.

Disclosure: Nothing to disclose.

References
P0683  HEPATITIS C SCREENING PROGRAMME IN MILITARY MEDICAL ACADEMY, SOFIA, BULGARIA - SINGLE-CENTRE EXPERIENCE

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Introduction: The prevalence of hepatitis C infection (HCV) in Bulgaria is estimated to be 1.28% in multicenter study in 2010, but no national representative study on HCV prevalence in general population exists so far.

Aims and Methods: The aim of this study is retrospectively to analyze HCV screening programme in Military Medical Academy (MMA), for the period January 2014 – December 2016.

HCV screening programme of the MMA consists of: risk-based screening for all clinics in in- and out-patient settings; voluntary screening offered to everyone admitted in clinics/services entering emergency department; obligatory screening for all blood donations; obligatory screening for all candidates for military services. Screening tests for anti HCV Ab were used. For the period January 2014 – December 2016 29,600 patients, 22,717 males/ 6,883 females, age between 18–87 years old, were screened.

Results: The prevalence of HCV in 29,600 screened patients was 0.65% (n=194). In the Group of blood donors (n=17,394) the HCV prevalence was 0.59% (n=104), but in first-time blood donors (n=6,709) 0.35% (n=27). In the Group of in/out-patients (n= 9,050) the HCV prevalence was 0.92% (n=84) and in Group of candidates for military service (n=3,156) 0.19% (n=6).

There was no gender difference in the HCV prevalence (0.68% in males and 0.55% in females). The most frequently affected age group was 31–40 years old (32.6%). Linkage to care was achieved in 82.5% (84/104) of HCV-infected blood donors and in 61% (61/100) of the out-patient candidates for military service.

Viiremic prevalence was found to be 73% (106/145) and out of them 68% (72/106) initiated antiviral treatment.

Conclusion: Screening for HCV in hospital setting is feasible options for the country where no national screening programme exists and provide excellent opportunity for linkage to care.

Disclosure: Nothing to disclose

P0684  PROCALCITONIN AS EARLY PREDICTOR OF ACUTE LIVER INJURY IN ACETAMINOPHEN POISONING - A PROSPECTIVE COHORT STUDY IN 116 PATIENTS

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Introduction: Acetaminophen is one of the most commonly prescribed drugs and the leading cause of poisoning and acute liver injury (ALI) in developed countries. For more than four decades, prediction of the risk of liver toxicity has been based on the Rumack-Matthew nomogram, which has helped determine when N-acetylcysteine (NAC) is indicated as preventive antidote. However, this nomogram is not validated 1) after repeated acetaminophen exposure; 2) if time of onset is unknown; 3) if initial AST is higher than 200 U/L; 4) to identify acetaminophen-poisoned patients with increased risk of ALI despite NAC administration. Consequently, there is a need for predictive biomarkers in addition to the nomogram to better identify acetaminophen-poisoned patients with increased risk of ALI despite NAC therapy. Since the liver has been considered as potential source of sepsis-related procalcitonin (PCT) production, we aimed to assess the prognostic value of plasma PCT, commonly used in the intensive care unit (ICU) to identify bacterial infections, in patients likely to develop acetaminophen-induced ALI.

Aims and Methods: All consecutive acetaminophen-poisoned patients admitted in our ICU and requiring NAC treatment were prospectively included between January 2011 and December 2017. The primary outcome was the occurrence of ALI defined as a peak of alanine aminotransferase (ALT) >100 IU/L. Liver function tests, PCT and acetaminophen levels were measured on admission. Data was reported as median (interquartile range) or absolute value (percentage) as required. Multivariate analysis based on a Cox proportional-hazard regression model was used to identify parameters associated with ALI. The corresponding hazard ratios and 95% confidence intervals (CI) were determined.

Results: 116 ICU patients were included [age: 72 (21–53), with a mean ingestion of 16 g (9–30) of acetaminophen. Multidrug ingestion was noted in 77% of the patients. The Rumack-Matthew nomogram could not be used in 47% of the cases. ALI occurred in 36 patients (31%) despite NAC treatment provided after a median 6-hour (4–12) delay. In these patients, plasma PCT concentrations were significantly increased as compared to patients without ALI (23.13 vs 0.08 ng/mL p < 0.001). The increase in PCT preceded the increase in ALT by 33 hours (19–74). Multivariate analysis showed that PCT levels > 1ng/mL was significantly associated with ALI [hazard ratio: 4.72 (95% CI, 1.76-12.66); p=0.002], independent from the dose of ingested acetaminophen, the delay of NAC administration and the presence of suspected community-acquired infection (Table 1). PCT levels predicted ALI with a sensitivity, specificity, and area under the ROC curve of 0.94, 0.83 and 0.88 (95% CI, 0.81-0.95), respectively.

Conclusion: Our results suggest that plasma PCT is predictive of acetaminophen-induced ALI. PCT is a potential useful biomarker for the early identification of 1) high-risk ALI patients whom may benefit from closer monitoring and should be referred to a specialized liver ICU and 2) lower-risk ALI patients requiring abbreviated NAC regimens and early discharge safely. Our findings require further validation in larger studies.

Disclosure: Nothing to disclose

P0685  POST-TRANSPLANT DE NOVO MALIGNANCIES: IS HCC AN ADDITIONAL RISK FACTOR?

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Introduction: Patients with hepatocellular carcinoma (HCC) are at higher risk for secondary primary malignancies compared with the corresponding general population. Such risk could be even higher after liver transplantation (LT) due to chronic immunosuppression. It has been consistently demonstrated that patients transplanted for alcoholic liver disease and primary biliary cholangitis are at higher risk for the development of post-LT de novo neoplasms (DNN). However, evidence on the additional risk that pre-LT HCC could confer to transplanted patients are lacking. As HCC has become the leading indication for LT, it is important to investigate whether such patients deserve more intensive post-LT DNN screening compared to other transplanted patients.

Aims and Methods: A cohort study was conducted using data collected among 9 Italian centers between 1985-2014. Patients were excluded if: ≤18 years old, follow-up shorter than 30 days after LT, cancer diagnosis within 30 days after LT. Person-years (PYs) at risk for DNN were computed from 30 days post-LT to the date of death, date of cancer diagnosis or end of follow-up, whichever came first. Hazard ratios (HR) of DNN development (excluding non-melanoma skin cancers) and 95% confidence intervals (95% CI) for patients transplanted for HCC (HCC-patients) compared to those undergoing LT without any pre-transplant neoplastic history (non-HCC patients), were estimated using Cox proportional hazards models, irrespectively from liver disease etiology. All models were adjusted for sex, age at transplant, and calendar year at transplant.

Results: A total of 2,801 patients were followed up for 18,021 PYs of observation [median follow-up: 5.3 years (IQR 2.4–9.9)] during which 194 (6.9%) developed 206 DNNs. Out of 991 HCC-patients (median age at LT 57 years, 86% males) 64 (6.4%) developed 66 DNNs, while out of 1,801 non-HCC patients (median age at LT 51 years, 69% males) 130 (7.2%) developed 140 DNNs. No significant association with the risk of all DNN emerged for HCC-patients as compared to non-HCC (HR = 1.18, 95% CI 0.85-1.64), after median follow-ups of 3.6 (IQR 1.9–6.71) and 6.2 years (IQR 2.7–11.1), respectively (p < 0.01). However, there was a significant difference in occurrence times: median time from LT to first DNN diagnosis was 2.5 years (IQR 1.5-4.3) for HCC-patients and 4.3 years (IQR 1.8-7.9) for non-HCC (p < 0.01). In the analysis by specific tumor types (Table 1), a significant increased risk emerged for bladder cancer only (HR = 8.66, 95% CI 1.7–74).

Conclusion: In our cohort, patients transplanted for HCC were not at higher risk for DNN than other transplant patients. Nonetheless, DNN seemed to occur earlier in HCC-patients, probably due to their higher susceptibility to carcinogens and shared risk factors with primary cancer, leading to a possibly accelerated carcinogenic process. Pre-LT liver neoplastic history could therefore represent an additional risk factor for early DNN occurrence and should be taken into account for surveillance-individualization, to improve early detection and management. Further investigations in wider cohorts with different patients’ characteristics are necessary to confirm these results.

Disclosure: Nothing to disclose
P0868 ASSOCIATION OF TOLL-LIKE RECEPTOR-2 GENOTYPIC POLYMORPHISM WITH ITS SERUM LEVEL AND INFECTIOUS COMPLICATIONS IN RECIPIENTS AFTER LIVING DONOR LIVER TRANSPLANTATION: A SINGLE CENTRE STUDY

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Introduction: Innate immune defenses against infection are altered after liver transplantation (LT) and may increase the risk of infection after transplantation. Toll like receptors (TLRs) are a large section of pathogen associated molecular patterns recognition (PAMP) receptors of the innate immunity. These receptors help stimulation of downstream signaling pathways in reaction to many antigens, mainly to Gram +ve and Gram-ve bacteria, all related to release of cytokines and enhancement of the inflammation. One of the most important elements of these innate defenses is Toll like receptors (TLRs) particularly TLR2.

Aims and Methods: The aim of this work is to assess Association of Toll-Like Receptor -2 single nucleotide genetic polymorphism and its serum level with infection in Recipients after living donor liver transplantation. Of out 125 subjects enrolled in our work, 109 subjects completed this cohort case control prospective study. Subjects were classified into two groups: 66 patients who underwent LDLT and 43 healthy donors as a control group. Serum TLR2 protein and 13th generation ELISA technique in the serum of the recipient’s pre and post transplantation and as well as in the serum of the donors before transplantation. In addition, single-nucleotide polymorphisms (SNPs) of 3 snips of Toll-like Receptor-2 (TLR2) gene (rs3804099 +597, rs5743708 +775, rs12191786 +677) were studied where the allelic genotyping of each DNA sample was performed using real-time PCR reaction.

Results: post liver transplantation developed in 84.8% of the recipients where 55.36% infected with single organisms while 54.69% with mixed infections. Serum TLR2 was significantly higher in recipients post transplant period when compared with recipients and donor in pre transplant period (p < 0.001).

Conversely, no significant difference was detected in post transplant serum TLR2 of recipients on comparing non infected group with infected groups (gram positive, gram negative and fungal infections) regarding blood, urine and sputum cultures (p = 0.9, p = 0.097 and p = 0.36) respectively. On the other hand, serum TLR2 in recipients post LDLT is significantly high in cases showing CMV infection when compared with those without CMV infection (p<0.02). And as regards the SNPs of TLR2 it was found that T allele of rs3804099, G allele of rs5743708 and the C allele of rs121917864 were significantly higher in non infected group when compared to both non infected (OR: 0.147, 0.148 and 0.1838 respectively, p < 0.05) and control groups (0.1238,0.2044 and 0.2528 respectively p<0.001) but no significant association was found with type of infections p > 0.05.

Conclusion: The current study showed that serum level of TLR2 was increased in the recipients post LDLT in comparison to pretransplant level but no significant association was found with the type of infection except CMV infection. The hepatic apelinergic system may be implicated in vasodilatory effects during hepatic I/R injury through increase the hepatic expression of eNOS which counteracts the pathologic effects of Ang II/AT1R system. These results clearly support the existence of a strong interactions between Apelin/APJ system, RAS and eNOS signaling pathways in hepatic I/R injury pathophysiology.

Disclosure: Nothing to disclose.

P0868 CORRELATES OF MORTALITY IN PATIENTS ON WAITING LIST OF LIVER TRANSPLANTATION: A 4-YEAR PROSPECTIVE COHORT STUDY

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Introduction: Liver transplantation (LT) is the most effective treatment for end stage liver disease but due to demand-supply imbalance and prolonged waiting time, LT candidates may die before transplantation. This study aimed to detect predictors of mortality and new predictors of mortality in LT candidates.

Aims and Methods: In this 4 years prospective cohort study, 544 LT adult candidates who referred to Shiraz LT center of Iran were followed on arrival and in 3 months intervals. A comprehensive examination of medical history, physical examination, laboratory and imaging data and death causes (in dead cases) was filled for each patient. Data analysis was performed in Nutritionist, SPSS and R software. Kaplan-Meier test was done and Cox proportional hazard (HRc) and LASSO Cox regression hazard (HRL) were measured.

Results: Mean age of patients was 46.7 ± 13.7 years while 336 (61.7%) were male. Till the end of study, 414 (76.1%) were alive and 130 (23.9%) dead, while 33.1%, 57.7% and 72.2% of deaths were occurred in the first 3, 6 and 12 months of waiting period. Hepatopulmonary syndrome (HRC = 4.7, HRL = 1.8), history of myocardial infarction (MI) (HRC = 3.3, HRL = 1.6) and low carbohydrate (CHO) diet (HRC = 2.7, HRL = 1.5) showed strong association with mortality of patients. In addition to the MELD score, CA 125, high PMN count, weight loss, high level of ALT, positive HBV markers, high MCV of RBCs, ascites, edema of gall bladder wall, high level of BUN and psychological problems showed significant association with death in LT candidates.

Conclusion: About one-fourth of patients die while they are waiting for LT. Therefore to achieve a better outcome besides MELD score, HPS, MI, malnutrition and psychological status of patients should also be considered and managed at the beginning and during the waiting time for LT.

Disclosure: Nothing to disclose.

P0867 PROTECTIVE EFFECT OF APELIN PRECONDITIONING IN A RAT MODEL OF HEPATIC ISCHEMIA REPERFUSION INJURY: POSSIBLE INTERACTION BETWEEN APELIN/APJ SYSTEM, ANGIOTENSIN II/ANGIOTENSIN I RECEPTOR (ANG II/AT1R) SYSTEM AND ENDOTHELIAL NITRIC OXIDE SYNTHASE (eNOS)

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Introduction: Hepatic ischemic reperfusion (I/R) injury, a major cause of liver damage, occurs in multiple clinical settings. It is responsible for nearly one third of delayed graft function cases in liver transplantation. Recently, a number of protective agents have been developed to attenuate hepatic I/R injury in several animal models. However, novel potent protective agents are still needed, hoping for promising results for alleviating hepatic I/R injury with the potential to increase the number of livers suitable for liver transplantation.

Apelin, a small regulatory peptide, is the endogenous ligand of the G protein coupled receptor APJ. It has various isoforms, among which Apelin-13 is the most active isoform. The apelin-APJ axis is widely expressed in hepatic parenchymal, Kupffer, stellate and endothelial cells.

Recently, exogenously administered apelin was shown to protect against I/R injury in different organs including the heart and the brain. However, the protective mechanism of apelin on hepatic I/R injury is not yet clear.

Aims and Methods: We aimed to evaluate the effect of apelin-13 preconditioning on hepatic I/R injury and its effect on hepatic expression of Angiotensin-I receptor (AT1R), endothelial Nitric Oxide Synthase (eNOS) and hepatic tissue level of apelin in an attempt to find the possible association between apelinergic, Renin-Angiotensin System (RAS) systems and eNOS.

Disclosure: Nothing to disclose.

60 male albino rats were randomly assigned to one of the following 4 groups (15 rats each): Control sham-operated (group I), ischemia reperfusion (group II), Angiotensin 1R (group III) and Apelin + L-NAME-treated I/R (group IV). Apelin-13 and L-NAME (N-nitro-L-arginine methyl ester) were administered intraperitoneally at dose of 2 µg/kg/day, 3 days prior to surgical hepatic I/R procedure and 0mg/kg/day, 2 weeks prior to the surgical procedure, respectively. Ischemia was induced for 30 minutes. After 2 hours of reperfusion, serum samples were collected for measurement of serum ALT and AST. Hepatic tissue specimens were harvested for biochemical (MDA; Malondialdehyde, apelin, gene expression of CASP-3, Caspase-3, eNOS and AT1R) and histopathological analyses.

Results: Compared to I/R group, apelin pretreatment provided marked hepatic protection with significant reduction in the serum levels of ALT and AST, hepatic MDA (oxidative stress marker), hepatic expression of CASP-3 (apoptosis marker) and AT1R, while hepatic apelin level and hepatic eNOS expression were significantly increased in group III. Moreover, apelin preconditioning reduced the hepatic histological damage induced by the I/R injury. Hepatic apelin level was positively correlated with hepatic expression of eNOS, while it was negatively correlated with serum liver enzymes, hepatic MDA, hepatic expression of CASP-3 and AT1R.

Conclusion: Exogenous apelin-13 preconditioning exerts protective effect against hepatic I/R injury, probably by modulating the antioxidant stress together with its antiapoptotic effect. Several signaling pathways may be involved including suppression of hepatic AT1R, antioxidant response and elevation of eNOS. These results clearly support the existence of a strong interactions between Apelin/APJ system, RAS and eNOS signaling pathways in hepatic I/R injury pathophysiology.

Disclosure: Nothing to disclose.
P0689 METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: LONG-TERM FOLLOW UP IN A PROSPECTIVE COHORT

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Introduction: Chronic hepatic syndrome (MS) is a common condition among liver transplanted patients, resulting in an increased mortality and morbidity in the long term after liver transplantation (LT).

Aims and Methods: This prospective study assessed the short and mid-term prevalence of MS and metabolic complications after LT. Patients who underwent LT at the Padova Liver Transplant Centre between April 2013 and August 2015 and regularly followed-up at Multivisceral Transplant Unit were prospectively included. Paediatric patients, multiorgan transplantation or re-transplantation and patients who had MS before LT were excluded. For each patient clinical and metabolic variables were collected at time of LT and at 3, 6, 12 and 24 months after LT. MS was evaluated according to the modified NCEP-ATP III criteria.

Results: Twenty-eight patients were included in the study (78% male, mean age 54.2 ± 8.1 years). The most common indication to LT was HCV cirrhosis (42.9%), 25% of the patients presented HCC and the mean MELD at transplantation was 23 ± 8.7. Prevalence of MS at 3, 6, 12 and 24 months after LT was 35.7%, 28.6%, 42.9% and 39.3% respectively (p = 0.003). After LT a significant increase in diabetes mellitus (46.4% vs. 17.9%, p = 0.02) and hypertension (25% vs. 7.1%, p = 0.07), as well as in total cholesterol (mean values 171.7 ± 46.7 vs. 94.5 ± 22.5, p = 0.01) and triglyceride levels (135.6 ± 62.2 vs. 95.4 ± 73.9, p = 0.01). The higher prevalence of MS, diabetes mellitus, and hypertension was observed at 12 months after LT, whereas cholesterol and triglyceride levels did not show significant differences overtime. Considering body weight, the proportion of those patients progressively increased overtime, moving from 4% at 6 months to 23% at 24 months.

Conclusion: Occurrence of MS is an early phenomenon after LT, affecting nearly half of patients at 12 months post-LT. Diabetes, hypertension and increased in body weight are the main responsible factors for developing post-LT MS. A strict metabolic and weight control is necessary, starting early after LT period.

Disclosure: Nothing to disclose

P0690 GENDER DISPARITY IN DONOR-RECIPIENT IN LIVER TRANSPLANTATION AND GRAFT FAILURE

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Introduction: The influence of donor-recipient sex mismatches on graft failure after liver transplantation (LT) is still controversial.

Aims and Methods: The aim of this study was to assess graft failure and to evaluate postoperative analytic outcomes after LT, regarding donor-recipient gender mismatches among 501 patients aged 80 and 85 years (study group admitted by the Liver Transplantation Unit of Hospital Curry Cabral from 2015 to 2019) and who were followed up for at least 12 months. The diagnosis of HCC was based on computed tomography scan and magnetic resonance imaging or liver biopsy. We evaluated the incidence of HCC among ETV treated patients and in untreated patients.

Results: A total of 75 patients were included (78% male, age = 57 ± 12 years, follow up for 37 ± 24 months). Our patients were classed Child Pugh A, B, C in 29%, 49% and 22% of cases respectively. After a median of 19 months, 15 patients developed HCC (20%). The HCC was classed BCLC A, B, C and D in 20%, 33%, 7% and 40% of cases respectively. The treatment was curative in one patient (radiofrequency) and palliative in the 14 others cases (transarterial chemo-embolization: 4 patients, Sorafendib 1 patient, symptomatic treatment: 9 patients).

In the ETV group, HCC developed in 8 patients (21%). In the untreated group, HCC developed in 7 patients (18.9%). Log rank test did not reveal a statistically significant difference between the incidence of HCC in the ETV group and the untreated group (p = 0.81).

Conclusion: HCC still develop in patients with HBV-related cirrhosis treated with ETV. For this reason, patients under effective long term nucleos (t) id analogues therapy should remain under surveillance for HCC.

Disclosure: Nothing to disclose

P0691 IMPACT OF ENTECAVIR IN REDUCING THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS B RELATED CIRRHOSIS

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Introduction: Chronic hepatitis B virus (HBV) infection is the most frequently identified cause of Hepatocellular carcinoma (HCC). The newer nucleos (t) id analogues such as Entecavir (ETV) or Tenofovir have been shown to be effective in terms of virological response and improvement of liver function. However their impacts on the incidence of HCC are still not clear.

Aims and Methods: The aims of this study were to investigate the incidence of HCC in patients with HBV-related cirrhosis and evaluate the effect of ETV in reducing this incidence. We performed a retrospective analysis of data from consecutive patients with HBV-related cirrhosis recruited from 2009 to 2019 and who were followed up for at least 12 months. The diagnosis of HCC was based on computed tomography scan and magnetic resonance imaging or liver biopsy. We evaluated the incidence of HCC among ETV treated patients and in untreated patients.

Results: A total of 75 patients were included (78% male, age = 57 ± 12 years, follow up for 37 ± 24 months). Our patients were classed Child Pugh A, B, C in 29%, 49% and 22% of cases respectively. After a median of 19 months, 15 patients developed HCC (20%). The HCC was classed BCLC A, B, C and D in 20%, 33%, 7% and 40% of cases respectively. The treatment was curative in one patient (radiofrequency) and palliative in the 14 others cases (transarterial chemo-embolization: 4 patients, Sorafendib 1 patient, symptomatic treatment: 9 patients).

In the ETV group, HCC developed in 8 patients (21%). In the untreated group, HCC developed in 7 patients (18.9%). Log rank test did not reveal a statistically significant difference between the incidence of HCC in the ETV group and the untreated group (p = 0.81).

Conclusion: HCC still develop in patients with HBV-related cirrhosis treated with ETV. For this reason, patients under effective long term nucleos (t) id analogues therapy should remain under surveillance for HCC.

Disclosure: Nothing to disclose

P0692 HEPATOCELLULAR CARCINOMA IN THE ELDERLY: CLINICAL CHARACTERISTICS, OUTCOMES AND TREATMENT EFFICACY, SAFETY IN OLDER THAN 75 YEARS


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Introduction: The number of elderly patients diagnosed with hepatocellular carcinoma (HCC) has been increasing because the increase in the longevity of the general population. But there is no proper management based on age stratification of elderly patients.

Aims and Methods: The aim of our study was to compare the clinical characteristics, outcomes and treatment efficacy and safety between oldest-old (aged more than 75 years), middle-old (aged 60–74 years) and youngest-old patients (aged between 75 and 80 years) patients with HCC from January 2010 to December 2016. A total of 550 elderly patients whose data included demographics, comorbidity, etiology of liver disease, presence of cirrhosis, staging of HCC, treatment modality and treatment related adverse event were evaluated retrospectively. Also overall survival was assessed in enrolled patient.

Results: Fifty-one patients (oldest-old; median 87 years old), 153 patients (middle-old; median 82 years old) and 346 patients (young-old; median 77 years old) were diagnosed with HCC. Both oldest-old and middle-old patients, compared to young-old patients, had significantly higher rate of hepatitis C-related disease (HCV antibody positivity 41.2% vs. 29.4% vs. 22.0%, p = 0.007) but had significantly lower rate of alcohol-related disease (11.8% vs. 19.3% vs. 30.3%, p = 0.002). The non were significant difference in underlying sex, body mass index, presence of co-morbidity, hepatitis B-related disease and stage of HCC. The Child-Pugh class (CPT class A 88.9% vs. 84.1% vs. 83.6%, CPT class B 11.1% vs. 15.9% vs.15.0% and CPT class C 0.0% vs. 0.0% vs. 1.3%, p = 0.912). And HCC was classed BCLC A, B, C and D in 29%, 49% and 22% of cases respectively. After a median of 19 months, 15 patients developed HCC (20%). The HCC was classed BCLC A, B, C and D in 20%, 33%, 7% and 40% of cases respectively. The treatment was curative in one patient (radiofrequency) and palliative in the 14 others cases (transarterial chemo-embolization: 4 patients, Sorafendib 1 patient, symptomatic treatment: 9 patients).

In the ETV group, HCC developed in 8 patients (21%). In the untreated group, HCC developed in 7 patients (18.9%). Log rank test did not reveal a statistically significant difference between the incidence of HCC in the ETV group and the untreated group (p = 0.81).

Conclusion: HCC still develop in patients with HBV-related cirrhosis treated with ETV. For this reason, patients under effective long term nucleos (t) id analogues therapy should remain under surveillance for HCC.

Disclosure: Nothing to disclose
the stemness properties of CD24 cells via promoting STAT3 Tyr705 phosphorylation. Blockade of HGF/c-Met or IL6/IL6R signaling significantly abolished the effect of CAFs on stemness properties, which compromised the activation of STAT3 pathway in CD24+ HCC cells. While knockdown of STAT3 in CD24+ HCC cells notably attenuated CAF-induced stemness characteristics of CD24+ HCC cells. Furthermore, in HCC patients, higher expression of phospho-STAT3 were also demonstrated to be positively correlated with poor clinical outcomes.

Conclusion: These findings suggested that HGF and IL6 secreted by CAFs promoted the stemness properties of CD24+ HCC cells through the activation of STAT3 signaling.

References: This work was supported by grants from the National Natural Science Foundation of China (81172063 and 81372352)

Disclosure: Nothing to disclose

P0696 LIVER STIFFNESS AS A PREDICTOR OF HEPATOCELLLULAR CARCINOMA BEHAVIOR IN PATIENTS WITH HEPATITIS C-RELATED LIVER CIRRHOSIS

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Introduction: Hepatocellular carcinoma (HCC) is a leading cause of death in cirrhotic patients. For improvement of patient outcome, early detection and treatment of HCC are mandatory, so strategies for screening, risk stratification and prognostication of HCC are important.

Aims and Methods: To explore the role liver stiffness measurement (LSM) inside HCC lesion, in peripheral tissue and in cirrhotic non-malignant liver tissues in the prediction of HCC clinical behavior. We included 121 naïve patients with hepatitis C related HCC. Liver biopsy profile as well as serum alpha-fetoprotein (AFP) were done. The aspartate aminotransferase (AST) ratio (APRI) score was calculated. HCC evaluation (number of lesions, maximum diameter, tumor capsule, vascular invasion, and extrhepatic spread) was done based on the triple CT. HCC staging was done (TNM, OUKUDA, CLIP and BCLC staging).

Results: Liver stiffness measurement (LSM) inside the tumor, and LSM in the peri-tumoral tissue (p = 0.001) could predict early HCC. The aspartate aminotransferase (AST) ratio (APRI) score was calculated. HCC evaluation (number of lesions, maximum diameter, tumor capsule, vascular invasion, and extrhepatic spread) was done based on the triple CT. HCC staging was done (TNM, OUKUDA, CLIP and BCLC staging).

Conclusion: LSM inside the tumor mass, within 1 cm around the tumor and at the non-malignant cirrhotic liver tissue [expressed as meter/second (m/s)] were assigned to appropriate treatment according to the BCLC stage. The recurrence-free interval was calculated from last CT evidence of HCC ablation to 1st CT evidence of recurrence.

Disclosure: Nothing to disclose

P0695 CANCER-ASSOCIATED FIBROBLASTS PROMOTE THE CANCER STEM CELL PLASTICITY OF CD24+ LIVER STEM CELLS VIA PARACRINE SIGNALLING

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Introduction: Cancer stem cells (CSCs) contribute to treatment resistance and tumour relapse in hepatocellular carcinoma (HCC). Cancer-associated fibroblasts (CAFs) have been reported to support tumor progress. However, the mechanisms by which CAFs contribute to stemness maintenance remain largely unknown. Here, we hypothesized that HGF and IL6 secreted by CAFs promote the stemness properties of CD24+ HCC cells through the activation of STAT3 signaling.

Aims and Methods: CD24+ cells were isolated from HCC cell lines, and their stemness characteristics were demonstrated in vitro and in vivo (Xenograft tumour models). CAFs isolated from fresh HCC samples and co-cultured with CD24+ HCC cells, and CSC functions were measured. HGF/c-Met, IL6/IL6R and STAT3 pathways were detected and then manipulated with pharmacologic and genetic approaches in CD24+ HCC cells with or without CAF-CM. Finally, the expression of CD24, alpha-smooth muscle actin (α-SMA) and phospho-STAT3 in tissues from HCC patients were examined by immunohistochemistry.

Results: We found that the expression of CD24 was high in HCC tissues, and positively correlated with the poor prognosis and α-SMA expression in CAFs. Meanwhile, CD24+ cells isolated from HCC cell lines exhibited higher self-renewal, chemotherapy resistance, invasion and migration abilities in culture, and formed more xenograft tumors in mice than CD24- cells. Moreover, CAF-derived HGF and IL6 enhanced the stemness properties of CD24+ HCC cells via promoting STAT3 Tyr705 phosphorylation. Blockade of HGF/c-Met or IL6/IL6R signaling significantly abolished the effect of CAFs on stemness properties, which compromised the activation of STAT3 pathway in CD24+ HCC cells. While knockdown of STAT3 in CD24+ HCC cells notably attenuated CAF-induced stemness characteristics of CD24+ HCC cells. Furthermore, in HCC patients, higher expression of phospho-STAT3 were also demonstrated to be positively correlated with poor clinical outcomes.

Conclusion: These findings suggested that HGF and IL6 secreted by CAFs promoted the stemness properties of CD24+ HCC cells through the activation of STAT3 signaling.

Disclosure: Nothing to disclose
The actual guidelines for liver cirrhosis recommend hepatocellular carcinoma (HCC) surveillance with ultrasound and alpha-fetoprotein every 6 months in a tertiary center.

Recent data suggested the efficacy and tolerability of Capecitabine in the treatment of advanced HCC, also in the case of patients intolerant to Sorafenib. Recently, Regorafenib (RESORCE trial) succeeded in improving survival in patients with advanced HCC, also in the case of patients intolerant to Sorafenib, which was not a good tool to predict the development of HCC in the Portuguese population. One reason for this could be the main etiologies of chronic liver disease in our population, namely alcoholic and non-alcoholic fatty liver disease, much different from the population where THRI was validated (the major causes were HCV infection and autoimmune liver diseases).

Disclosure: Nothing to disclose.

P0699 Combined blood indices and MELD score as prognostic predictors for early recurrence of hepatocellular carcinoma after transarterial chemoembolization

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Introduction: The first-line treatment option for intermediate-stage Hepatocellular Carcinoma (HCC) was Transarterial chemoembolization (TACE). Inflammation has been proved to play an important role in tumor progression and invasion. Inflammation profile, such as lymphocyte-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), Monocyte Granulocyte Lymphocytic Ratio (MGLR) and Red blood cell distribution width (RDW) have been identified as prognostic biomarkers in multiple cancers.

Aims and Methods: We aimed to investigate these different blood indices and MELD score as prognostic predictors for early recurrence of hepatocellular carcinoma after TACE.

Methods: NLR, LMR, MGLR, RDW and PLR were calculated and values determined in 147 patients (111 male and 36 female). Sensitivity and specificity of different indices for HCC recurrence were estimated by receiver operating characteristic curve. Relation between best predictors and recurrence free time in TACE treatment of HCC cases was studied by Kaplan-Meier curve.

Results: MGLR had the best diagnostic performance for detection of early recurrence of HCC after TACE at cut off value 2.75 with sensitivity 70.7%, specificity 59.2%, MELD score at cut off value 9.3 had the best diagnostic performance for detection of early recurrence of HCC after TACE with 80% sensitivity and 55.8% specificity; also risk estimates for HCC recurrence was 2.489 with 95% confidence interval (1.280–4.838).

Conclusion: This study concluded that higher both MGLR and MELD score were associated with increased risk of HCC recurrence after TACE and could be used as novel, simple, low-cost, non-invasive prognostic tests for HCC patients.

Disclosure: Nothing to disclose.

P0700 Quality of sleep in patients with liver transplant: A multicenter, prospective study in a cohort from South Italy

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Introduction: Patients with liver cirrhosis and liver transplant (LT) candidates show sleep disturbances that negatively impact their quality of life. Data about the quality of sleep after LT are scanty.

Aims and Methods: We aimed to evaluate the quality of sleep in a cohort of adult LT patients from Southern Italy. Adult LT patients were recruited from two Liver Following Transplant Centers of Southern Italy (Salerno and Gragnano). We collected the following data: age, gender, marital status, cause of transplantation, presence of hepatocarcinoma at the time of transplantation, early liver rejection, time from transplantation, type of immunosuppression, and presence of comorbidities. Age- and gender-matched healthy controls (HC) were also enrolled. All participants completed the Pittsburg Sleep Quality Index (PSQI), the Zung Self-rating Depression Scale and the State-Trait Anxiety Inventory (STAI).

Results: 129 LT patients (91 males, mean age 60.2 ± 9.8 years) and 51 HC (29 males, mean age 60.3 ± 8.6 years) were enrolled. The most common indications for LT were HCV-related cirrhosis (44.3%), HBV-related cirrhosis (35%),...
Introduction: A rare disease is defined by the European Health Commission (EHC) as a disorder found in less than 5/10,000 population. The importance of the sleep pattern of LT patients are needed because a better sleep may promote more than half of LT patients had sleep disorders. Age, gender, type of immunosuppressive therapy, indication for LT did not relate to the presence of sleep disorders. The improved LT patients survival stresses the importance of characterizing psychosocial aspects, including anxiety, depression, and sleep. The improved LT patients survival stresses the importance of the sleep pattern of LT patients are needed because a better sleep may promote a better quality of life.

Table 1 Mood disorders in LT patients compared to HC. Data were expressed as percentage (%) or mean (Standard Deviation).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>LT patients (N = 129)</th>
<th>Healthy Controls (HC) (N = 51)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSQI mean (SD)</td>
<td>6.7 (3.9)</td>
<td>6.4 (3.6)</td>
<td>0.7</td>
</tr>
<tr>
<td>% pathological sleep (PSQI &gt; 5)</td>
<td>49 (53.9)</td>
<td>27 (52.9)</td>
<td>0.9</td>
</tr>
<tr>
<td>STAI Y1</td>
<td>40.2 (13.0)</td>
<td>36.9 (8.9)</td>
<td>0.08</td>
</tr>
<tr>
<td>STAI Y2</td>
<td>38.6 (10.2)</td>
<td>36.4 (8.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>ZUNG</td>
<td>38.7 (10.0)</td>
<td>33.7 (6.0)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Disclosure: Nothing to disclose

P0701 TRANSLATING POLICY TO REAL WORLD IN RARE LIVER DISEASES REGISTRIES; A EUROPEAN PERSPECTIVE

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Introduction: A rare disease is defined by the European Health Commission (EHC) as a disorder found in less than 5/10,000 population. The importance of collaborations in the field of rare diseases where data is scarce and fragmented is well-known. The OrphanXchange project was set up by Orphanet to promote collaborations between academia and industry. Moreover, the European Union Committee of Experts on Rare Diseases (EUCERD) encouraged the exchange of relevant experience, policies and practices in rare diseases among member states and promoted cooperation across Europe and beyond, including Japan. The committee identified multiple important challenges for successful registry utilisation: discrepancy in coverage with multiple fragmented registries for some conditions, complete lack of registries for other conditions and registries that were mainly academic rather than clinical. A critical output of EUCERD was the provision of a basic framework for European data collection and registration in rare diseases across 6 domains:

- International Operability
- Sources Of Data
- Collection Of Data
- Good Practices
- Use Of Data For Regulatory Purposes
- Sustainability

There are approximately 20 rare liver diseases (RLD), meaning the hepatology community can be influential in informing and developing such registries.

Aims and Methods: Our aim was to identify how many of the defined non-cancer orphan conditions have an established registry in keeping with EHC’s recommendations. A PubMed and google scholar search using the MESH terms “registries”, “database management systems”, “database” and the non-MESH terms “database$$”, “registry”, “repository” and “repositories” for English literature in humans was performed. The results were screened manually.

Results: Registries were identified for most RLD in the table below. The results are summarised in the table below. Slovenia, Slovakia, FYROM, Malta, Luxemburg, Lithuania, Estonia and Cyprus do not appear to have RLD registries.

Abbriviation: Alpha 1 antitrypsin deficiency (A1AD), autoimmune hepatitis (AIH), acute liver failure (ALF), biliary atresia (BA), Caroli’s disease, hereditary haemorrhagic telangectasia (HHT), IgG4 disease, primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), polycystic liver disease (PLD), porphyria, vascular liver disorders (VLD), Wilson disease (WD) and hemidrosis (HDV).

Conclusion: Despite concerted efforts of the European Union, there is variability in the number of registries for RLD. The EUROPLAN was set up to provide a framework and support EU countries in developing their national strategies. Currently, 24/28 member countries have rare disease strategies. Thus far, action plans could not be found on the EU portal for Estonia, Finland, Malta, Poland. Interestingly, despite whilst not demonstrating a national strategy for rare diseases, Poland and Finland currently have registries for RLD and surprisingly, countries with established national policies such as Lithuania, Luxemburg, Cyprus, Slovenia, Slovakia and FYROM do not.

Disclosure: MP: Advisory board Dr Falk pharma. Speaker fees Intersect. CK: Nothing to disclose SdL: is supported by the Eli Lilly fund a Real-World Evidence Centre in diabetes; Astra-Zeneca diabetes study; and Takeda gastroenteritis. AA: Advisory board for Wilson Therapeutics, Yivel, Univar, Interpect, unrestricted educational grants from Alexion and Bayer, Grant support from Wilson therapeutics and Interpect.

Abstract No: P0701

<table>
<thead>
<tr>
<th>Name of Country</th>
<th>Number of registries identified</th>
<th>Diseases with registries</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>13</td>
<td>A1AD, AIH, ALF, BA, Caroli’s, HHT, IgG4, PBC, PLD, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Germany</td>
<td>13</td>
<td>A1AD, AIH, ALF, BA, Caroli’s, HDV, HHT, PBC, PLD, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>France</td>
<td>12</td>
<td>AIH, ALF, BA, Caroli’s, HH, HHT, PBC, PLD, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Spain</td>
<td>8</td>
<td>A1AD, HDV, PBC, PLD, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Netherlands</td>
<td>8</td>
<td>A1AD, BA, PBC, PLD, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Italy</td>
<td>8</td>
<td>A1AD, BA, HDV, PBC, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Belgium</td>
<td>7</td>
<td>A1AD, BA, PBC, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Austria</td>
<td>6</td>
<td>A1AD, BA, HDV, PSC, VLD, WD</td>
</tr>
<tr>
<td>Switzerland</td>
<td>6</td>
<td>A1AD, BA, Porphyria, PSC, VLD, WD</td>
</tr>
<tr>
<td>Poland</td>
<td>5</td>
<td>BA, PBC, Porphyria, PSC, WD</td>
</tr>
<tr>
<td>Sweden</td>
<td>4</td>
<td>A1AD, Porphyria, PSC, VLD</td>
</tr>
<tr>
<td>Portugal</td>
<td>4</td>
<td>A1AD, BA, VLD, WD</td>
</tr>
<tr>
<td>Norway</td>
<td>4</td>
<td>Porphyria, PLD, PSC, WD</td>
</tr>
<tr>
<td>Greece</td>
<td>4</td>
<td>HDV, PBC, PSC, WD</td>
</tr>
<tr>
<td>Denmark</td>
<td>4</td>
<td>WD, BA, PSC, VLD</td>
</tr>
<tr>
<td>Romania, Ireland, Czech Republic, Finland</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Serbia, Iceland, Croatia, Bulgaria, Latvia</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
Identification of patients through analysis of archival laboratory results and chart review is feasible. Disease severity is unknown in a significant part of the LTFU population. These patients could be at risk for serious complications. Together with the high percentage of LTFU patients observed in this centre, this emphasizes the need for a nationwide retrieval project to bring this group back in care.

Disclosure: This investigator-initiated study was funded by an unrestricted grant from MSD.
hepatologists, the RCGP (Royal college of General Practitioners), the NIHR (National Institute of Health and Research), patient groups, charities and industry partners.

Results: The design process of creating a registry can be primarily divided into three main phases (theoretical, technical and data collection) and spans across 9 domains. The blueprint for these is shown in the table below:

<table>
<thead>
<tr>
<th>1</th>
<th>Aims, objectives and endpoints</th>
<th>What is the purpose of the registry?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Define study population</td>
<td>Define the disease ontology and case eligibility</td>
</tr>
<tr>
<td>3</td>
<td>Information, research and clinical governance</td>
<td>1. Safety &amp; Wellness of patients and investigators 2. Competence and adequate qualifications 3. Scientific and Ethical Conduct. Peer-reviewed research proposal 4. Patient, service user and public Involvement 5. Integrity, quality and transparency 6. Protocol to clearly explain the design of the study 7. Legality 8. Benefits and Risks to patients should be identified and stated 9. Approval by regional ethics committee, confidentiality advisory group (if necessary) and ultimately by the health research authority 10. Information about the research to be made publically available 11. Accessible findings (positive or negative) 12. Respect autonomy of participants and afford respect and choice in relation to consent or refusal of consent. Develop robust opt-out mechanisms. 13. Insurance and Indemnity to cover liabilities 14. Respect for Privacy by practising strict information governance rules and ensuring safekeeping of data 15. Compliance</td>
</tr>
<tr>
<td>4</td>
<td>Sponsorship &amp; Funding</td>
<td>Seek locoregional, national and international collaborations</td>
</tr>
<tr>
<td>5</td>
<td>Identify stakeholders &amp; set up collaborations</td>
<td>1. Define data fields and set core/mandatory and desired components 2. Is there a need for patient-identifiable information? 3. Create pseudonymised record identifier for each patient recruited 4. Create various levels of access for users 5. Build in data validation check points 6. Engage with patients, the public and relevant charities</td>
</tr>
<tr>
<td>6</td>
<td>Registry design and data quality</td>
<td>1. Define the disease ontology and case eligibility</td>
</tr>
<tr>
<td>7</td>
<td>Data entry</td>
<td>1. Enable remote access and data entry 2. User-friendly interface for quick data entry</td>
</tr>
<tr>
<td>8</td>
<td>Data processing</td>
<td>1. Data linkage to other repositories available 2. Develop a strategy for handling missing data 3. Presentation of outcomes in local, regional and international meetings</td>
</tr>
<tr>
<td>9</td>
<td>Ensure sustainability</td>
<td>1. Form a steering committee 2. Regular consultations with stakeholders including patients and the public 3. Long-term funding 4. Continental/ international data feeding into bigger datasets</td>
</tr>
</tbody>
</table>

### Blueprint for the design of a comprehensive registry for rare liver diseases

### Conclusion

Overall, the development of a bespoke registry for rare liver diseases is complex and requires a wide array of skills and expertise including clinical, IT, cyber security and information governance. Our experience was that the key element is clearly defining both the study population and the purpose of the registry. This will provide a solid foundation for the design and utility of the database which can be then be expanded appropriately and sustainably. The efforts should be guided by a carefully-selected steering committee which should also promote the establishment of loco-regional, national and international collaborations.

### Disclosure

CK: Nothing to disclose. MP: Advisory board Dr Falk pharma. Speaker fees Intercpect. SDF: is supported by the Eis Lily fund a Real-World Evidence Centre in diabetes; Astra-Zeneca diabetes study; and Takeda gastroenteritis. AA: Advisory board for Wilson Therapeutics, Vivet, Univar, Intercpect, unrestricted educational grants from Alexion and Bayer, Grant support from Wilson therapeutics and Interceptor.

### P0705 OBESITY STARTS WITH THE ACCUMULATION OF FAT IN THE SUBCUTANEOUS ADIPOSE TISSUE IN ASSOCIATION WITH NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Adiposity due to a positive energy balance starts with the accumulation of fat in the subcutaneous adipose tissue, with relatively less influence on insulin sensitivity, until the limit is expanded through adipose tissue dysfunction. The lipid then overflow and the accumulation of visceral and ectopic fat sets in, resulting in insulin resistance and related cardiometabolic problems. Several factors differentiate the subcutaneous and visceral adipose tissues, including adipokine and cytokine production, adipogenic potential, and the ability to store and mobilize lipids. It has been widely accepted that liver fat is a type of ectopic fat that is strongly associated with visceral obesity. However, there is not yet a unified view about the association between nonalcoholic fatty liver disease (NAFLD) and subcutaneous obesity.

### Aims and Methods: NAFLD is recognized as a hepatic manifestation of metabolic syndrome because of the association with visceral obesity. However, the association between NAFLD and subcutaneous fat is less investigated. Hence, the aim of the study is to examine the association between NAFLD and subcutaneous obesity. The study population included 3197 subjects who consumed <20 g of alcohol per day. They were divided according to the quartiles of subcutaneous (SFA) or visceral (VFA) fat areas on CT. Fatty liver was diagnosed using ultrasonography (FL-US).

### Results:
The prevalence of FL-US increased across the SFA categories, even after adjusting for the VFA, in men (S-Q1, 13.7; S-Q2, 37.8; S-Q3, 52.3; S-Q4, 75.4%, p < 0.001, Mantel-Haenszel test) and women (S-Q1, 8.4; S-Q2, 19.0; S-Q3, 33.6; S-Q4, 50.4%, p < 0.001). The risk of FL-US increased with SFA—indipendently of VFA—in men (Odds ratio [95% confidence interval]: S-Q1, 1; S-Q2, 2.21 [1.54–3.18]; S-Q3, 3.57 [2.48–5.13]; S-Q4, 6.67 [4.52–9.86] and women (S-Q1, 1; S-Q2, 1.74 [1.07–2.84]; S-Q3, 3.03 [1.90–4.82]; S-Q4, 4.12 [2.60–6.54]). In addition, the prevalence of FL-US increased across the VFA categories, even after adjusting for the SFA in men (V-Q1, 13.2; V-Q2, 41.9; V-Q3, 54.9; V-Q4, 69.4%, p < 0.001) and women (V-Q1, 8.4; V-Q2, 19.0; V-Q3, 33.6; V-Q4, 50.4, p < 0.001). The risk of FL-US increased with the VFA, independently of the SFA, in men (V-Q1, 1; V-Q2, 2.21 [1.54–3.18]; V-Q3, 3.57 [2.48–5.13]; V-Q4, 6.67 [4.52–9.86] and women (V-Q1, 1; V-Q2, 1.74 [1.07–2.84]; V-Q3, 3.03 [1.90–4.82]; V-Q4, 4.12 [2.60–6.54]). In addition, this significant association between FL-US and the SFA was already detected from the second SFA quantile. It is noteworthy that the mean BMI values of the subjects in the second quantile were 23.7 kg/m² in men and 22.6 kg/m² in women, as they were significantly close to the in normal body weight range according to the Japanese criteria (obesity ≥ 25 kg/m² in both men and women). On the other hand, the components of metabolic syndrome were independently associated with the VFA, but were less associated with the SFA.

### Conclusion

NAFLD may be independently associated with both visceral and subcutaneous adiposity, which is a characteristic that distinguishes NAFLD from other components of metabolic syndrome.

### Disclosure: Nothing to disclose.
Patients who underwent surgical resection after preoperative examinations were included in this study. Between January 2004 and September 2015, patients who underwent mapping biopsy under X-ray fluoroscopy (ERC) without POCS were included (CHF group, n = 56). POCS using CHF-B260 was performed only when ERC-guided mapping biopsy findings were unreproducible because of possible discrepancy between the mapping biopsy findings and other examinations, such as ERC, intraduodenal ultrasonography, EUS, CT, and MRI. Between October 2015 and March 2017, SpyGlass DS accompanied by POCS-guided mapping biopsy was used in all candidates for surgery (SpyDS group, n = 14). The accuracy of overall preoperative diagnosis of lateral cancer extent, which was defined based on all examinations, including POCS, and was compared with the final diagnosis confirmed using the resected specimen, was the main outcome. The accuracies of optical evaluation by POCS, which was retrospectively reviewed by authors, and accuracy of EUS-guided mapping biopsy were evaluated.

Results: Accuracy of the overall preoperative diagnosis of lateral cancer extent for both the liver side and the ampullary side were 93% and 100%, respectively, for the CHF group and 97% and 100%, respectively, for the SpyDS group (p = 0.34 for the liver side; p, not available for the ampullary side). Sensitivity and specificity for liver-side estimation were 92% and 93%, respectively, for the CHF group, and 70% and 100%, respectively, for the SpyDS group (p = 0.13 for the liver side and p = 0.10 for specificity). Both the sensitivity and specificity for ampullary-side estimation were all 100% for both groups.

Diagnostic accuracy of simple optical evaluation by using POCS for both the liver side and the ampullary side were 91% and 100%, respectively, for the CHF group, and 69% and 80%, respectively, for the SpyDS group (p = 0.44 for the liver side; p = 0.26 for the ampullary side). When comparing groups, the accuracy rates seemed lower for the SpyDS group, although statistical significance was not detected.

The accuracy of the ERC-guided mapping biopsy in the CHF group was 80% (44/51) for the liver side and 92% (12/13) for the ampullary side. The reasons why the tumor spread toward the liver side was misdiagnosed in seven patients were contamination in five patients (false positive), inappropriate biopsy site (i.e., unintended upstream bifurcation of which the tumor spread did not reach) in one patient (false negative), and impossibility of advancement of the biopsy forceps beyond the obstruction in one patient (specimen was not obtained).

Conclusion: The SpyGlass DS system was found to be acceptable for the diagnosis of lateral cancer extent when cholangioscopy-guided biopsy was applied, although the accuracy rates of simple optical evaluation seemed lower than those using the traditional cholangioscope. It could be a standard approach for the tumor spreading to the liver side and the ampullary side.

Patients with less than 90 days of follow-up were excluded from the study. The outcomes were compared at 3, 6, and 12 months, and were evaluated regarding its risk factors.

Aims and Methods: The aim of this study was to investigate the risk factors for RBO after endoscopic MS placement in unresectable malignant distal biliary obstruction. Between January 2005 and June 2017, 200 patients (mean age, 76 ± 11 yrs.; 117 males, 83 females) with unresectable malignant distal biliary obstruction were included in this study. Patients with less than 90 days of follow-up were excluded from the study. The primary outcome measurements were time to RBO and risk factors for RBO. RBO was defined as stent occlusion and stent migration. Time to RBO was analyzed by using the Kaplan-Meier method and risk factors for RBO were analyzed by using log-rank test and Cox regression analysis.

Results: One hundred and seventeen patients had pancreatic cancer, 57 had bile duct cancer, 11 had gallbladder cancer 11 had lymph node metastases from other cancers, and 6 had ampullary cancer. The stents used were uncovered MS in 31 patients, partially covered MS in 66, and fully covered MS in 103. Stents used in patients with RBO were uncovered MS in 70 patients (44/51) for the liver side and 92% (12/13) for the ampullary side. The reasons for RBO were contamination in 5 patients, inappropriate biopsy site, and impossibility of advancement of the biopsy forceps beyond the obstruction in one patient. The mean time to RBO was 583 days (median, 324 days). Non-RBO rate at 3, 6, and 12 months after MS placement was 90%, 71%, and 44%, respectively. Univariate analysis including 17 factors revealed that sex (male, p = 0.088), bile duct cancer (p = 0.088), MS except WallFlex (Boston Scientific, Co., Ltd., USA) (p = 0.023), and cholangitis at the time of MS placement (p = 0.001) were risk factors for RBO. Multivariate analysis showed that cholangitis at the time of MS placement (HR 2.0, 95% CI 1.3–3.2, p = 0.003) and MS except WallFlex (HR 1.9, 95% CI 1.1–3.1, p = 0.017) as the significant risk factors for RBO.

Conclusion: Endoscopic MS placement for unresectable malignant distal biliary obstruction should be considered after improvement of cholangitis due to the high risk of RBO. WallFlex is recommended as a MS for unresectable malignant distal biliary obstruction.
P0710 PROPERATIVE BILIARY DRAINAGE USING PLASTIC STENTS VERSUS SELF-EXPANDABLE METAL STENTS FOR PERIAMPULLARY CANCER
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Introduction: Periampullary cancers frequently present as obstructive jaundice, with signs and symptoms of liver dysfunction, coagulation disorders, cholangitis, and immune system dysfunction. Preoperative drainage has become popular for patients with periampullary cancers suffering from acute cholangitis or intense pruritus, or receiving neoadjuvant chemotheraphy or delayed surgery. If the stent dysfunction occurs during the preoperative period or neoadjuvant chemotherapy, surgery must be postponed or chemotherapy must be interrupted, so it is increasingly important to place self-expandable metal stents (SEMSs) that have a longer stent patency than plastic stents (PSs).

Aims and Methods: The aim of this study was to investigate the superiority of fully covered SEMSs over PSs as preoperative drainage for patients with resectable periampullary cancers and obstructive jaundice. We retrospectively reviewed 26 consecutive patients from September 2015 to February 2018 with resectable periampullary cancers who received preoperative biliary drainage with PSs or SEMSs (13 patients each). We excluded cases that received SEMS placement for repeated occlusion of PSs. Stent patency rates, time from endoscopic retrograde cholangiopancreatography (ERCP) to surgery, adverse events of stent placement, operating time, amount of bleeding during surgery, rate of negative resection margins (R0), and adverse events of surgery were compared between the PS and SEMS groups.

Results: In the PS group, the preoperative stents patency rates were significantly lower than in the SEMS group (54% vs. 100%, p<0.005). There were no significant differences between the PS and SEMS groups for median time from ERCP to surgery (33 vs. 35 days, p=0.78), median operating time (528 vs. 542 minutes, p=0.77), median amount of bleeding during surgery (644 vs. 660 ml, p=0.69), rate of R0 (15% vs. 0%, p=0.54), adverse events of stent placement (elevated serum pancreatic enzyme levels alone: 8% vs. 0%, p=0.50), or adverse events of surgery (pancreatic fistula: 15% vs. 15%, p=1; surgical site infection: 23% vs. 15%); and gastric emptying: 44% vs. 15%, p=0.50).

Conclusion: Preoperative biliary drainage with SEMSs in patients with resectable periampullary cancers showed higher patency rate than that with PSs and a low complication rate similar to that with PSs.

Disclosure: Nothing to disclose.

P0711 ASSOCIATION BETWEEN APPENDICECTOMY AND RISK OF PRIMARY SCLEROSING CHOLANGITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS
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Introduction: Appendectomy is one of the most commonly performed surgeries worldwide. Recent epidemiologic studies have suggested that appendectomy could be a risk factor for primary sclerosing cholangitis (PSC) although the results were inconsistent.

Aims and Methods: This systematic review and meta-analysis was conducted to summarize all available evidence with the aim to better characterize the relationship between the two conditions. A comprehensive literature review was conducted using MEDLINE and EMBASE database through January 2018 to identify all studies that reported the risk of PSC among individuals who had appendectomy versus those with no history of appendectomy. Effect estimates from each study were extracted and combined together using the random-effect, generic inverse variance method of DerSimonian and Laird.

Results: A total of 6 case-control studies with 2,432 participants met the eligibility criteria and were included in the meta-analysis. The risk of PSC in individuals who had appendectomy was significantly higher than those with no history of appendectomy with the pooled odds ratio of 1.37 (95% CI, 1.15–1.63). The statistical heterogeneity was insignificant with an I² of 0%. Moreover, the funnel plot is relatively symmetric and does not suggest the presence of publication bias in favor of positive studies.

Conclusion: A significantly increased risk of PSC among individuals who had a history of appendectomy was found in this study.

Disclosure: Nothing to disclose.

References

P0712 SERVICE EVALUATION OF A DEDICATED PSC PROGRAMME: IDENTIFYING NEEDS AND BARRIERS TO TRANSITIONING TO A 21ST CENTURY APPROACH TO CARE
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Introduction: PSC is a rare auto-immune liver disease with significant impact on quality and quantity of life for patients. Modern health care delivery has the potential to change care for rare disease but before appropriate changes can be made to improve patient care, we must understand the healthcare burden and natural history of the disease.

Aims and Methods: We sought to evaluate our current service over a 10 year period, to identify patient and clinical themes of relevance to service redesign. We performed a retrospective service evaluation of all pre-transplant patients with PSC who were first seen at our centre between October 2005 and October 2015, to allow for a minimum of 5 years of follow up data. Data was gathered on patient demographics, geographical location, referral source, symptom burden and clinical events.

Results: 484 patients were identified and their electronic records reviewed; 64% were male with a mean age of 44 years (range 16–84 years). 85% were Caucasian and 72% had large duct involvement, with 65% having co-existing inflammatory bowel disease. Median ALP at first clinic appointment 461 (range 48–5051) with median UKELD of 48 (range 40–66). Median distance travelled via road from the patient’s home to our centre was 48 miles (range 2–380) with a median travel time by road of 80 minutes (range 9–500). In total we received referrals from 64 different centres; 88% of patients were from outside our local area; 20% were referred from another UK tertiary liver centre, 45% from secondary care services and 25% were referred for ongoing management, 20% for transplant assessment and 12% due to possible cholangiocarcinoma. The diagnosis of PSC was preceded by chronic symptoms in 23%, an acute hospital admission in 17% and incidentally on blood tests in 22%, often due to monitoring for pre-existing IBD. 85% of patients experienced PSC-related symptoms at some point in their follow up; 36% described significant pruritus, 32% fatigue, 28% recurrent cholangitis and 16% right upper quadrant pain. During this period, median number of clinic appointments was 8 (range 1–74) with 38% of patients requiring at least one hospital admission; 11% required EUS and 7% underwent ERCP at our centre during their follow up. Overall, 39% have been assessed for transplantation, 85% of which were activated on our transplant list. Of the entire cohort there was a 21% mortality rate, with 23% undergoing transplantation and 3% were diagnosed with cholangiocarcinoma.

Conclusion: Parallel to the essential development of new treatments for PSC, is a need for clinicians to recognise the total burden PSC places on patients and to use such insights when considering a patient-centred service redesign relevant to 21st century healthcare. Given the large distances many PSC patients travel for specialist care, novel alternatives to conventional management, such as the use of telemedicine, should be considered.

Disclosure: Nothing to disclose.

References
P0713 INVESTIGATING THE ACCEPTABILITY TO PATIENTS OF INTRODUCING A VIRTUAL CLINIC INTO TERTIARY HEPATOPATHY OUTPATIENT CARE: AN AUDIT OF PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

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Introduction: Telemedicine is the use of telecommunication systems to deliver healthcare at a distance. It is potentially one way of improving access to healthcare as well as efficiency. However, the 2016 Cochrane review concluded that questions remain about the acceptability of this to patients (1). Patients with rare diseases face geographical hurdles to accessing disease specific care that may be improved by the introduction of telemedicine. Primary sclerosing cholangitis (PSC) is a rare auto-immune liver condition and University Hospitals Birmingham (UHB) is preparing to introduce a virtual clinic via video link, commencing first in the PSC clinic.

Aims and Methods: We aimed to investigate the patient burden of attending specialist care and the acceptance of the virtual clinic, in this patient group. We distributed questionnaires to all patients attending the weekly PSC clinic over a 5 week period. The questionnaire included questions on demographics, employment, travel to appointments, diagnosis and opinions on the introduction of the virtual clinic. Analysis was completed including Fisher’s exact test where appropriate to provide a test statistic for statistical significance.

Results: A total of 101 questionnaires were completed; a 66% return rate. 74% stated they would accept a virtual appointment when commencing first in the PSC clinic. 47% had a diagnosis of a rare auto-immune liver disease, 83% of which was PSC. 47% of all respondents had previously received a liver transplant. 79% of respondents stated that UHB was their local hospital and 34% of patients travelled for over 2 hours for appointments. There was an overall mean travel cost of £28.72 per patient visit. Overall, 59% stated they would accept a virtual appointment however 22% would not and 13% were unsure. 84% stated they used a desktop computer, laptop or tablet at least weekly and this was associated with increased acceptance of the virtual clinic (p = 0.001). Travel time was not associated with acceptance. In the post-transplant group only, patients seen at 6 monthly intervals were more likely to accept a virtual appointment than those seen at 3 monthly intervals (p = 0.026).

Conclusion: This audit shows that despite time and financial burdens placed on many patients attending our specialist centre for their PSC care, patient acceptability of the virtual clinic is not universal. We are planning further research to more fully understand patient opinions about the use of virtual clinics, via a series of semi-structured interviews.

Disclosure: Nothing to disclose

Reference

TUESDAY, OCTOBER 23, 2018
Paediatric: Liver, Biliary and Pancreas – Hall X1

P0714 ASSESSMENT OF RISK FACTORS OF POST-PARACENTESIS CIRCULATORY DYSFUNCTION WITH MULTIPLE LARGE VOLUME PARACENTESIS IN CHILDREN WITH CHRONIC LIVER DISEASE: PROSPECTIVE LONGITUDINAL STUDY

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Introduction: Asciets is a common complication of cirrhosis and is associated with poor prognosis. Post-paracentesis circulatory dysfunction (PPCD) is overall seen in one-third of cirrhotic children who undergo single-time large volume paracentesis (SLVP). It is not known whether PPCD occurs with multiple LVP (MLVP).

Aims and Methods: Our study aimed to analyse the safety, complications and effect of albumin infusion during MLVP on PPCD in children with severe ascites due to liver disease. Complications of severe ascites underwent single time or multiple LVP with albumin infusion. Plasma renin activity (PRA) assessed at baseline and day 6 of last performed LVP. Maximal PRA value in MLVP was noted. Delta PRA was defined as PRA difference on day 6 and baseline. Worsening PPCD was defined as ≥1.5 times increase of delta PRA of any 2 sessions of LVP in MLVP group. “At-risk” group was defined as any cirrhotic child with ≥2 worsening PPCD episodes. Their outcome at 3 months and maximal follow-up were noted. Poor outcome was defined as failure of definitive therapy, need for liver transplantation or mortality.

Results: Table 1 shows baseline characteristics of 37 children (SLVP, n = 17; MLVP, n = 20). 92% had high PRA at the onset. The overall incidence of PPCD was 43% (SLVP: 12%, MLVP: 70%; p = 0.003). Baseline pediatric end-stage liver disease (PESLD) was associated with PPCD (sensitivity: 90%; specificity: 50%; p = 0.01) in MLVP group. Worsening PPCD (n = 28; 54%) and at-risk children (n = 9; 45%) were identified in 52 sessions of MLVP. In the MLVP group, PPCD occurred if cumulative ascitic fluid extraction volume was > 855 mL/kg/week (sensitivity: 90%; specificity: 50%; p = 0.01). Cumulative albumin infusion < 4.2 g/kg/week (sensitivity: 93%; specificity: 55%; p = 0.03) and frequency of sessions were > 2.3/week (sensitivity: 91%; specificity: 57%; p = 0.02). In those who developed PPCD, lowest volume of ascites extracted in SLVP and MLVP groups were 117 and 143 mL/kg/week respectively. MLVP patients (80%) were susceptible to asymptomatic, persistent hypo-natremia (baseline vs. day 6 from first LVP, 131 ± 4 vs. 124 ± 4 mEq/L; p = 0.001), hemodynamic changes (25%), renal impairment (35%), recurrence of ascites (60%) and hospital readmission (70%). At risk patients had worsening of PELD scores (baseline: 25 ± 8 vs. follow-up 31 ± 6; p = 0.01) at 3 months. Poor outcome at maximal follow-up (18.7±4.7 months) was seen in 35% (n = 1, SLVP; n = 12, MLVP) especially in the at-risk group (n = 8; 89%).

Conclusion: PPCD occurs in multiple LVP and baseline PPCD > 27, cumulative extracted ascites > 855 mL/kg/week, cumulative albumin infusion < 4.2 g/kg/week and frequency of sessions > 2.3/week. One third have poor outcome, more in the at-risk group. Risk factors of PPCD with multiple LVP are baseline PPCD > 27, cumulative extracted ascites > 855 mL/kg/week, cumulative albumin infusion < 4.2 g/kg/week and frequency of sessions > 2.3/week.

Disclosure: Nothing to disclose

Reference

P0715 HEMODYNAMIC CHANGES IN THE VESSELS OF THE ABDOMINAL CAVITY IN THE POSTPRANDIAL PHASE IN HEALTHY CHILDREN

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Introduction: The postprandial test provides valuable information about the state of the digestive system. It is most often used to determine the function of the pancreas. Changes in the parameters of regional circulation of the abdominal cavity during the postprandial phase are analyzed much less frequently. There are no standards of postprandial reaction of hemodynamic parameters in arteries and veins of the abdominal cavity in children. That fact complicates its evaluation in patients with gastroenterological pathology.

Aims and Methods: The aim of the work is to characterize the reaction of abdominal vessels to the food load in healthy children and to determine the reference values of postprandial changes in the regional blood flow.

44 healthy children aged 3 to 15 years were examined. Doppler study of hemodynamics in abdominal veins was performed twice: on an empty stomach and 30 minutes after a standard breakfast. The parameters of blood flow in veins (inferior vena cava, portal vena) and arteries (abdominal aorta, ventral trunk, superior mesenteric, common hepatic and splenic) were evaluated. Vessel
diameters, resistance index (IR) and volumetric blood flow velocity (BFV) were determined.

Results: It was found that changes in hemodynamic parameters after eating in healthy children of different ages and sex has no statistically significant differences. The diameters of the abdominal aorta and the inferior vena cava after eating remain in 73% and 74% of cases significantly higher (p < 0.05) and the effective cross-sectional area of the inferior vena cava changes significantly (p < 0.05). The maximum growth rates of BFV are observed in large vessels – abdominal aorta (5%) and in the inferior vena cava (13%).

Conclusion: In healthy children dilation of the ventral trunk, superior mesenteric, hepatic and splenic arteries, portal and splenic veins is registered in the postprandial phase. The transverse dimensions of the abdominal aorta and the inferior vena cava in most cases remain the same or change slightly. There is a significant increase in the volume rate of blood flow in all the vessels studied, which reflects the intensification of blood circulation in the abdominal cavity.

Disclosure: Nothing to disclose.

P0716 THE NATURE OF THE HEMODYNAMIC CHANGES OF THE ABDOMINAL CAVITY IN CYSTIC FIBROSIS IN CHILDREN
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Introduction: Disorders of the hepatobiliary system are diagnosed in 80% of children with cystic fibrosis (CF), in 5–10% of cases multilobular cirrhosis of the liver is formed accompanied by portal hypertension syndrome.

Aims and Methods: The aim of the work was to determine the nature of hemodynamic changes in abdominal vessels in children with cystic fibrosis and their relationship with the degree of structural disorders of the liver. The transverse dimensions of the abdominal aorta and the inferior vena cava in most cases remain the same or change slightly. There is a significant increase in the volume rate of blood flow in all the vessels studied, which reflects the intensification of blood circulation in the abdominal cavity.

Results: It was found out that in the absence, as well as in the moderate severity of changes in liver parenchyma in patients with CF, the average value of the diameters of the abdominal cavity vessels corresponds to the indicators of healthy children. In the group of patients with significant violations of the structure of the organ, dilation of celiac trunk (on average by 25.5% compared to the normal range), superior mesenteric (23.4%), common hepatic (28.8%) and splenic (74.1%) arteries was recorded. BFV in these patients increases significantly in the common hepatic artery (by 41.2%), portal (59.7%) and splenic (62.3%) veins. The IR rises in the ventral trunk by 0.75 ± 0.006 and 0.78 ± 0.02 against the 0.71 ± 0.007 and 0.75 ± 0.006 in healthy children (p < 0.05). The postprandial test revealed a significant decrease in the growth of the diameter of the abdominal cavity arteries and veins after eating, which had already been determined in the group of patients with normal liver structure. In the group of patients with significant organ impairment postprandial response of abdominal vessels was practically absent. It is known that under normal conditions, eating causes a significant (in some cases, multiple) increase in the volume rate of blood flow in the abdominal cavity arteries and veins. At CF there is a sharp decrease or absence of BFV growth in the postprandial phase. Dopper changes are observed in the group of children whose standard ultrasound examination results have not yet revealed structural disorders of the liver. This makes it possible to consider the change in Doppler indices (the degree of increase in vascular diameters and BFV in them) as the signs of early liver damage at CF.

Conclusion: Standard Doppler imaging of abdominal vessels in children with cystic fibrosis reveals changes in regional hemodynamics only in the presence of pronounced structural disorders of liver. This is manifested by dilation of abdominal vessels, increased arterial inflow and venous outflow in the vascular system of the liver, an increase in the resistance index in the ventral trunk and common hepatic artery. Postprandial test can detect a reduction of adaptive reserve of the abdominal cavity vascular system before structural changes in the liver are detected by ultrasound. This is manifested by the lack of adequate vasodilatation and increase in the volume of blood flow in arteries and veins after eating.

Disclosure: Nothing to disclose.

P0717 PEDIATRIC SUB-ACUTE HEPATIC FAILURE IN DEVELOPING COUNTRIES: RISK FACTORS THAT DETERMINE OUTCOME
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Introduction: Sub-acute hepatic failure (SAHF) is a grey zone area of liver dys- function which has a smouldering, variable course and is poorly understood. Though spontaneous recovery is known, case fatality is high. Pediatric experience of SAHF is poorly highlighted in literature.

Aims and Methods: We aimed to identify the high risk subet that determine poor outcome of SAHF in children. Children with SAHF (appearance of ascites and/or coagulopathy occurring from 4th-24th week of onset of acute hepatitis with coagulopathy in the absence of pre-existing liver disease) were analysed. Poor outcome (PO: death or liver transplantation within 90 days) were compared with spontaneous recovery (SR: complete normalisation of liver functions in native liver for risk factors). End-stage liver disease score and King’s College’s criteria (KCC) were applied as measures of outcome.

Results: SAHF (n = 60) constituted 15% of all liver failure (n = 351) referrals. Seven had cirrhosis on biopsy and were excluded. Etiological workup (n = 53) was hepatitis A (n = 19), co-infection hepatitis A and E (n = 7), hepatitis B (n = 6), hepatitis E (n = 1), cytomegalovirus (n = 1), autoimmune hepatitis type 2 (n = 1) and indeterminate etiology (n = 18). Table 1 compares SAHF (n = 14, 26%) with follow-up of 6 (1-24) months versus PO (n = 30, 57%).

Disclosure: Nothing to disclose.

Table 1: Baseline clinical and laboratory data of poor outcome versus spontaneous recovery groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Poor outcome (n = 30)</th>
<th>Spontaneous recovery (n = 14)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>5.5 (2-16)</td>
<td>6 (3-15)</td>
<td>0.79</td>
</tr>
<tr>
<td>Male</td>
<td>22 (73%)</td>
<td>8 (57%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Duration of illness (days)</td>
<td>52 (30-180)</td>
<td>50 (30-150)</td>
<td>0.33</td>
</tr>
<tr>
<td>Jaundice to ascites/</td>
<td>30 (22-150)</td>
<td>30 (22-120)</td>
<td>0.85</td>
</tr>
<tr>
<td>portal vein encephalopathy interval (days)</td>
<td>19 (63%)</td>
<td>13 (93%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Prorome</td>
<td>28 (93%)</td>
<td>13 (93%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Pulior</td>
<td>20 (67%)</td>
<td>5 (36%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Emeda</td>
<td>19 (63%)</td>
<td>7 (50%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>19.4 (4-41.6)</td>
<td>25 (2-39.6)</td>
<td>0.29</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>2.4 (1-6.3)</td>
<td>2.7 (2-13.9)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

P0718 CONGENITAL DILATATION OF THE BILIARY TRACT: RADIOLOGICAL ASPECTS AND THERAPEUTIC MANAGEMENT
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Introduction: Congenital dilation of the biliary tract (CDBT) is a rare and heterogeneous congenital malformation affecting the bile ducts in variable way. The aim of this study was to describe the various radiological aspects of this pathology and analyze its therapeutic management in our medical center.

Aims and Methods: From 2002 to 2017 all the patients with the diagnosis of congenital dilatation of the biliary tract were retrospectively enrolled. The diagnosis of CDBT was based on the imaging data (MRI and / or ERCP) and histology in operated patients. Biliary duct anomalies were classified according to Todani’s classification. Therapeutic modalities whether surgical or endoscopic were identified for each patient.

Results: 32 patients were enrolled. The mean age was 46 years and the sex ratio was 1.1 [M / F = 17/15]. According to the Todani’s classification, patients were
classified as type I = 13 cases (40%), III = 4 cases (12.5%), IV = 4 cases (12.5%), V = 1 case (3.4%). Therapeutic management was based on this radiological classification. Indeed, in the case of malformations type I, IVb: 6 patients were operated (resection of the choledochal cyst with hepaticojejunal anastomosis). One of them was secondary operated after a non-controlled cholangitis (after ERCP). In 7 other cases endoscopic sphincterotomy in ERCP was indicated according to the bad state of the patient’s field or the good spontaneous evolution of symptoms and biology. Regarding the 4 cases of choledochocoele, endoscopic treatment (based on the ERCP with pre-cutting on the top of the choledochocoele) was recommended, only one patient was complicated of duodenal perforation leading to a surgical treatment. For the 11 cases of Caroli: 3 had congenital liver fibrosis indicating liver transplantation. This one was however not carried out for lack of availability. For the 8 other cases it was a left caroli diverticulum in 5 patients without anatomy in 4 cases and biliodigestive anastomosis in 1 case. The remaining 3 patients were treated with ursodeoxycholic acid with endoscopic treatment in case of complications (acute cholangitis, lithiasis). No cases of degeneration were observed in our series.

Conclusion: Our study underlines the complexity of the therapeutic management of the congenital biliary tract dilatation. Surgery, whenever possible can prevent the risk of degeneration. However, endoscopic treatment has a fundamental place in case of impossibility of operating the patients or the occurrence of complications.

Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00

Pancreas II – Hall X1

P0719 ANTIBIOTICS IN ACUTE PANCREATITIS IN THE LAST
YEARS – EXPERIENCE OF A TERTIARY REFERRAL CENTER
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Introduction: Antibiotic therapy in acute pancreatitis (AP) does not influence clinical course and mortality and it is not endorsed by current international guidelines [1]. Concerns regarding the increase in multidrug resistant bacteria has led to the implementation of measures to mitigate inappropriate antibiotic use in our center.

Aims and Methods: We aimed at comparing the patterns of antibiotic use and associated clinical outcomes over two different timelines. We included 200 patients with AP: 100 admitted between 2012 and 2017 (retrospective cohort, group A) and 100 patients admitted after 2017 (prospective cohort, group B). We defined inappropriate antibiotic therapy if: (1) no bacterial agent was isolated in microbiological tests, (2) infected necrosis was not present, and (3) antibiotics were not due to documented extra-pancreatic infection. Statistical analysis was performed with SPSS®. A p value <0.05 was considered significant.

Results: No differences were found between demographics, etiology and severity of AP in both groups (table). In group A there was a significant higher use of anti-biotics (52% vs 24%; p=0.009), therapeutic management was based on this radiological classification. Indeed, in the case of malformations type I, IVb: 6 patients were operated (resection of the choledochal cyst with hepaticojejunal anastomosis). One of them was secondary operated after a non-controlled cholangitis (after ERCP). In 7 other cases endoscopic sphincterotomy in ERCP was indicated according to the bad state of the patient’s field or the good spontaneous evolution of symptoms and biology. Regarding the 4 cases of choledochocoele, endoscopic treatment (based on the ERCP with pre-cutting on the top of the choledochocoele) was recommended, only one patient was complicated of duodenal perforation leading to a surgical treatment. For the 11 cases of Caroli: 3 had congenital liver fibrosis indicating liver transplantation. This one was however not carried out for lack of availability. For the 8 other cases it was a left caroli diverticulum in 5 patients without anatomy in 4 cases and biliodigestive anastomosis in 1 case. The remaining 3 patients were treated with ursodeoxycholic acid with endoscopic treatment in case of complications (acute cholangitis, lithiasis). No cases of degeneration were observed in our series.

Conclusion: Our study underlines the complexity of the therapeutic management of the congenital biliary tract dilatation. Surgery, whenever possible can prevent the risk of degeneration. However, endoscopic treatment has a fundamental place in case of impossibility of operating the patients or the occurrence of complications.

Disclosure: Nothing to disclose

P0720 PREDICTIVE NATURE AND CLINICAL CHARACTERISTICS
OF PAIN ON ADMISSION IN ACUTE PANCREATITIS
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Introduction: Pain is a very common symptom in acute pancreatitis (AP), therefore, understanding its characteristics and predictive role is important. Until now, the detailed characteristics have not been investigated. Here, we aimed to analyze the predictive role and clinical characteristics of pain on admission in AP.

Aims and Methods: The Hungarian Pancreatic Study Group (HPISG) has prospectively collected multicenter clinical data of 1435 adult patients between 2012 and 2017. The specific pain questionnaire contained data in four categories: intensity (visual analog scale, 1–10, mild (modP):1–3, moderate (modP): 4–6, severe (sevP):7–10), duration of pain prior to admission (hours), localization (upper, middle, and lower abdomen), and type (sharp, dull, or cramping). These data were compared with parameters on admission and with the outcome of AP. Statistical analyses were performed accordingly.

Results: Most of the patients had abdominal pain (modP: 5.23%, modP: 24.48%, sevP: 70.29%). The intensity of pain was directly associated with the severity of AP (modP: 0% severe AP, modP: 2.81%, sevP: 4.50%; p<0.05), mortality (modP:5% moderate: 1.98% severe: 1.76%; modP vs sevP: p<0.05), local (modP:28.09% sevP:25.25% modP vs modP and sevP: p<0.05) and systemic complications (modP:9.55% sevP:7.83%; modP vs modP and sevP: p<0.05), higher white blood cell count, elevated lipase and amylase levels, but not with CRP level. The duration of pain was not associated with mortality and severity; however, it markedly influenced the laboratory parameters on admission. The level of amylase and lipase, the amount of RBC and hemoglobin, and pain intensity were decreasing, whereas the level of CRP and the amount of thrombocyte were increasing. Concerning the localization of the pain, 46% of the patients had upper abdominal pain.25% had epigastric pain. However, localization was not associated with the above-mentioned parameters. Sharp pain was associated with higher mortality, severity, and systemic complications.

Conclusion: Higher intensity of pain is associated with worse clinical outcome; therefore, its role should be investigated in clinical trials. The duration of pain prior to admission strongly influence the laboratory parameters on admission, therefore, it should be incorporated into the on admission scoring systems in AP. Disclosure: Nothing to disclose

P0721 PRE-EXISTING DIABETES ELEVATES RISK OF RENAL
FAILURE AND LOCAL COMPLICATIONS IN ACUTE
PANCREATITIS
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Introduction: Acute pancreatitis (AP) is an inflammatory condition which commonly requires hospitalization and shows increased incidence. The prevalence of diabetes mellitus (DM) has duplicated in the last 35 years. Acute pancreatitis may therefore, its role should be investigated in clinical trials. The duration of pain

Reference
incidence of organ failures and intensive care unit admission. The meta-analysis was performed using the PRISMA Protocol. PubMed, EMBASE and Cochrane databases were searched, articles with AP patients including DM and non-DM groups were included, and complications, length of hospitalization (LOH), intensive care unit (ICU) admission and mortality were analyzed. The odds ratio (OR) and standardized mean difference (SMD) with 95% confidence intervals (CI) were calculated with Comprehensive Meta-Analysis software.

Results: 1417 articles were found, of which 9 articles involving 354,880 patients were analyzed. More systematic complications were seen in diabetic patients, than in non-diabetic patients (OR = 1.553 [CI:1.266–1.904], p < 0.011). ICU admission (OR = 1.799 [CI:1.442–2.243], p < 0.001) and renal failure (OR = 1.585 [CI:1.278–1.966], p < 0.001) were more frequent in DM patients than in non-DM patients. There was a trend of higher mortality and local complications (60% vs 50% [CI:0.991–1.645], p = 0.059; and OR = 1.267 [CI:0.964–1.650], p = 0.090, respectively) in the pre-existing DM group. LOH was longer in DM patients than in non-DM patients (SMD = 0.217 [CI:0.075–0.360], p = 0.003).

Conclusion: Pre-existing DM negatively influences the outcome of AP and increases the risk of renal failure, ICU admission, local complications and mortality. More attention is necessary for AP patients with pre-existing DM.

Disclosure: Nothing to disclose
Several studies have confirmed that obesity (BMI ≥ 30) is strongly associated with the development of the metabolic syndrome (MS), and the rate of severe AP elevates with the number of affected components of MS. Obesity, hypertension, hyperlipidemia, and diabetes are the four components of the WHO classification of BMI and the presence of the components of MS, which are independent risk factors for severity and mortality in acute pancreatitis (AP), however, information is available about whether its effect is independent or joint with the components of metabolic syndrome (MS).

**Aims and Methods:** Our aim is to investigate whether chronic statin and/or ASA use of peri-procedural NSAIDs; the incidence of Post-ERCP Acute Pancreatitis (PEP) in patients consuming aminosalicylic acid (ASA), a NSAID, is unclear. Some prophylactic strategies spread application of the technology to some extent. Post-ERCP pancreatitis (PEP) is the most common complication of ERCP. To date, although several clinical studies have suggested prophylactic use of nonsteroidal anti-inflammatory drugs (NSAIDs) is effective on PEP prevention, the effects of NSAIDs on PEP prophylaxis are still in debate. Meanwhile, the underlying mechanism by which NSAIDs prevent PEP remains poorly understood. As cyclooxygenase-2 (COX-2) is implicated in inflammatory response, thus we speculate that NSAIDs exert its protective effect mainly through inhibiting COX-2 expression.

**Aims and Methods:** In the present study, we aimed to determine the prophylactic effects of two different types of NSAIDs, indomethacin (COX-1 and COX-2 inhibitor) and parecoxib (selective COX-2 inhibitor) on PEP occurrence in rat model and investigate the underlying mechanisms. Thirty-two Wistar rats were equally and randomly assigned to 4 groups: PEP model group, indomethacin group, parecoxib group and pseudo-operation group. PEP rat models were established via retrograde injecting 0.4ml 30% olive oil into bile ducts at 50mmHg pressure. NSAIDs prophylaxis rats received rectal administration of indomethacin suppository at 10mg/kg or intramuscular parecoxib injection at 4mg/kg 45 minutes prior to surgical operation. The serum amylose, IL-6, IL-10 and TNF-α were tested, and the pancreatic histological alteration were assessed. For mechanism study, the expression of COX-1, COX-2 and apoptosis-relative protein BAX was further determined.

**Results:** The amylose level in PEP rat dramatically increased compared with pseudo-operation rats (p < 0.05). Indomethacin and parecoxib treatment decreased 14% and 13% amylose levels compared with PEP rats, respectively, but without significant difference. Histological assessment showed that compared with pseudo-operation rats, the pancreatic edema, hemorrhage, acinar necrosis and inflammatory cell infiltration scores in PEP rats obviously increased, respectively. However, indomethacin and parecoxib prophylaxis effectively declined the histological scores above mentioned (p < 0.05). Likewise, the serum amylose and IL-10 and TNF-α levels in PEP rats dramatically increased compared to pseudo-operation rats, respectively (p < 0.05), and indomethacin and parecoxib remarkably declined the serum inflammatory cytokines levels (p < 0.05). Western blot analyses revealed that compared with PEP rats, indomethacin markedly inhibited the pro-inflammatory COX-1 (0.99 ± 0.11 vs. 1.30 ±1.03), COX-2 (1.04 ±0.13 vs. 1.50 ±0.12, p < 0.05) proteins expression while parecoxib selectively inhibited COX-2 expression (0.90 ±0.08 vs. 1.50 ±0.12, p < 0.05). Furthermore, indomethacin and parecoxib treatment decreased the expression level of BAX proteins (1.17 ±0.13 vs. 1.62 ±0.12, p < 0.05; 1.03 ±0.09 vs. 1.62 ±0.12, p < 0.05).

**Conclusion:** Prophylactic use of indomethacin and parecoxib could histologically mitigate pancreas injury and suppress inflammatory cytokines levels in PEP rats. NSAIDs could effectively protect pancreatic acinar cells from apoptosis via inhibiting COX-2 expression.

**Disclosure:** Nothing to disclose

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The obesity prevalence in our AP cohort is 29.5%, therefore it is representative of the Hungarian population (prevalence of obesity: 30.0%). High BMI is associated with higher rates of mortality and morbidity of AP, respiratory and renal failure and more severe comorbidities. The prevalence of diabetes, hypertension and hyperlipidemia are growing with higher BMI. The rate of severe AP elevates with the number of affected components of MS (26.6%, 4.7%, 6.1%, 8.5% and 6.0% with 0, 1, 2, 3 and 4 components respectively), however, the increase was significant only in case of three components of MS compared to cases without any MS components (OR = 3.439 95% CI: 1.145–10.326). In a logistic regression model, out of the four components only hypertension is a predictive factor for severity (OR = 3.805 95% CI: 1.704–9.002) and mortality (OR = 5.900 95% CI: 1.330–26.165). Concerning complications, hyperlipidemia elevates the risk of diabetes as a complication (OR = 2.373 95% CI: 1.945–7.117) and obesity increases the risk of renal failure (OR = 2.908 95% CI: 1.343–6.559). Hypertension is a strong predictive factor for respiratory failure (OR = 2.667 95% CI: 1.139–6.243) and renal failure (OR = 7.565 95% CI: 1.769–32.516).

**Conclusion:** Metabolic syndrome, in particular hypertension factor, strongly deteriorates the outcome of AP. Obesity, hyperlipidemia and diabetes are not independent risk factors for severity and mortality in AP, however strongly elevate each other’s detrimental effects.

**Disclosure:** Nothing to disclose
P0728 META-ANALYSIS AND TRIAL SEQUENTIAL ANALYSIS OF PROPHYLACTIC ANTIBIOTICS FOR ACUTE PANCREATITIS

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Introduction: Prophylactic antibiotics (AB) are not recommended for treatment of acute pancreatitis (AP). Their use is still widespread despite several trials showing no firm evidence of efficacy.

Aims and Methods: To evaluate the effects of prophylactic antibiotics (PAB) for AP in a meta-analysis and investigate the need for further research by trial sequential analysis (TSA).

Results: A total of 18 trials with 1134 pts were included in the analysis. PAB were recommended by 10 trials and -2 within the pancreas. Acute pancreatitis (AP) occurs when the inhibitory capacity of TATI is exceeded. Inflammation leads to leakage of pancreatic -trypsinogen 1 (cathelic T-1, T-2, and -2, and complex between trypsin-2 and -antitrypsin (trypsin-2-AAT) have been studied as markers for AP but their prognostic value in detecting developing OD has not been cleared.

Conclusions: Our aim was to explore if on-admission serum levels of TATI, trypsinogens 1, -2, and -3, and trypsin-2-AAT can be used to evaluate the severity of AP and predict development of OD in AP patients, with and without OD.

Disclosure: Nothing to disclose

P0730 INFLAMMATION PLAYS A KEY ROLE IN PANCREATIC CARCINOGENESIS INDUCED BY ELECTROPORATION

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Introduction: Pancreatic cancer (PC) is one of the deadliest cancers. Because of the high lethality, PC becomes a hot spot of research. Over the last decade, many experimental models for PC have been developed. It is worth noting that the LI and EP models have induced PC. However, the LI model can not format PC by altering the existence of pancreatitis. The characteristic of acinar-to-ductal metaplasia in PC has not been cleared.

Aims and Methods: To investigate the difference in cancer formation mechanism of the new two humanized genetically-modified adult mouse model of PC. A reporter plasmid driven by green fluorescent protein (GFP) expression was constructed. After laparotomy, it is possible to make the pancreas accessible for intra-parenchymal injection of experimental vectors. The study of transgenic mouse models might make up for shortcoming in other animal models, such as lentivirus-infected (LI) model and another model which induced by electroporation (EP). By using genetic alterations of Kras and P53, the EP model has induced PC. However, the LI model can not format PC by altering the cancer genes above Kras, P53, until Cre/loxP and Cre/loxP are added. They indicate that the mechanisms of tumour formation between the two adult PC models are not similar. Moreover, inflammation, a tumour risk factor, can contribute to carcinogenesis when combined with characterized mutational events.

Disclosure: Nothing to disclose

P0729 SERUM TATI, TRYPsinOGENS 1-3, AND COMPLEX OF TRYPsinIN 2 AND α2-ANTITRYPsin IN THE DIAGNOSIS OF ACUTE PANCREATITIS

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Introduction: Human pancreatic juice contains three trypsinogen isozymes: Trypsinogen-1 (cathelic T-1), trypsinogen-2 (anionic T-2), and trypsinogen-3 (mesotryptogen, T-3). Tumor-associated trypsinogen inhibitor (TATI), also called pancreatic secretory trypsin inhibitor (PSTI) inhibits activated T-1 and -2 within the pancreas. Acute pancreatitis (AP) occurs when the inhibitory capacity of TATI is exceeded. Inflammation leads to leakage of pancreatic enzymes into the circulation. This can lead to 100-fold increases in the serum concentrations of TATI and trypsinogens in plasma and urine a few hours after onset of the disease. Concentrations of T-2 may stay elevated for weeks. α-macroglobulin and α-antitrypsin form complexes with and inactivate trypsin.

When their inhibitory capacity exceeds, other proteolytic enzymes activate TATI, lead to complications and organ dysfunction. The characteristic of OD has not been cleared.

The existence of pancreatitis. The characteristic of acinar-to-ductal metaplasia in PC has not been cleared.

Aims and Methods: To investigate the difference in cancer formation mechanism of the two new humanized genetically-modified adult mouse model of PC. A reporter plasmid driven by green fluorescent protein (GFP) expression was constructed. After laparotomy, it is possible to make the pancreas accessible for intra-parenchymal injection of experimental vectors. The study of transgenic mouse models might make up for shortcoming in other animal models, such as lentivirus-infected (LI) model and another model which induced by electroporation (EP). By using genetic alterations of Kras and P53, the EP model has induced PC. However, the LI model can not format PC by altering the cancer genes above Kras, P53, until Cre/loxP and Cre/loxP are added. They indicate that the mechanisms of tumour formation between the two adult PC models are not similar. Moreover, inflammation, a tumour risk factor, can contribute to carcinogenesis when combined with characterized mutational events.

Disclosure: Nothing to disclose

Results: A total of 18 trials with 1134 pts were included in the analysis. PAB were received by 576 pts, while 558 were assessed as controls. Most of trials were assessed as being of high risk of bias. Overall mortality rate was similar in both groups with RR 0.85 (95% CI 0.64-1.14; p = 0.27; I2 = 0%), while the risk for infectious complications was significantly reduced in pts receiving PAB (RR 0.34, 95% CI 0.22-0.51; p < 0.0001; I2 = 59%). This reduction was mainly due to the decreased risk of sepsis (RR 0.36, 95% CI 0.19-0.68; p = 0.02; I2 = 11%), while a trend in risk reduction of IPN was shown with RR 0.78 (95% CI 0.60-1.00; p = 0.08; I2 = 82%). There was no significant difference in risk of other infectious, fungal infectious, organ failure, and surgical interventions. Length of hospital stay was diminished in the intervention group by MD 10.75 days. For the detection of RRR of 30% in a 10% mortality rate among controls the required sample size is 2714 pts, while only 959 are included so far. A 30% RRR of infectious complications has been achieved at 428 included pts, while a 10% mortality rate among controls requires 1725 pts, while only 959 are included so far. A 30% RRR of infectious complications has been achieved at 428 included pts, while a 10% mortality rate among controls requires 1725 pts, while only 959 are included so far. A 30% RRR of infectious complications has been achieved at 428 included pts, while a 10% mortality rate among controls requires 1725 pts, while only 959 are included so far. A 30% RRR of infectious complications has been achieved at 428 included pts, while a 10% mortality rate among controls requires 1725 pts, while only 959 are included so far. A 30% RRR of infectious complications has been achieved at 428 included pts, while a 10% mortality rate among controls requires 1725 pts, while only 959 are included so far. A 30% RRR of infectious complications has been achieved at 428 included pts, while a 10% mortality rate among controls requires 1725 pts, while only 959 are included so far.
Conclusion: These observations suggest the difference of process for cancer induc- tion but not between the two adult animal PC models. Apart from this mutation with Kras and P33, the EP model requires inflammation cooperated with genomic aberrations to build tumour. However, only if altering several cancer genes, PC in L1 model can be induced. This finding provides considerable insight for different research purposes, the proper use of animal model is an important step for gaining significant scientific observation. Additionally, inflammation inhibi- tion might be a potential target in treating parts of PC whose formation required inflammation.

Disclosure: Nothing to disclose

P0731 INCREASED CATHEPSIN D EXPRESSION HAS A NEGATIVE PROGNOSTIC EFFECT ON SURVIVAL IN GEMCITABINE TREATED PATIENTS WITH Pancreatic Ductal ADENOCARCINOMA

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Introduction: The lysosomal asparagine protease Cathepsin D (CatD) is overex- pressed and hypersecreted in many cancers and hereby influences cell death. Previous studies, in the ESPAC-3 cohort we determined a significantly increased median overall survival in cathepsin D low expressing PDAC patients. Gemcitabine treatment was significantly less effective in patients with high CatD expression compared to 5FU treated patients. Here, we present a prospective validation study.

Aims and Methods: Sample size calculation based on the catD H-score [3.58] from our previous study warranted 76 gemcitabine treated patients asking for a power of 0.8 and p < 0.05. Tumor tissue microarrays of 79 patients from the “informative patients” with PDAC receiving adjuvant gemcitabine treatment recruited at a single center with anti-CatD (C-20) antibody. Patients were dichotomously distributed in lower and higher H-scores (H-score cut-off: 22.35) for further analysis.

Conclusion: Subject to prospective validation within a randomized trial, gemic- tabine is less effective for patients with high CatD expression and could serve as a stratification marker for biomarker driven pancreatic cancer therapy.

Disclosure: Nothing to disclose

P0732 THE IMPORTANCE OF BIOMARKERS IN EARLY DIAGNOSIS OF Pancreatic Cancer: GLYPICAN

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Introduction: Recently ion mobility spectrometry-based electronic nose has been shown to detect pancreatic cancer from urine (1). Until now it is not known which volatile compounds in urine are specific for pancreatic cancer. Polyamines are volatile organic compounds with strong odour and play an impor- tant role in cell proliferation, signaling, gene expression, apoptosis and organ development. Urine polyamine concentrations increase in malignant and proliferating cells (2).

Aims and Methods: To determine if pancreatic cancer can be detected from urine sample by quantitative analysis of urinary polyamines with low tandem mass spectrometry (LC-MS/MS).

For a proof-of-concept study in two Finnish hospitals, patients with pancreatic cancer, pancreatic pre-malign lesions, acute pancreatitis and chronic pancreatitis were prospectively recruited during January 2014 and June 2016. Patients provided urine sample at the time of the diagnosis. Controls were patients undergoing hernia repair or elective cholecystectomy and were recruited during the same period. Midstream urine was collected before the operation and stored in −70°C until analysis the urinary concentration of 14 polyamines including their mono- and diacylated forms in a single run with LC-MS/MS (3). To our knowledge, this is the widest panel of polyamines analysed in a single run. Results were calculated as absolute concentration and urinary creatinine normalized concentration. To find optimal polyamine profiles for detection of cancer, the data was analyzed with linear discriminant analysis and cross-validated with leave-one-out cross-validation.

Results: 82 patients with pancreatic cancer, 36 with acute pancreatitis, 17 with chronic pancreatitis and 8 with pre-malign pancreatic lesion and 44 controls were recruited. 72% had stage III-IV pancreatic cancer and 27% went to radical pancreaticectomy. A profile of five specific polyamines in urine putrescine,
acetylputrescine, spermidine, diacetylpiperdine, cadaverine, and spermine distinctly
highlighted the cancer from controls with a sensitivity of 79% and specificity of 79% and area under curve (AUC) was 0.86. We also compared pancreatic cancer and pancreatic pre-malign lesions with controls when LC-MS/MS revealed a sensitivity of 80% and specificity of 83% and AUC was 0.88.

Conclusion: We specified urine volatile organic compounds in urine of cancer patients. Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive types of pancreatic cancer and is a significant public health burden. The present study was designed to evaluate the potential of urinary volatile organic compounds as a diagnostic marker for PDAC.

Disclosure: Nothing to disclose
A retrospective comparative study including non-metastatic PDAC patients who underwent surgery at Nagasaki University Hospital between January 2014 and December 2017. Data obtained by different preoperative imaging modalities including contrast enhanced computed tomography (CECT), magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) were compared with the final pathological diagnosis. The clinical parameters for comparison were: tumor size, common bile duct (CBD) gall bladder (GB) invasion, duodenal wall (DU) invasion, regional lymph node (LN) spread, adjacent organs infiltration including stomach, colon, spleen, left adrenal, retroperitoneal fat and coeliac plexus, portal vein (PV) invasion/encasement, arterial (ART) invasion/encasement including coeliac artery (CA), hepatic artery (HA) and superior mesenteric artery (SMA), and the overall tumor resectability. Sensitivity, specificity, PPV, NPV and diagnostic accuracy (DA) with the corresponding 95% confidence interval (95% CI) were calculated for each imaging modality. Tumor invading the PV, CA, HA and SMA was defined as unresectable. When the lesion was assessed as resectable by the imaging modality, the test was defined as positive.

**Results**: A total of 64 PDAC patients, 28 females, with mean age 70 years (range: 37-87 years) and mean body mass index (BMI) of 24.4 (range: 16.4-35.7) were enrolled in the study. The sensitivity, specificity, PPV, NPV, and accuracy of CECT, MRI and EUS respectively, for CECT, MRI and EUS were 34% (CI: 18-54) for MR, 29% (CI: 17-44) for CECT and 15% (CI: 3-38) for EUS. For evaluation of regional LN affection, CECT had the highest specificity (90%, CI: 68-99) and PPV (82%, CI: 52-95) while MR had the highest sensitivity (31%, CI: 11-59) and NPV (50%, CI: 30-69), while that for DU infiltration was 89% (CI: 67-97), 88% (CI: 76-95) and 73% (CI: 67-89) respectively. For the overall resectability assessment, EUS had the highest DA of 85% (CI: 62–97), the lowest overstaging rates.

**Conclusion**: For non-metastatic PDAC, CECT is the most useful preoperative imaging modality for assessing DU infiltration and ruling out regional LN affection and accuracy of EUS-FNA increased by 21.9% (p<0.001), respectively. For CBD/GB infiltration, EUS was the best modality for ruling out invasion and ART invasion. For PV invasion, DA of EUS, CECT and MR was 89% (CI: 65-99), 80% (CI: 67-90) and 76% (CI: 67-85) respectively. While that for PV infiltration was 89% (CI: 67-97), 88% (CI: 76-95) and 73% (CI: 67-89) respectively. For the overall resectability assessment, EUS had the highest DA of 85% (CI: 62–97), the lowest overstaging rate (0%) and the lowest understaging rate (15%) versus 76% (CI: 62-87), 5.8% and 17.6% for CECT, and 72% (CI: 53-87), 6.8% and 20.6% for MR respectively. Our study was a retrospective one on a small number of patients and it did not include a cost minimization analysis.

**Disclosure**: Nothing to disclose.

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**Reference**


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**P0739**

**K-RAS MUTATION ANALYSIS BY DIGITAL PCR IN EUS-GUIDED FNA CYTOLOGY SPECIMENS AND CTDNA IMPROVE PANCREATIC CANCER DIAGNOSIS**

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**Introduction**: Pancreatic cancer is a dismal disease and the fourth leading cause of cancer-related death in western countries. Novel methods for early diagnosis is the necessary path forward to improve the situation for patients with pancreatic cancer. Our primary aim in this study was to explore the potential value of detecting the K-ras gene mutation to supplement histo/cytopathologic evaluation of pancreatic masses. Our secondary aims of the current study were to compare the quantities of K-ras mutation of ctDNA in the circulation with FNA tissue samples in pancreatic mass of the same patients and investigate the prognostic value of K-ras gene mutation in advanced pancreatic adenocarcinoma.

**Aims and Methods**: Our study comprised 149 consecutive patients who underwent EUS-FNA of pancreatic solid masses between September 2014 and May 2016 at the Endoscopy Center of Tongji Hospital. After lesions were identified by EUS, aspirated samples were separated into 2 parts each for cyto/histopathological evaluation and K-ras point mutation analysis. ctDNA in serum was extracted from cell-free ctDNA in serum blood samples from these patients. We used droplet digital PCR (ddPCR) to analyse K-ras mutations (G12V, G12D, and G12R). The final diagnosis was based on pathological examinations of specimens obtained by surgical resection or following up for at least 2 years.

**Results**: We prospectively evaluated 149 PDAC patients, including 110 pancreatic ductal adenocarcinoma (PDAC) patients [age 58.38 ±11.01 years; male 69/105 (65.71%) and 44 cases with non-malignant pancreatic masses [age 52.66 ±13.81 years; male 36/44 (81.82%)]. The sensitivity, specificity, PPV, NPV, and accuracy of the cyto/histopathological examination alone were 71.4%, 86.4%, 92.6%, 55.9% and 78.5%, respectively, whereas these values of the K-ras mutation ddPCR analysis combined with Cyto/histopathological analysis were 93.3%, 79.1%, 91.6%, 82.9% and 88.6%, respectively. The sensitivity and accuracy of EUS-FNA tissue samples and ctDNA were evaluated by 21.9% and 52.66 years, respectively. When K-ras mutation ddPCR analysis was added to standard cyto/histopathological assessment. Aiming for further investigation in a non-invasive method in highly sensitive detection of KRAS mutations, we evaluated K-ras mutation ddPCR analysis of ddPCR in all matched plasma samples. We identified KRAS mutations in 56.2% of the ctDNA in plasma samples from patients with pancreatic cancer. 26.3% of the plasma ctDNA were positive for G12D, 8% for G12V, and 3.3% for G12R. The sensitivity and specificity of combined K-ras mutation and ctDNA mutations in plasma samples were 78.9% and 76.2%, respectively. The median survival time was significantly shorter in patients with G12D mutations (180 days) compared with patients with other mutations (240 days) in their EUS-FNA tissue samples and ctDNA samples (log-rank test, p=0.0001, respectively). Multivariate analysis demonstrated that both G12D mutation in EUS-FNA tissue samples (HR, 0.495, 95% CI 0.325-0.753, p=0.001) and ctDNA (HR, 0.417, 95% CI 0.199-0.870, p=0.0199) were independently associated with poor overall survival.

**Conclusion**: We observed that combining K-ras mutation qPCR analysis and histo/cytological findings increases the accuracy in diagnosing pancreatic cancer. K-ras mutation ddPCR analysis of ddPCR complements the diagnostic techniques in the diagnosis of pancreatic cancer in clinical practice. G12D mutation in EUS-FNA tissue samples and ctDNA were independent risk factors for poor prognosis of pancreatic cancer.

**Disclosure**: Nothing to disclose.

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**P0740**

**COST-EFFECTIVENESS OF PANCREATIC CANCER SURVEILLANCE IN HIGH-RISK INDIVIDUALS: AN ECONOMIC ANALYSIS**

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**Introduction**: Surveillance of high-risk individuals (HRI) with magnetic resonance imaging (MRI) or endoscopic ultrasound (EUS) can detect resectable pancreatic cancer (PC) and may reduce cancer-related mortality. There is controversy whether systematic screening and surveillance is cost-effective or not. We aim to perform an economic analysis to identify the different clinical and cost determinants of PC screening in HRI. Three strategies
P0740 IMPACT OF INCONCLUSIVE OR NEGATIVE ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION RESULTS IN THE MANAGEMENT OF SUSPICIOUS SOLID PANCREATIC MASSES

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Abstract No: P0740

Baseline: Higher risk of PC Relative risk: 5:1-120 Cost (U.S. dollars) $54,741 $47,750 $27,617

Relative risk: 1:20 Highest risk of PC Relative risk: ≥ 20 Cost (U.S. dollars) $110,441 $64,875 $66,639

Effective QALYs gained ICER ($/QALY) 19.477 21.225 21.532

Further details available in the full manuscript.

POTENTIAL DIFFERENCES IN SURVIVAL OF RESECTABLE PANCREATIC CANCER BETWEEN MODERATE DEVIATION AND WHIPPLE'S PROCEDURE

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Abstract No: P0742

Introduction: Endoscopic ultrasound (EUS) plays a key role in the evaluation of solid pancreatic masses, obtaining tissue for diagnosis through EUS-fine needle aspiration (EUS-FNA). However, the diagnostic accuracy is variable, with relatively high rate of inconclusive results after the first EUS-FNA. There are currently no consensus regarding the best diagnostic method after negative or inconclusive EUS-FNA of a highly suspicious solid pancreatic mass.

Aims and Methods: The aim of this study was to evaluate the diagnostic methods and predictive factors of malignancy after a negative or inconclusive EUS-FNA of a highly suspicious solid pancreatic mass.

Retrospective study of all cases of EUS-FNA of highly suspicious solid pancreatic masses in a tertiary center (from Jan 2012 to Dec 2016), with inconclusive or negative result for malignancy.

Results: We included 118 EUS-FNA in a total of 277 EUS-FNA, of 85 patients, 65.9% male, with mean age of 60.3 ± 14.27 years. The majority of the pancreatic masses were located in the head (56.8%) and 54.2% had an estimated size between 2 and 4 cm. The mean number of passes was 3.0 (+/-1.4) and the most common needle size was 25G (55.9%). Ninety-four (79.7%) of the 118 EUS-FNA were inconclusive and the other 24 EUS-FNA were negative for malignancy. After this result, 41.5% repeated EUS-FNA, 17.8% underwent surgical exploration, 16.1% kept in close follow-up and 13.6% were referred to palliative care.

More than 3 passes in EUS-FNA was statistically associated with malignancy (p = 0.022), as well as higher values of CA 19.9 (p = 0.025). The size of the lesion was statistically associated with obtaining tissue for diagnosis (p = 0.016). After a first negative/inconclusive EUS-FNA, 72% of the cases were diagnosed as malignant (75.4% as pancreatic adenocarcinoma), being EUS-FNA and surgery the main methods for the diagnosis. Seven patients (33%) that were submitted to surgery due to high suspicion of malignancy, revealed benign lesions.

Conclusion: EUS-FNA is the best method for the evaluation of pancreatic solid masses. However, in some cases, EUS-FNA does not lead to conclusive cytolo- ulogy diagnosis. After a negative or inconclusive EUS-FNA of a highly suspicious solid pancreatic mass EUS-FNA appears a reasonable choice to achieve the definite diagnosis.

Disclosure: Nothing to disclose.
Abstract No: 0742

Parameter | p-value | Hazard Ratio (HR) | 95% HR Confidence Lower Limit | 95% HR Confidence Upper Limit
--- | --- | --- | --- | ---
Age 60-69 | 0.8219 | 0.877 | 0.280 | 2.745
Age 70-79 | 0.6140 | 1.313 | 0.435 | 3.790
Age ≥80 | 0.1441 | 2.808 | 0.703 | 11.225
Tumor Size 20-29 mm | 0.1272 | 7.921 | 0.568 | 93.659
Tumor Size 30-39 mm | 0.2378 | 5.109 | 0.341 | 76.628
Tumor Size 40-49 mm | 0.1244 | 8.031 | 0.563 | 114.458
Tumor Size ≥50 | 0.0043 | 53.724 | 3.478 | 829.890
Moderate Differentiated Tumor | 0.1939 | 0.551 | 0.224 | 1.354
Well Differentiated Tumor | 0.1835 | 1.226 | 0.141 | 10.661
Median cfDNA level in plasma of PDAC patients (12.6 ng/ml, range: 80–400 ng/ml). Statistical analyses were routinely assessed by multivariate Cox regression model estimation.

Conclusion: THBS2 and CA19-9 panel assessed in human blood using a conventional ELISA assay may improve the definition of pancreatic lesions as PDAC even at early stages of disease. While total ctDNA amount differs between patients with benign and malignant pancreatic lesions, ctDNA genotyping for KRAS mutations failed to improve non-invasive diagnostic strategies in resectable PDAC most likely due to a low tumor load.

Disclosure: No disclosure.

P0743 A COMPOSITE LIQUID BIOMARKER FOR NON-INVASIVE DIAGNOSIS OF RESECTABLE PANCREATIC DUCTAL ADENOCARCINOMA
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Introduction: Pancreatic ductal adenocarcinoma (PDAC) has a dismal prognosis. Biomarkers are needed to facilitate early and preferably noninvasive detection of PDAC, which may enable early diagnosis and therefore influence patients’ prognosis. Circulating tumor DNA (ctDNA) has been examined several times in metastatic PDAC, but is yet to be evaluated in resectable PDAC with lower tumor load. Recently, KRAS mutations in ctDNA detectable by highly sensitive ddPCR have been identified as a strong predictor of PDAC diagnosis. The clinical utility of the KRAS mutation panel was therefore assessed in a prospective translational analysis.

Material and Methods: A prospective, single-center, observational study was performed at the University Medical Center Goettingen, Germany. Five hundred and eighty-three consecutive patients with newly diagnosed PDAC (44%) and in none of the IPMN patients. In contrast, parallel assessment of both, THBS2 and CA19-9 levels, was found to be most suitable to discriminate the PDAC% cohort from the IPMN cohort, with a sensitivity of 77% and a specificity of 100%.

Results: The chi-square test and Student’s t-test were used for statistical analysis, where applicable. Proper immune response to either HBV or HCV is necessary for the development of HCC. The guidelines strongly recommend that these patients routinely undergo abdominal imaging surveillance for HCC, regardless of whether they have symptoms.

Aims and Methods: This study aimed to evaluate whether patients with HBV- and HCV-related chronic liver disease were diagnosed with PC at early stages during abdominal imaging surveillance for HCC. This prospective study examined 50 consecutive patients with PC who were diagnosed at the Ehime University Hospital and its affiliated centers (including a cancer institute, tertiary care hospital, and community hospital) between 2011 and 2013. Data were collected regarding HBV and HCV status, likelihood of PC diagnosis, and Union for International Cancer Control (UICC) stage. Based on the aim of the present study, 73 patients without test results for viral hepatitis markers were excluded. The chi-square test and Student’s t-test were used for statistical analysis, where appropriate. Outcomes were analyzed using the Kaplan-Meier method and Cox proportional hazards regression. Differences in survival analyses were determined using the log-rank test. Local ethic boards approved the study but written consent form was waived due to the retrospective manner.

Results: The cohort included 447 patients (240 men and 207 women) with PC, who had a mean age of 72 ± 10 years (range: 33–91 years). Forty-five patients (10.0%) were positive for either HBsAg (N=18, 4.0%) or anti-HCV (N=27, 6.0%), although none of them had coinfection. Among the 45 patients, 26 patients had newly diagnosed HBV/HCV infections at the PC diagnosis.

Conclusion: The chi-square test and Student’s t-test were used for statistical analysis, where applicable. Proper immune response to either HBV or HCV is necessary for the development of HCC. The guidelines strongly recommend that these patients routinely undergo abdominal imaging surveillance for HCC, regardless of whether they have symptoms.
P0745 IMAGING AND HISTOLOGICAL DIAGNOSTIC ABILITY OF PANCREATIC NEUROENDOCRINE NEOPLASMS LESS THAN 20 MM IN SIZE

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Introduction: For diagnosis of pancreatic neuroendocrine neoplasms (PNNs), the usefulness of various imaging examinations has been reported. However, the diagnostic ability of imaging and pathological examinations for small lesions is uncertain.

Aims and Methods: The aim of this study was to examine the diagnostic ability of ultrasonography (US), computer tomography (CT), magnetic resonance imaging (MRI), endoscopic US fine-needle aspiration (FNA) for PNNs < 20 mm in size. From April 2004 to December 2017, 93 patients with PNNs were treated in our hospital. Thirty-four patients (48 lesions) who underwent surgery after US, CT, MRI, and EUS/EUS-FNA and whose tumours had pathology ≥20 mm were included in this study. The primary endpoints were detectability of each imaging modalities and calculated the cut-off line of detectable size of PNNs and the secondary endpoint was accuracy of the pathological examinations and concordance rate of the World Health Organization (WHO) grade by EUS-FNA.

Results: Ten lesions were in the pancreatic head, and 38 were in the pancreatic body or tail. The median tumour diameter was 10 mm (2–20). Four lesions were functional PNNs, and 44 were non-functional PNNs. The pathological diagnosis was based on WHO classification, and 41 lesions were G1 and 7 were G2. We performed US for 46 lesions and detected 24 (52%). On CT, 38 lesions (79%) were observed. Thirty-six lesions were contrasted in the early phase, and 2 showed delayed enhancement. MRI revealed 29 lesions (60%), of which 26 showed high signal intensity in diffusion-weighted images. On EUS, 44 lesions (83%) were detected. The boundary was clear/unclear in 43/1 lesions, the surface was adjusted/irregular in 42/2, and the internal echogenic gain was hypechoic/hyperchoic/isoechoic in 38/4/2.

The diameters of the 38 lesions detected on CT were all > 5 mm, and lesions of <5 mm could not be detected. The cut-off size of the detectable lesions in the receiver-operating characteristic curve analysis was 8 mm on US (sensitivity, 0.87; area under the curve [AUC], 0.92), 8 mm on MRI (sensitivity, 0.86; AUC, 0.84), and 5 mm on EUS (sensitivity, 0.95; AUC, 0.97). EUS-FNA was performed for 26 lesions, and 25 (96%) were diagnosed as PNNs. The Ki-67 index was evaluated for 23 lesions. Regarding the pathological classification of the FNA specimens, 17 lesions were G1 and 2 were difficult to assess. However, after surgery, 17 lesions were diagnosed as G1 and 6 as G2. In the analysis of pathological classifications, 16 lesions (70%) were properly assessed using FNA specimens.

Conclusion: The most useful examination for the diagnosis of small PNNs was EUS. Although the pathological diagnostic ability of EUS-FNA was high, the grading classification tended to be underestimated.

Disclosure: Nothing to disclose

P0746 IGFBP RNA-BINDING PROTEINS: POTENTIAL REGULATORS OF EPIGENETIC FACTORS IN PANCREATIC NEUROENDOCRINE TUMOR-CELLS

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Introduction: Pancreatic neuroendocrine tumors (PNET) are highly angiogenic tumors which – despite of various systemic targeted options including mTOR and VEGF inhibition – frequently develop secondary drug resistance. IGF2BP (IGF2 mRNA-binding proteins) represent a family of RNA-binding proteins (RBP) comprised of three members (IGF2BP1-3) which have been described as potentially oncomigenic factors in different solid tumors. As posttranscriptional regulators of gene expression they control the transport, translation and degradation of their target mRNAs, thereby influencing proliferation, migration and chemoresistance of tumor cells. However, the oncotelic proteins IGF2BP2 and IGF2BP3 can not be associated with an aggressive carcinoma, e.g. pancreatic ductal adenocarcinoma (PDAC), but their role and function in PNETs is still unknown.

Aims and Methods: We aim to analyze the functional role and clinical potential of IGF2BPs in PNETs to identify novel therapeutic avenues overcoming therapy resistance. Thereby the methods RNA interference, Flow Cytometry, Mutation-Assay, CPU, Western Blot, qRT-PCR, RNA-IP, RNA-deacy were used.

Results: In the PNET cell line BON1, we observed an exuberant expression of IGF2BP1 and MYC. Remarkably, IGF2BP depletion in BON1 cells significantly extenuated cell proliferation, migration and colony formation by posttranscriptional reduction of c-MYC, PCNA, CCNE1, CCNA2, CCNB1 and the methyltransferase EZH2. Simultaneously, mRNA and protein levels of p21, p53 and BCL-2 were upregulated, resulting in BCL-2 were upregulated, resulting in cell cycle arrest. Interestingly, no sign of apoptosis, senescence or reduced viability were observed. Using RNA Immunoprecipitation (RIP) we could confirm binding of IGF2BP1 to the EZH2 mRNA as well as to its known target mRNA MYC. The posttranscriptional regulation of EZH2 and MYC could explain the depressed proliferation of cell cycle arrest genes and BCL-2 in BON1 cells. In contrast to our findings on IGF2BP1, the depletion of IGF2BP2 and IGF2BP3 had no effect on the oncospecific capacity of BON1 cells. These data on EZH2 and MYC could explain the development of therapy resistance. Thereby the methods RNA interference, Flow Cytometry, Mutation-Assay, CPU, Western Blot, qRT-PCR, RNA-IP, RNA-deacy were used.

Conclusion: Our findings suggest that IGF2BP2 acts as a posttranscriptional modulator of oncogenic and epigenetic factors in PNET-cells, thereby enhancing or sustaining oncogenic hallmarks in support of an aggressive and chemoresistant phenotype.

Disclosure: Nothing to disclose

P0747 EXENDIN-IRDEy700DX FOR PHOTODYNAMIC THERAPY OF GLP-1R POSITIVE LESIONS

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Introduction: Insulinoma and focal lesions in congenital hyperinsulinism (CHI) can be treated by ethanol-monotherapy characterized by excising insulin producing lesions by heat and thereby causing severe hypoglycaemia. The therapy of choice is surgery, however, these surgical procedures are challenging because of the necessity to preserve as much healthy pancreatic tissue as possible and in some cases due to the localization of lesions near the ducts or large vessels. Targeted photodynamic therapy (PDT) could provide selective destruction of tumour tissue without causing damage to surrounding tissues. The glucagon-like peptide-1 (GLP-1) analogue exendin specifically binds the GLP-1R expressed on pancreatic beta cells. GLP-1R imaging using 64G-labelled exendin is a successful pre-operative imaging technique for insulinoma and is under investigation in CHI. We hypothesise that (PDT using exendin labelled with the near-infrared (NIR) sensitive photosensitiser IRDye 700DX enables specific destruction of GLP-1R positive lesions.

Aims and Methods: Exendin-IRDye700DX was characterized in vitro and in vivo. A competitive binding assay was performed using CHL-cells transfected with the GLP-1R. The feasibility of inducing specific cell death was assessed by incubating different cell-types (CHL-GLP1R, INS-1 cells and PCAN-1 cells) with 300 nM exendin-IRDye700DX and exposing them to various intensities of NIR LED light. Cell viability was measured using a cell titer glo assay. Tracer biodistribution was determined in BALB/c nude mice bearing subcutaneous GLP-1R positive tumours. To determine therapy response, tumours of 2 groups of mice (N = 8 per group, 1 group injected with 20 μg exendin-IRDye700DX and 1 control group injected with PBS) were exposed to 120 J/cm² of NIR LED light of 690 nm. Mice were sacrificed when tumours reached a size of 1000 mm³. Ex vivo imaging was performed with exendin-IRDye700DX PET/CT.

Disclosure: Nothing to disclose

P0748 LOCALIZATION OF INSULINOMAS WITH 68Ga-NODAGA-SCH 900916-4 PET/CT

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Introduction: Insulinomas are usually small, single benign tumors. Surgery is the therapy of choice and precise preoperative anatomical localization of the tumor is essential. Imaging techniques like CT, MRI as well as somatostatin receptor (SSTR) imaging have limited sensitivity (1,2). The stable glucagon like peptide-
indicate that false positive results can be excluded following 68Ga-NODAGA-exendin-4 PET.

Patients, all other imaging modalities were negative and an insulinoma NODAGA-exendin-4 PET, while Sst-receptor PET was negative in 5 of these lesions produced insulin leading to recurrent hypoglycaemia. In one MEN1 patient, multiple NETs were visualized by conventional imaging as well as Sst-receptor PET. In 2 patients, conventional imaging could not confirm the presence of an insulinoma while Sst-receptor PET as well as 68Ga-NODAGA-exendin-4 PET were positive. In one patient, an insulinoma was found using conventional imaging and 68Ga-NODAGA-exendin-4 PET, while Sst-receptor PET was negative. In 5 patients, all other imaging modalities were negative and an insulinoma could only be visualized by 68Ga-NODAGA-exendin-4 PET. The PET images were obtained one hour and two hours after injection of (5–7 µg) 95–105 MBq 68Ga-NODAGA-exendin-4. Current standard imaging was performed within 8 weeks of 68Ga-NODAGA-exendin-4 PET in all patients, consisting of CT or MRI and SSTR PET imaging.

Results: 68Ga-NODAGA-exendin-4 PET imaging confirmed insulinoma, i.e., GLP-1R positive lesions, in 25 of the 33 patients with suspected insulinomas. Insulinomas were also confirmed by conventional imaging as well as Sstr-receptor PET. In 2 patients, conventional imaging could not confirm the presence of an insulinoma while Sst-receptor PET as well as 68Ga-NODAGA-exendin-4 PET were positive. In one patient, an insulinoma was found using conventional imaging and 68Ga-NODAGA-exendin-4 PET, while Sst-receptor PET was negative. In 5 patients, all other imaging modalities were negative and an insulinoma could only be visualized by 68Ga-NODAGA-exendin-4 PET. The MEN1 patient, multiple NETs were visualized by conventional imaging and Sst-receptor PET, but no decisive answer could be given on which of these lesions produced insulin leading to recurrent hypoglycaemias. In three patients, 68Ga-NODAGA-exendin-4 PET was positive and confirmed the insulinoma's GLP-1R positive lesion. In all patients, GLP-1R positive lesions were pathologically confirmed to be insulinoma. In 7 patients, insulinoma could not be confirmed despite a positive Whipple's triad with any of the imaging techniques other than 68Ga-NODAGA-exendin-4 PET. This result may indicate that false positive results can be excluded following 68Ga-NODAGA-exendin-4 PET.

Conclusion: In conclusion, 68Ga-NODAGA-exendin-4 PET/CT performed better than standard imaging methods, which indicated it is a promising new technique for non-invasive pre-operative detection of insulinomas.

Disclosure: Nothing to disclose

References
P0752: ENDOSCOPIC VACUUM THERAPY FOR THE TREATMENT OF UPPER GASTROINTESTINAL TRANSMURAL DEFECTS: INITIAL EXPERIENCE

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Aims and Methods: The objective of this study was to evaluate the preliminary efficacy and impact of EVT in the treatment of upper gastrointestinal transmural defects.

Results: EVT was performed using the Endo Spong system (B. Braun, Melsungen, Germany). Continuous negative pressure of 100 mmHg, generated by an electronic vacuum pump system was applied. When possible the sponge was placed in an intracavitary position. Sponge replacement was performed every 3–7 days.

Conclusion: EVT is a promising approach in the treatment of upper gastrointestinal transmural defects.

Disclosure: Nothing to disclose

P0754: THE EFFECTIVENESS AND SAFETY OF ORAL PHLOROGLUCIN AS PREMEDICATION FOR STUDY PAPILLOMIESSPHAGIAGOASTRODUDENOSCOPY: A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED CLINICAL TRIAL


Aims and Methods: This study aimed to evaluate the effectiveness and safety of oral Phloroglucin (Flospan®) as premedication for study papillomiesphagastroduodenoscopy. Patients were administered 30 mg intravenous lansoprazole twice on the day of ESD. Postoperative day2, patients in group V received 20 mg/day vonoprazan and those in group L received 30 mg/day lansoprazole. Esophagastroduodenoscopy was performed 4 and 8 weeks after the ESD.

Results: The 263 patients who underwent ESD from April 2015 to December 2017, 182 patients (90 in group V and 92 in group L) were eligible for the study. Thirteen patients were excluded during follow-up because of complications or the need for additional surgery. Finally, 85 patients were allocated to group V and 84 to group L. The age, sex, status of Helicobacter pylori infection, tumor location, and ESD ulcer index of the two groups did not differ significantly. The 4-week healing rate for artificial ulcers was not significantly higher in group V (75.8% vs. 20.0%, p<0.001). There were no significant differences between the 4-week shrinkage rates of group V (92.4%) and group L (92.5%). Delayed bleeding was observed in 3 subjects of group L; however, no subject of group V had delayed bleeding. One patient in group V presented delayed perforation 2 days after ESD.

Conclusion: Vonoprazan was not superior to lansoprazole in its ability to heal artificial gastric ulcer after ESD.

Disclosure: Nothing to disclose

Additional information:

P0753: A PROSPECTIVE, RANDOMIZED CONTROLLED TRIAL OF VONOPRAZAN VERSUS Lansoprazole IN THE TREATMENT OF ARTIFICIAL GASTRIC ULCERS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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Aims and Methods: We aimed to evaluate the effectiveness of vonoprazan in healing artificial ulcers after ESD. Patients with gastric tumor were randomly assigned to the vonoprazan group (group V) or the lansoprazole group (group L) after ESD. The exclusion criteria were as follows: recent stomach, administration of antimicrobial agents, complication during and after ESD, need for additional surgical or endoscopic intervention. Patients were administered 30 mg intravenous lansoprazole twice on the day of ESD. Postoperative day2, patients in group V received 20 mg/day vonoprazan and those in group L received 30 mg/day lansoprazole. Esophagastroduodenoscopy was performed 4 and 8 weeks after the ESD. During the following endoscopy, the length and width of the artificial ulcer were evaluated using measure forceps. The EVT ulcer index was calculated by multiplying the length with the width of the resected specimen. The 4- and 8-week ulcer index were also calculated by multiplying the length with the width of the artificial ulcer at 4 and 8 weeks after ESD, respectively. The primary endpoint was the healing rate for the artificial ulcer at 4 weeks after ESD. Secondary endpoints were the healing rate at 8 weeks, shrinkage rates for the artificial ulcers at 4 and 8 weeks; and complications, such as delayed bleeding and perforation.

Results: Of the 263 patients who underwent ESD from April 2015 to December 2017, 182 patients (90 in group V and 92 in group L) were eligible for the study. Thirteen patients were excluded during follow-up because of complications or the need for additional surgery. Finally, 85 patients were allocated to group V and 84 to group L. The age, sex, status of Helicobacter pylori infection, tumor location, and ESD ulcer index of the two groups did not differ significantly. The 4-week healing rate for artificial ulcers was not significantly higher in group V (78.5% vs. 20.0%, p<0.001). There were no significant differences between the 4-week shrinkage rates of group V (92.4%) and group L (92.5%). Delayed bleeding was observed in 3 subjects of group L; however, no subject of group V had delayed bleeding. One patient in group V presented delayed perforation 2 days after ESD.

Conclusion: Vonoprazan was not superior to lansoprazole in its ability to heal artificial gastric ulcer after ESD.

Disclosure: Nothing to disclose

Additional information:
P0756 LAUNCHING AN ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) PROGRAM IN A EUROPEAN ACADEMIC HOSPITAL: REVIEW OF THE FIRST 34 MONTHS OF EXPERIENCE

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Introduction: Launching a professional program of endoscopic submucosal dissection (ESD) for the treatment of early gastrointestinal neoplasia in Western countries may be fastidious and is still debated.

Aims and Methods: This retrospective study included all 313 patients with peptic ulcers who were treated using monopolar soft coagulation in our department between January 2005 and December 2015. Endoscopic hemostasis with soft coagulation was performed if a patient with hematemesis or melena was admitted and presented with an actively bleeding ulcer (spurring or oozing), a non-bleeding visible vessel, or an adherent clot. Endoscopic hemostasis with soft coagulation was performed on 215 monopolar hemostatic forceps (FD-410LIR, Olympus Co., Tokyo, Japan or HDB2418W, Pentax Co., Tokyo, Japan) and an electro-surgical unit (ICC-200, ERBE, Tübingen, Germany) at soft-mucosal coagulation with a 70W current. If hemostasis was not achieved using this method, injection of hydrocortisone, heparin, heparin alone, or argon plasma coagulation was applied. If the additional endoscopic treatment was still unable to stop the bleeding, intervention radiology or surgical treatment was performed. Rebleeding was defined as blood in the stomach and stigmata of a recent hemorrhage in the ulcer base when second-look endoscopy was performed, or fresh hematemesis and/or melena accompanied by either instability of vital signs or reduction in hemoglobin level of greater than 2g/dl within 24 hours. Factors associated with treatment failure of soft coagulation were analyzed.

Results: The study subjects were 207 men and 106 women at a median age of 69 (range, 28–97) years, with 242 gastric ulcers and 71 duodenal ulcers. Initial hemostasis with soft coagulation was achieved in 296 patients (94.6%). Of the 17 patients with treatment failure, additional endoscopic methods were required in 17 cases for the treatment of counter bleeding. Rebleeding in 21 patients (6.7%). Minor perforation occurred in 2 patients, and was managed conservatively in both patients. Three patients died of ulcer bleeding within 30 days of the occurrence of initial bleeding. Initial hemostasis with soft coagulation was not achieved with an exposed vessel. In multivariate analysis, rebleeding was significantly related to duodenal ulcer and elderly patients.

Conclusion: Soft coagulation using a monopolar hemostatic forceps is effective and safe for patients with gastroduodenal ulcer bleeding. However, duodenal ulcer bleeding, exposed vessels and elderly patients are risk factors for treatment failure.

Disclosure: Nothing to disclose
Anticoagulants to heparin replacement, and those who underwent hemodialysis. This was encountered with a historical control group that included patients who underwent SLE after gastric ESD between November 2015 and March 2017 (the SLE group). Data were analyzed using propensity score-matching methods. We used the size of the ESD specimen and comorbidity of diabetes mellitus as covariates according to previous reports [2, 3]. The primary endpoint was POB.

[Study 2] In the entire cohort, the rate of POB after gastric ESD in HRSs was 4.7% (5/106 specimens). However, there was no difference in the other risk factors between the two groups. No significant differences were observed in the rate of POB between the two groups (SLE group, 3.8%; non-SLE group, 10.5%).

Conclusion: SLE did not reduce the rate of POB after gastric ESD in HRSs. SLE may not be recommended after gastric ESD in HRSs, as in the case in LRP; however, it is necessary to accumulate and analyze more cases.

Disclosure: Nothing to disclose

References

P0759 OLGA AND OLGIM STAGE ACCORDING TO AGE AND RISK FACTORS INFLUENCE HIGH RISK OF GASTRIC CANCER M. Zhang1, B. Li2,3
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Introduction: Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) are superordinate staging systems for risk stratification in gastric cancer.

Aims and Methods: The study aimed at evaluating the distribution of OLGA and OLGIM staging and the relationship with age and other risk factors analysis. 632 patients who underwent endoscopy for functional dyspepsia. Helicobacter pylori status and histologic changes were assessed using the updated Sydney system. At least three biopsy pieces (one from the lesser curvature of antrum and corpus, respectively, one from incisura angularis) were acquired. Helicobacter pylori status and histologic changes graded by senior gastrointestinal pathologists according to the updated Sydney system.

Stage III and OLGIM staging, the proportion of high-risk OLGA stages was low (6.9%) before the age of 50, but increased to 9.5%, 11.7%, and 25.7% for those in their 50s, 60s, and older than 70 years, respectively, smoking (OR = 2.07, 95% CI: 1.09-3.95, p < 0.001), and H. pylori infection (OR = 2.46, 95% CI: 1.37-3.79, p = 0.002) were independent risk factors for high-risk OLGA stages. These risk factors were also for high-risk OLGIM stages. The H. pylori infection was positive correlation with the OLGA and OLGIM staging, the H. pylori positive rate of OLGA and OLGIM Stage 0 was 5.8% (4/69 cases) vs. 3.3% (2/61 cases). and 22.4% and 22.9% and 34.4% and 30.8%, 39.5% and 39%, 45.0% and 30.0%, respectively, the proportion of high-risk OLGA stages was low (6.9%) before the age of 50, but increased to 9.5%, 11.7%, and 25.7% for those in their 50s, 60s, and older than 70 years, respectively. High-risk OLGIM stages showed a similar trend.

Conclusion: High-risk OLGA and OLGIM stages are uncommon under the age of 50. The H. pylori infection was positive correlation with the OLGA and OLGIM staging, thus eradication of H. pylori before that age may reduce the requirement for endoscopic surveillance for gastric cancer.

Disclosure: Nothing to disclose

P0760 ARGON PLASMA COAGULATION FOR SUPERFICIAL SQUAMOUS CELL CARCINOMA IN THE RESIDUAL ESOPHAGUS AFTER ESOPHAGECTOMY K. Saisho, T. Tanaka, S. Matono, M. Naoki, H. Haruhiko, A. Yoshito
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Introduction: Patients with esophagectomy for esophageal squamous cell carcinoma (SCC) often develop metachronous SCC in the residual esophagus. Although most of the lesions are detected as superficial SCC at follow-up endoscopy, it is difficult to perform endoscopic resection for lesions near the anastomosis. We have performed argon plasma coagulation (APC) for such superficial SCC in the residual esophagus. The aim of this study is to evaluate the usefulness of APC for superficial SCC in the residual esophagus after esophagectomy.

Aims and Methods: The aim of this study is to evaluate the usefulness of APC for superficial SCC in the residual esophagus after esophagectomy. At patients who underwent endoscopy for functional dyspepsia.

Results: [Study 1] Eighty-two patients (96 specimens) underwent gastric ESD, assessing (OR 2.46, 95% CI: 1.37–3.95, p < 0.002) were independent risk factors for high-risk OLGA stages. These risk factors were also for high-risk OLGIM stages. The H. pylori infection was positive correlation with the OLGA and OLGIM staging, the H. pylori positive rate of OLGA and OLGIM Stage 0 was 5.8% (4/69 cases) vs. 3.3% (2/61 cases). and 22.4% and 22.9% and 34.4% and 30.8%, 39.5% and 39%, 45.0% and 30.0%, respectively, the proportion of high-risk OLGA stages was low (6.9%) before the age of 50, but increased to 9.5%, 11.7%, and 25.7% for those in their 50s, 60s, and older than 70 years, respectively. High-risk OLGIM stages showed a similar trend.

Conclusion: High-risk OLGA and OLGIM stages are uncommon under the age of 50. The H. pylori infection was positive correlation with the OLGA and OLGIM staging, thus eradication of H. pylori before that age may reduce the requirement for endoscopic surveillance for gastric cancer.

Disclosure: Nothing to disclose

Disclosure: Nothing to disclose

P0761 THE EFFECTIVENESS OF “HANDMADE MULTI-BENDING SYSTEM OF THE ENDOSCOPE” FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF THE LESSER CURVATURE OF GASTRIC NEOPLASMS K. Yamamoto1, K. Tanaka2, S. Hayashi2, N. Tatsuumi1, T. Michida1, T. Ito1
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Introduction: Maintaining good operative field is crucial in performing endoscopic submucosal dissection (ESD) for early stage gastrointestinal tumors, but it often requires high skill or special equipment depending on the lesion location. In ESD for the lesions at the lesser curvature of the gastric body, it is often difficult to approach the lesion with conventional gastroscopy and it is also often difficult to maintain good operative field. A multi-bending endoscope (Olympus) is a good option for such a situation, but it is difficult for most operators to prepare it due to its particularity or cost.

Aims and Methods: We therefore recently developed handmade multi-bending system (HMBS) and performed ESD using it for 11 lesions which were located at the lesser curvature of the gastric body and tended to be difficult to approach. A fishing line was passed through the external tube (Crusher catheter, Zeon Medical, Japan), and the tip of external tube was fixed about 15–20 cm apart from the tip of the gastronomy (Olympus or Fujifilm). The fishing line was then inserted into the lesions and fixed at the original first bending portion. Second bending portion was created by pulling the fishing line through the external tube, and fixed with three-way stopcock according to the situation during the procedure. HMBS was used at our hospital from February 2017 and August 2017. In this study, we retrospectively investigated the treatment outcome of ESD with HMBS (N = 11) for the lesions located at the lesser curvature of the gastric body and difficult to approach, and compared it with the treatment outcome before the adoption of HMBS (Conventional, N = 11). ITknife2 (Olympus), Flusknife BT (Fujifilm), or both endoknives were used for ESD. This study was approved by the ethical committee.

Results: Average tumor diameter and resected specimen diameter of Conventional and HMBS were 16.6mm vs 16.5mm, and 36.2mm vs 37.3mm (not significant), respectively. In all cases to which we applied HMBS, the tip of the endoscope could be closely approached to each lesion just after using HMBS, although it was difficult to approach the lesion without HMBS. Procedure time of HMBS (34.3minutes) was significantly shorter than that of conventional (61.5 minutes) (p = 0.01). In all cases, en bloc resections were achieved, and no perforation or other complication occurred.

Conclusion: This study demonstrated that our handmade multi-bending system may greatly shorten the procedure time of ESD for the lesions which are located at the lesser curvature of the gastric body and difficult to approach.

Disclosure: Nothing to disclose

P0762 CLINICAL EFFICACY OF THE OVER-THE-SCOPE CLIP DEVICE: A SYSTEMATIC REVIEW N. Bartelli1, A. Rajabalian2, V. Kaul1, T. Kothari1, K. Bittner1, S. Kothari1
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Introduction: The over-the-scope clip (OTSC) is a technology that is increasingly incorporated into endoscopic practice and is utilized for applications including fistula closure, control of bleeding, perforation, management of anastomotic

Disclosure: Nothing to disclose

 disclosure
leaks, endoscopic full thickness resection (EFTR), and luminal stent fixation. Our study evaluated a large body of literature to determine the overall efficacy and safety of OTSC. **Aims and Methods:** A Medline search was conducted from inception to October 1st, 2017. The following search terms were used: “over the scope clip”, “OTSC”, “fistula closure”, “over the scope clip bleeding”, and “endoscopic perforation closure”. Publications selected for inclusion consisted of case reports, case series, as well as prospective and retrospective single-arm clinical studies. Data were collected from each study on technical success, clinical success, and reported adverse outcomes. Weights were calculated (Table 1) to adjust for sample size. **Results:** 238 papers were selected that met the search criteria: 81 case series/retrospective reviews/prospective studies (Group A) and 157 case reports (Group B). In Group A, technical success of OTSC placement was 95.3%, with a clinical success of 77.2% (n = 2285 patients). Indications for OTSC placement were fistula closure (30.6%), bleeding (28.9%), perforation closure (16.3%), leaks (15.1%), EFTR (8.4%) and stent fixation (0.7%). Clinical success for each indication (weighted means) is listed in Table 1. Complete luminal obstruction (one) was the only reported adverse event across all studies. 24/81 papers reported the need for surgery despite OTSC placement. In these 24 papers, 18 were the only OTSC-related adverse events reported. Overall, the role of endoscopic surgery-sparing, endoscopic tool in today’s GI practice with 77.96% of patients achieving clinical success without the need for further treatment. Technical success of > 95% has been reported across all indications. Surgical salvage is still needed in a minority of patients. **Disclosure:** Nothing to disclose

<table>
<thead>
<tr>
<th>Sample Size</th>
<th>Weighted Mean</th>
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<td>Overall Clinical Success</td>
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<td>Fistula Closure</td>
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<td>Bleeding</td>
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<td>EFTR</td>
<td>191</td>
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<tr>
<td>Stent Fixation</td>
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</table>

**Table 1:** Observation Studies Pooled Sample Sizes and Weighted Means of Overall Clinical Success and Individual Indications for OTSC Placement

**Conclusion:** pCLE seems comparable to standard biopsies in detection of persistent/recurrent IM in 2 patients (5%, 2/39), another 2 patients had IM present in biopsies but not in pCLE. pCLE diagnosed one patient in in whom microscopic visible tongue arising from neo-Z-line, which was not confirmed in biopsies. Sensitivity and specificity of pCLE in detection of persistent/recurrent IM was 83% (95% CI 51.6–97.9) and 93% (95% CI 75.7–99.1), respectively, with a positive predictive value of 83% (95% CI 56.3–95.1) and a negative predictive value of 93% (95% CI 77.8–97.8). Agreement of pCLE and histopathological findings was 90%.

**Disclosure:** Nothing to disclose
Aims and Methods: The study was to find the factors affecting size discrepancy occurred after formalin fixation, respectively. 69 lesions including 50 gastric adenomas and 19 adenocarcinomas were analyzed for age, sex, location, gross shape, histologic finding, complete resection of ESD, and size immediately after ESD and after fixation formalin.

Results: Size of resected specimen decreased after formalin fixation (3.75 mm vs 35.8 mm, p<0.05). Mean size of long diameter of the lesion was 20.3 ± 7.7 mm in the time of pre-fixation, 13.4 ± 7.9 mm after fixation. Size discrepancies in the diagnosis of endoscopic submucosal dissection (ESD) method in the gastric adenoma or superficial adenocarcinoma. The one of major parameter to determine the resection method is the size of the lesions. Previous study showed that there were a significant discrepancy between endoscopic and pathologic sizes. Aims and Methods: The aim of the study was to compare size of gastric and P-EGC. (Odds ratio [OR] 2.53, 95% confidence interval [CI], 1.11–6.5 vs 2.5 ± 5.8, p<0.001). In multivariate analysis, tumor size ≥20mm of the lesion was independent factor affecting size increases after formalin fixation (p<0.05).

Conclusion: Endoscopic evaluation of horizontal extent of the lesions before ESD may be incorrect in large tumors more than 20mm in size. It must be restected with more careful procedure to avoid incomplete resection.

Disclosure: Nothing to disclose

P0768 THE DIAGNOSIS OF INVASION DEPTH IN SUPERFICIAL ESOPHAGAL SQUAMOUS CELL CARCINOMA: EFFICACY OF ENDOSCOPIC ULTRASONOGRAPHY — A SINGLE CENTER TRIAL

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Introduction: The diagnosis of cancer invasion depth is crucial for selecting the appropriate treatment strategy. In Japan, magnifying endoscopy with narrow-band imaging (ME-NBI) has been used for diagnosis by observing the esophageal microvasculature architecture. This modality represents a rapid and simple diagnostic procedure without the need for additional equipment. However, some lesions with microvascular patterns without invasion cannot be observed because the intra-epithelial papillary capillary loop is inaccessible. Endoscopic ultrasonography (EUS) is regarded as the standard modality for diagnosing esophageal cancer invasion depth in the West. EUS is an effective tool for determining the depth of tumor invasion; however, the ability to distinguish invasive carcinoma from normal or hyperplastic tissue, and its exact effectiveness is unknown. We investigated the role of EUS in diagnosing invasion depth in superficial esophageal cancer.

Aims and Methods: Patients with superficial esophageal squamous cell carcinoma (SECSC) and suspected muscularis mucosa or submucosal invasion in non-magnifying white light imaging (WLI) were included. All patients received WLI and ME-NBI observation. T1b High Confidence in EUS showed higher accuracy of invasion depth in WLI followed by ME-NBI and WLI, ME-NBI was used as the reference standard.

Results: From May 2015 to January 2018, 119 patients with esophageal SCC with suspected muscularis mucosa or submucosal invasion in WLI were examined. Of the 119 patients, 31 were excluded from analysis because histologic specimens were not obtained. 38 lesions treated by esophagectomy (n=26) or endoscopic resection (n=62) were included in the final analysis. Histologic diagnosis was T1a in 44 lesions and T1b in 44 lesions. The accuracy of invasion depth in WLI followed by ME-NBI and WLI, ME-NBI followed by EUS was 70% (p=0.30), respectively. The accuracy of diagnosing invasion depth for lesions with protrusions in WLI followed by ME-NBI and WLI, ME-NBI followed by EUS was 74% (29/39 lesions) and 85% (35/41 lesions) (p=0.06), respectively.

Conclusion: EUS showed a possible additional benefit to WLI followed by ME-NBI for lesions with protrusions. T1b High Confidence in EUS showed higher PPV compared with T1b Low Confidence in EUS which showed marginal accuracy of invasion depth in WLI followed by ME-NBI and WLI, ME-NBI followed by EUS was 74% (29/39 lesions) and 85% (35/41 lesions) (p=0.26), respectively. The positive predictive value (PPV) in EUS T1b High Confidence and T1b Low Confidence was 47% (9/19) and 79% (19/24) (p=0.06).
statistical benefit. Therefore, the confidence level in EUS may affect the diagnosis of invasion depth for SESCC.

Disclosure: Nothing to disclose

Reference

P0769 EVALUATION OF FACTORS TO DECIDE ON ESD INDICATION FOR GASTRIC ADENOMAS DIAGNOSED WITH ENDOSCOPIC BIOPSY

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Introduction: Although the adenoma is a benign neoplasm, those diagnosed with biopsy specimen were sometimes prove to be malignant by pathological evaluation after ESD, indicating that the accuracy of the diagnosis for neoplasm based on a small biopsy specimen is limited. Thus, it is difficult to decide on the indication of endoscopic submucosal dissection (ESD) for adenomas. In addition, therapeutic strategy for gastric adenoma has not been well established and none has reported the appropriate approach to adenomas for the future metachronous multiple lesions. In this study, factors contributing to the decision for removing gastric adenomas diagnosed preoperatively with biopsy specimen were evaluated.

Aims and Methods: Five hundred and thirty-nine lesions of gastric epithelial tumor pathologically diagnosed after complete en-bloc curative resection by ESD between 2009 and 2017 were retrospectively reviewed. Among 539 lesions, 62 lesions, diagnosed preoperatively as adenomas, were enrolled in this study. The preoperative endoscopic findings under white light (WL), known as signs of potential size over 20 mm, red color, tall protrusion, central depression, and positive finding in the assessment under magnified-NBI (M-NBI) were analyzed using Fisher’s exact test. The assessment under M-NBI was based on VS classification system by Yao. The removed specimens, pathologically assessed by cutting with every 2 mm of interval, were classified as either cancer or adenoma. In addition, the specimens of well differentiated adenocarcinoma (tub1) were classified into 2 groups, low-grade tub1 and regular tub1. While adenomas are characterized of lesions without A (dysplasia of nucleus and disappearance in superficial area) and B (dysplasia of glandular structure with or without invasion to submucosal layer), regular tub1 was characterized of that with A and B. Low-grade tub1 was defined as lesion with A but without B.

Results: Among 62 lesions preoperatively diagnosed as adenoma, 24 (38.7%) proved to be cancer by detailed pathological assessment after ESD. These 24 lesions (tub1) were all pathologically classified as low-grade intestinal type tub1. Among 24 lesions diagnosed as tub1 after ESD, the preoperative endoscopic findings described above under WL were found in 10 (2.4/2 lesions (41.7/3/16.7/8.3/3/16.7/8.3/3/16.7/8.3/3/16.7/8.3%), respectively, indicating that the rate of each factor was higher in tub1 than adenoma although no statistically significant difference was observed. However, the rate of above factors with more than 1 preoperative finding was significantly higher in tub1 group (62.5%/12/24 vs 34.2%/12/38, p = 0.038). The rate of positive findings under M-NBI was also higher in tub1 group (54.2%/13/24 vs 23.7%/9/38, p = 0.028). We experienced 2 metachronous cases with a scar of previous ESD for benign adenoma. The treatment time was extremely long (252, 323 min, respectively) because of the technical difficulty.

Conclusion: It is important to evaluate macroscopic findings under white light as well as magnified-NBI assessment to decide on the ESD indication for lesions with a preoperative diagnosis of benign adenoma with biopsy specimens. Considering the difficulty to remove lesions with an ESD-related scar in case with endoscopic depth of invasion, lesions without risk factors of cancer can be carefully followed-up to avoid the consequent ESD-related scar because of pathologically low-grade malignancy in all cancer lesions diagnosed postoperatively.

Disclosure: Nothing to disclose

P0770 HOW DOES LINKED COLOR IMAGE (LCI) WHICH IS ONE MODALITY OF IMAGE ENHANCED ENDOSCOPY (IEE) CONTRIBUTE TO DETECT THE SHORT TO SMALL EARLY GASTRIC CANCER? A PILOT STUDY

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Introduction: How can you detect minute to small early gastric cancer effectively? It is the theme that is the most important to gastric cancer screening. If minute to small early gastric cancer is detected by untechnical Endoscopist it is effective at all.

Therefore we examined whether a detection rate of the early gastric cancer was raised by using LCI which was one of the modality of IEE which Fuji Film Company developed.

Aims and Methods: LCI expands color differences so that reddish color becomes redder and whitish color becomes whiter for image obtained by simultaneously eradiating laser light and white light with appropriate balance. Therefore, LCI enhances slight color differences close the mucosal color and may increase the visibility of the lesion as compared with the conventional white light observation. Detectability of neoplastic lesions in stomach using ultra slim endoscope and LCI: a randomized comparison trial.

The aim of this study is to evaluate usefulness of LCI compared with White light observation for detectability of neoplastic lesions in Stomach.

Registered cases: - WL 750 cases
- LCI 750 cases

Total 1500 cases

Study term: March, 2017-Feb. 2022 (5 years)

Pilot Study (100 cases) is finished

Results: In Japan, the differentiated type early gastric cancer with H. pylori (+) was said to tend to be multiple around 10–15% and did field setting of this study after early gastric cancer endoscopic treatment primarily. We report pilot study in 100 cases.

Conclusion: Both cancer and adenoma were a few in the LCI group, but there was a tendency that a discovery rate was high in with a significant difference. We may detect to provide the minute–small early gastric cancer by LCI in the detection of the early gastric cancer after eradication in future while H. pylori eradication states increases.

Disclosure: Nothing to disclose

P0780 COMPARATIVE STUDY OF ESD AND SURGICAL RESECTION FOR GASTRIC SETS ORIGINATED FROM MUSCULARISPROPRIA

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Introduction: Endoscopic resection for gastric subepithelial tumors (SETs) originated from the muscularispropria (GSET-PM) has offered less invasive alternatives to surgical resection.

Aims and Methods: The aim of this study was to compare endoscopic submucosal dissection (ESD) with surgical resection for the removal of GSET-PM. This study involved 17 patients with GSET-PM removed by ESD and 76 patients who underwent curative surgical resection.

Results: ESD group were more likely to have upper portion (10/17, 58.8%) and surgery group were more likely to have mid portion (41/76, 53.8%, p = 0.039). ESD group were smaller median tumor size (25.6 mm vs 35.9 mm, p = 0.037) and higher endoluminal ratio (58.5 ± 9.1% vs 45.8 ± 15.4%, p = 0.002). ESD group were mostly to have Yamada type III (10/17, 58.8%) and surgery group were mostly Yamada type I (52/76, 68.4%, p = 0.001). Complete resection by ESD was very high by surgical resection (82.4% vs 100%, p = 0.001). In ESD group, 3 performed surgical resection after ESD (1 incompletely resection and 2 uncontrolled bleeding) and 1 showed perforation was completely resected with endoscopic closure. In surgery group, complications occurred in 6 patients (1 leakage, 1 stricture, 1 hernia and bowel obstruction, 1 wound infection and 2 worsened general condition after surgery). Although surgery group were lower in complication rate than ESD group (p = 0.006), severity of complications were higher in the surgery group and there were no mortalities in the ESD group compared with 2 in the surgery group. There was no statistical difference of recurrence and the follow-up period between two groups.

Conclusion: ESD can be one of good options for the resection of endoluminal GSET-PM and could be replace treatment by surgical resection in Yamada type III with a high endoluminal ratio.

Disclosure: Nothing to disclose
**P0772 SHOULD NARROW BAND IMAGING (NBI) BE ROUTINELY USED DURING ESOPHAGUS INSPECTION? A RANDOMIZED PROSPECTIVE STUDY**

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**Introduction:** Heterotic gastric mucosal patch of cervical esophagus (gastric inlet patch, GIP) is a common endoscopic finding, however, its origin, prevalence and clinical significance are not well understood. Recently gastric inlet patch detection rate (GIPDR) has been proposed as potential quality indicator of upper gastrointestinal endoscopy [1] and first guidelines mentioned about cervical inlet patches (BSG and AUGIS) [2]. Endoscopists awareness as well as endoscopy using narrow band imaging (NBI) are proposed as main factors that affect its detection, however there is lack of prospective randomized trials that may answer the question if this imaging technique should be used routinely [3-5].

**Aims and Methods:** The aim of the study was to investigate whether routine use of NBI and endoscopist’s attention improves the GIPDR. 1000 patients were randomized into NBI or standard white light endoscopy (WL) in 1:1 ratio. During the endoscopic examination, heterotic patches were exclusively evaluated. Both as monotherapy and dual therapy in UGIB.

**Results:** There was neither significant difference in GIPDR between NBI and WL groups (9.4% vs 6.6%, p = 0.1), nor in ‘attentive’ and ‘inattentive’ (9.4% vs 6.6%, p = 0.1). Detection rate remained the same in WL and NBI groups (WL inattentive 7.6% vs WL attentive 7.6%, p = 0.37; NBI inattentive 7.6% vs NBI attentive 12.2%, p = 0.17). NBI and enhanced attention improved GIPDR in comparison to WL and standard attention (11.2% vs 5.6%, p = 0.001). GIPDR in the study was greater than in control group (8% vs 4.1%, p = 0.006), however only increased attention was superior to the control group (inattentive p = 0.09; attentive p = 0.001). NBI was superior to the control group (NBI total p = 0.001, NBI inattentive p = 0.047, NBI attentive p = 0.003), in WL group only increased attention was superior to the control group (WL total p = 0.09, WL inattentive p = 0.36, WL attentive p = 0.047).

**Conclusion:** NBI enables CIP detection at the same level as standard endoscopy with enhanced attention. Increased attention of GIP enhances GIPDR especially when using NBI.

**Disclosure:** Nothing to disclose

**References**

**P0773 EFFICACY OF HAEMOSPRAY THERAPY ON RE-BLEED AFTER A MORTAL SINGLE-CASE EXPERIENCE**

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**Introduction:** Dual endotherapy including epinephrine injection, thermal and mechanical methods have been shown to be superior to monotherapy in reducing the risk of re-bleed (20% vs 10%) and need for surgery in patients with upper gastrointestinal bleed (UGIB) [1]. Heamospray, an inorganic powder is a chemical mechanism to achieve haemostasis. The aim of the study was to describe a single centre district hospital experience in the United Kingdom with haemospray both as monotherapy and dual therapy in UGIB.

**Aims and Methods:** Retrospective data for all patients who were treated with haemospray for UGIB were collected retrospectively between January 2016 to June 2017 using EndoSoft®, Sunquest ICE8, Medisc and case notes. The primary endpoints were short-term haemostasis (24 hours), long-term haemostasis (7 days) and mortality in patients where haemospray was used either as primary haemostatic agent or combination therapy with a second haemostasis modality.

**Results:** Haemospray was applied during 50 examinations in 48 patients - 21 male (44%) and 27 female (56%), mean age 71.9 (range 40 to 92) years. The mean Blatchford score was 9.6 (range 0–18). 33 (69%) patients were treated for peptic ulcer. The rest were used for treating 2 (4%) gastric antral vascular ectasia, 2 (4%) oesophagitis, 2 (4%) post psychiatric, 8 (16%) non-specific bleeding source and 1 (2%) gastric tumour. Of the 48 procedures, re-bleeding occurred in 8 patients. Overall, short-term haemostasis was achieved in 46 (95%) patients and long-term haemostasis was achieved in 42 (87.5%). A total of 12 (25%) patients died, out of which 4 (8%) died due to a re-bleed and 2 (4%) failed to achieve initial primary haemostasis. The reminder 6 patients died from non-UGIB cause.

**Conclusion:** In this single-centre audit, the role of haemospray as combination and monotherapy in achieving haemostasis has been shown to be comparable to other modalities of endotherapy with statistical significance. This data needs to be replicated in a larger number of patients across other centres.

**Disclosure:** Nothing to disclose

**Reference**

**P0774 MUCOSAL LOSS IS THE CRITICAL MECHANISM OF ESOPHAGAL STRIURE AFTER MUCOSAL RESECTION: A PILOT EXPERIMENT IN A PORCINE MODEL**

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**Introduction:** Esophageal stricture is a major complication of endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). To date, the critical mechanism of esophageal stricture has not been fully elucidated and there is no effective treatment.

**Aims and Methods:** We designed this experiment to explore the underlying mechanism of esophageal stricture after mucosal resection in a porcine model. Twelve swines were used for this study and were randomly divided into two groups. Firstly, in all the swines, two submucosal tunnels, 5 cm in length and 1.3 cm in width, were made on the anterior and posterior wall of the submucosal layer over each tunnel. In the second group. The process of stricture formation was evaluated by endoscopic inspection after one, two and four weeks respectively. Histological examination was performed after humanely execution.

**Results:** Ulcer formation was inspected on endoscopic observation and incisional edges tended to grow and conglutinate with each other in each group after one week. All of the swines in the first group developed mild to severe esophageal stricture with weight loss whereas no esophageal stricture was evident in the ones of the second group after two and four weeks respectively.

**Conclusion:** The loss of esophageal mucosa should be the crucial factor for esophageal stricture after mucosal resection. Inflammation and scar formation slightly attribute to esophageal stricture formation. These results are important for developing a suitable treatment method for esophageal stricture.

**Disclosure:** The two authors were involved in this work, agreed to submit it to UEGW 2018, and assumed responsibility for the accuracy and completeness of the data. The authors declare that there are no conflict of interest.
P0775  ENDOSCOPIC SUBMUCOSAL DISSECTION WITH SPLASH MICROKnife: A CENTER CONSOLE CASE SERIES
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Introduction: Endoscopic submucosal dissection (ESD) is widely accepted as a standard endoscopic treatment for early stage gastrointestinal (GI) neoplasms having a small risk of lymph-node metastasis, which could not resect by traditional endoscopic methods. However, completion of the procedure is very laborious in some cases due to bleeding and fibrosis. The Splash M-knife is a new multifunctional ESD device with water irrigation function. In addition, a metal plate attached to its distal sheath is better for hemostasis and cutting the fibrotic tissue than conventional devices. Aims and Methods: We aimed to elucidate the technical outcomes of ESD for GI neoplasms by using the Splash M-knife, because no consecutive case series in the whole GI tract have been reported so far. A retrospective single-center study was conducted at the University of Tokyo Hospital between January 2015 and December 2017 in patients who had received ESD with the Splash M-knife, because no consecutive case series in the whole GI tract have been reported so far. Results: During the study period, 435 patients (esophagus (E)/stomach (S)/colon (Cr): 89/146/200) were treated by ESD with the Splash M-knife. The gender ratio (S/E/C) was 1:3:1. Patients aged 65-75 years, 37.0/40.2/38.9 mm, and 21.7/18.8/29.4 mm, respectively. As for the short-term outcomes, procedure time, en bloc resection rate, complete resection rate, post procedure bleeding rate and perforation rate were evaluated in each organ. Conclusions: ESD with Splash M-knife resulted in favorable outcomes through the GI tract. Further prospective comparative studies are needed to elucidate the advantages of this knife over other conventional knives. Disclosure: Nothing to disclose.

References

P0776  DEVELOPMENT AND VALIDATION OF ENDOSCOPIC PREDICTION MODEL FOR GASTRIC CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH RENAL TRANSPLANTATION
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Introduction: Cytomegalovirus (CMV) is a very common viral pathogen after organ transplant patients. However, endoscopic characteristics of gastric CMV infection have not been established. Aims and Methods: We aimed to develop and validate a prediction model using endoscopic findings for gastric CMV infection in patients with renal transplantation. A retrospective study was performed in a tertiary referral hospital enrolling 354 kidney transplant recipients who received endoscopy with biopsy for suspected CMV infection from Jan. 2005 to Nov. 2015. The development phase, endoscopic parameters were selected by univariate logistic regression analyses. Then, the prediction model was established on the basis of β coefficients of the multivariate logistic regression. For the validation of the model, the same regression equation was tested on the other group. Results: Age, days from renal transplantation to endoscopic biopsy, erosion at antrum, erosion with exudate, raised erosion, and ulcer at antrum were selected as the predicting factors for gastric CMV infection. In the development set (n=176) using these five markers, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 92.3, 80.8, 87.16, and 88.06, respectively. In the validation set (n=178), the sensitivity, specificity, PPV, and NPV were 83.87, 82.35, 83.87 and 82.35, respectively. Conclusion: This endoscopic prediction model using 5 risk factors can be a reliable diagnostic tool for gastric CMV infection after renal transplantation. Disclosure: Nothing to disclose.

P0777  AN AUSTRALIAN EXPERIENCE WITH ENDOSCOPIC SLEEVE GASTROPLASTY (ESG) FOR WEIGHT LOSS
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Introduction: The pioneering centres for endoscopic bariatric therapies have demonstrated the strong efficacy and safety profile of endoscopic sleeve gastoplasty (ESG). However, data outside these expert centres remain scant. We report a single-centre experience of ESG performed in Australia (Sydney Adventist Hospital, Sydney).

Aims and Methods: All patients undergoing ESG between May-October 2017 had data prospectively collected. All patients had previous unsuccessful attempts at diet and exercise programs. ESG was performed by 2 Gastroenterologists. The Apollo OverStitch device (Apollo Endosurgery) was used to place full-thickness endoscopic sutures from the incisura angularis to the fundus, creating a ‘sleeve effect’ using the technique previously described in detail. All patients received regular follow-up with a multidisciplinary team. Measured outcomes included absolute weight loss, change in body mass index (BMI), total body weight loss (%TBWL) and excess weight loss (%EWL) at 1 and 6 month follow-up. The proportion of patients achieving ≥10% TBWL, ≥15% TBWL, and ≥25% EWL at 6 months was also assessed. Intention-to-treat (ITT) analysis considered patients lost to follow-up as failing to meet these thresholds.

Results: A total of 66 patients (75.8% female) underwent ESG. The mean age was 45.2±10.2 years, mean baseline weight was 112.5±17.0kg and mean BMI was 39.3±4.7kg/m2. The outcomes at 1 and 6 month follow-up (mean±SD) are summarised in table 1.

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Weight loss (kg)</th>
<th>Δ BMI (Kg/m2)</th>
<th>%TBWL</th>
<th>%EWL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month 66</td>
<td>9.7 ± 3.3</td>
<td>3.4 ± 1.0</td>
<td>8.6 ± 2.5</td>
<td>25.3 ± 11.7</td>
</tr>
<tr>
<td>6 months 64</td>
<td>16.5 ± 7.3</td>
<td>5.8 ± 2.5</td>
<td>14.6 ± 5.7</td>
<td>42.7 ± 20.1</td>
</tr>
</tbody>
</table>

[Weight loss outcomes at 1 month and 6 months post-ESG]

Of the 64/66 (97.0%) of patients with 6 month follow-up data, 81.3% achieved ≥10% TBWL, 45.3% achieved ≥15% TBWL, and 85.9% achieved ≥25% EWL. In the ITT analysis, 78.8% achieved ≥10% TBWL, 43.9% achieved ≥15% TBWL, and 83.3% achieved ≥25% EWL at 6 month follow-up. There were 2 (3.0%) serious adverse events. Both were peri-gastric inflammatory collection requiring hospitalisation (4 and 8 days), intravenous antibiotics, laparoscopic washout and percutaneous drainage. Both patients recovered uneventfully without long-term sequelae.

Conclusion: This single-centre study of 66 consecutive patients undergoing ESG for obesity demonstrates reproducibility of the strong efficacy and safety profile of ESG outside the core facilities where the procedure was developed. Patients achieved 14.6% TBWL and 42.7% EWL at 6 months. These results are comparable to the multicentre study across the pioneering centres, in which 248 patients undergoing ESG achieved 15.2% TBWL at 6 months. In ITT analysis, at 6 months 83.3% achieved ≥25% EWL, which is the 12 month efficacy threshold for a bariatric procedure to be incorporated into clinical practice, as determined by the American Society of Gastroenterology (ASGE) Bariatric Task Force.

The limitations of this study are the lack of control group and limited long-term follow up. Weight loss at 6 months has been shown to predict weight maintenance and further weight loss at 2 years, so we would anticipate the majority of our patients to have favourable longer-term results. This study adds to the growing evidence that ESG is a highly effective, reproducible and safe treatment option for patients with obesity.

Disclosure: Nothing to disclose.

References
Aims and Methods:

The gastric mucosal change after eradication was classified into three histological categories. A group A, B, C viewpoint (easy, moderate, difficult) was histologically examined. The easy group (group A) classified the mucosal surface to easy observation due to the development of mucous adhesion and swollen gastric fold. The moderate group (group B) comprised the gastric folds, endoscopic appearance did not change before and after eradication in this group. The difficult group (group C) classified the gastric folds not clearly appeared after eradication and this change made it obviously complicated and difficult to detect. The age, sex and other variables did not have significant difference in each group. We analyzed this gastric mucosal surface irregularity in histologically. We found that the reason of gastric mucosal irregularity consisted of gastric foveolar epithelial hyperplasia and intestinal metaplasia after eradication. In other words, gastric surface irregularities after eradication became gradually apparent with atrophic changes after eradication. We considered that the main reason of surface irregularities in the gastric mucosa after eradication was the development of gastric foveolar epithelial hyperplasia and intestinal metaplasia after eradication. Therefore, we examined the stomach after eradication, the endoscopic examination should be done with sufficient consideration that endoscopic diagnosis becomes complicated and becomes difficult in the eradicated stomach.

Results:
The gastric mucosal change after eradication was classified into three groups (A, B, C) from the viewpoint of easiness (difficulty) of endoscopic observation. Group A is the easy group after eradication: 92.7% (175/352). This group is easy to observe after eradication due to the development of mucous adhesion and swollen gastric fold. Group B is the unchanged group after eradication: 24.7% (87/352), endoscopic appearance did not change before and after eradication in this group. Group C is the difficult group after eradication: 25.6% (90/352), endoscopic appearance occurred after eradication and this change made it obviously complicated and difficult to detect. The age, sex and other variables did not have significant difference in each group. We analyzed the gastric mucosal surface irregularity in histologically. We found that the reason of gastric mucosal irregularity consisted of gastric foveolar epithelial hyperplasia and intestinal metaplasia after eradication. In other words, gastric surface irregularities after eradication became gradually apparent with foveolar epithelial growth and metaplastic change after eradication. Approximately one fourth of the stomach after eradication, it is considered that endoscopic diagnosis of detecting GC becomes difficult. In the gastric mucosa where proper gastric glands remain, foveolar epithelial hyperplasia occurs in the process of repair and regeneration after inflammation. This is considered that the main cause of surface irregularities in the gastric mucosa after eradication. On the other hand, it seems that such a change does not occur in the gastric mucosa which has been completely replaced by intestinal metaplasia without proper gastric gland remaining.

Conclusion:
The aim of this study is to elucidate what changes are occurring on the gastric mucosal surface after Hp eradication. Endoscopic images of 352 cases who received Hp eradication therapy were collected (from Jan. 2015 to Nov. 2017). We examined the presence of gastric mucosal changes on all endoscopy files before and after eradication in each case. We checked the presence of irregularities on the gastric mucosal surface, and all cases were examined histologically with biopsy samples. In the histological evaluation, we analyzed the cause of surface irregularity and were measured the thickness of gastric foveolar epithelial and proper gastric glands.

Nothing to disclose

Disclosure:
Nothing to disclose

Conclusion:
Both treatments are effective in promoting weight loss; however, the combination with liraglutide seems to promote an even greater weight loss without increasing complication. Liraglutide shows to be a great adjuvant drug for the intragastric balloon therapy.

Disclosure:
Nothing to disclose

Introduction:
Onset of amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease with bulbar impairment. Weight loss is one of the major factors affecting the progress and survival in ALS. Weight loss is also an independent prognostic factor for survival. Thus, the use of nutritional support is important for ALS patients. Numerous studies have been performed on the use of percutaneous endoscopic gastrostomy (PEG) to deliver nutritional support. The effects of PEG insertion on patients with ALS have been published in many studies. The majority of patients placed a 20Fr PEG (63%) and under sedation with midazolam (80%), all under non-invasive ventilation (NIV). There were no immediate complications during and after the procedure (no episodes of aspiration or orotracheal intubation) and mortality. The 30-day, 180-day and 360-day mortality rates were, respectively, 5.1, 7.1% and 11.6%.

Conclusion:
The PEG insertion is performed in patients with ALS to improve the swallowing function and the postpone the mechanical ventilation. We aimed to evaluate the efficacy and complications of intragastric balloon and liraglutide single therapies are used worldwide to treat excess weight and obesity. However, there is no published study with both treatments combined.

Aims and Methods:
We aimed to evaluate the efficacy and complications of intragastric balloon therapy alone and combined with liraglutide. Patients with BMI above 27 kg/m² were included. Patients at risk of baseline gastroesophageal reflux disease (Type II diabetes, age greater than 60 years) were excluded. Patients were randomly divided into two groups. One group was submitted to the isolated therapy with Orbera intragastric liquid balloon, with permanence of 6 months. The second group, besides the IGB implant, received a daily dose of liraglutide (1.8 mg, mean). Data were analyzed using descriptive statistical methods, Student’s t-test and analysis of variance followed by the Tukey post-test.

Results:
30 patients (64 women) were randomly divided into two groups of 45 people with the same composition (32 women and 13 men). The mean age was 34.4 (21–57), the mean initial BMI in group 1 was 33.93 and in group 2, 33.95. 42 patients in group 1 completed treatment compared to 31 patients in group 2.

The results regarding the initial and final BMI, TBLW EWL, weight loss in kg are shown in Table 1.

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
</tr>
<tr>
<td>initial</td>
<td>33.93 ± 1.94</td>
</tr>
<tr>
<td>final</td>
<td>27.72 ± 1.66</td>
</tr>
<tr>
<td>reduction</td>
<td>6.21 ± 0.88</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>initial</td>
<td>97.98 ± 8.87</td>
</tr>
<tr>
<td>final</td>
<td>80.08 ± 7.34</td>
</tr>
<tr>
<td>Weight loss (kg)+</td>
<td>17.90 ± 2.87</td>
</tr>
<tr>
<td>TWL (%)+</td>
<td>18.29 ± 2.16</td>
</tr>
<tr>
<td>EWL (%)+</td>
<td>71.81 ± 14.50</td>
</tr>
</tbody>
</table>

*p < 0.001 comparing final and initial values, p+ < 0.001 between groups

Disclosure:
Nothing to disclose

Introduction:
Onset of amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease with bulbar impairment. Weight loss is one of the major factors affecting the progress and survival in ALS. Weight loss is also an independent prognostic factor for survival. Thus, the use of nutritional support is important for ALS patients. Numerous studies have been performed on the use of percutaneous endoscopic gastrostomy (PEG) to deliver nutritional support. The effects of PEG insertion on patients with ALS have been published in many studies. The majority of patients placed a 20Fr PEG (63%) and under sedation with midazolam (80%), all under non-invasive ventilation (NIV). There were no immediate complications during and after the procedure (no episodes of aspiration or orotracheal intubation) and mortality. The 30-day, 180-day and 360-day mortality rates were, respectively, 5.1, 7.1% and 11.6%.

Conclusion:
The PEG insertion is performed in patients with ALS to improve the swallowing function and the postpone the mechanical ventilation. We aimed to evaluate the efficacy and complications of intragastric balloon and liraglutide single therapies are used worldwide to treat excess weight and obesity. However, there is no published study with both treatments combined.

Aims and Methods:
We aimed to evaluate the efficacy and complications of intragastric balloon therapy alone and combined with liraglutide. Patients with BMI above 27 kg/m² were included. Patients at risk of baseline gastroesophageal reflux disease (Type II diabetes, age greater than 60 years) were excluded. Patients were randomly divided into two groups. One group was submitted to the isolated therapy with Orbera intragastric liquid balloon, with permanence of 6 months. The second group, besides the IGB implant, received a daily dose of liraglutide (1.8 mg, mean). Data were analyzed using descriptive statistical methods, Student’s t-test and analysis of variance followed by the Tukey post-test.

Results:
30 patients (64 women) were randomly divided into two groups of 45 people with the same composition (32 women and 13 men). The mean age was 34.4 (21–57), the mean initial BMI in group 1 was 33.93 and in group 2, 33.95. 42 patients in group 1 completed treatment compared to 31 patients in group 2.

The results regarding the initial and final BMI, TBLW EWL, weight loss in kg are shown in Table 1.
**P0781** DIAGNOSTIC ACCURACY USING ARTIFICIAL INTELLIGENCE-ASSISTED ENDOSCOPY FOR SESSILE SERRATED ADENOMA/POLyps

Y. Ogawa1, S. Kudo1, Y. Mori1, M. Misawa1, K. Takeda1, S. Katozka1, Y. Maeda1, K. Ichimasa2, T. Ishigaki2, H. Nakamura1, N. Ogata1, T. Kudo1, K. Wakamura1, T. Hayashi1, F. Ishida1, H. Inoue2, H. Isoh1, M. Oda1, K. Mori1
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Introduction: sessile serrated adenoma/polyps (SSA/Ps) should be resected because they are known to be precursors of CRCs. Accurate endoscopic criteria for differentiating SSA/Ps from hyperplastic polyps (HPSs) are necessary. However, endoscopic differentiation with histological eyes is difficult. In this study, we evaluated the performance of the newly developed artificial intelligence (AI) in endoscopic identification of SSA/Ps.

Aims and Methods: We developed the AI system based on the previously proposed model. The AI system was combined with endoscopy which enables in vivo observation of cellular images at 300-fold magnification (CF-H290EC1 or CF-Y0058, prototype from Olympus Co.). The diagnostic algorithm of the AI consisted of the sequence of image acquisition, extraction of 312 visual features from nuclear images and contrast difference of the whole image and classification into two pathological groups (SSA/P and non-SSA/P).

We designed this retrospective study to assess the performance of the AI system for prediction of SSA/Ps by using 18 SSA/Ps (641 images) and 49 HPSs (1228 images) resected between Sep. 2017 and Feb. 2018.

The main outcome measures were diagnostic sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the AI system in identifying SSA/P in high confidence (probability > 90%).

Machine learning for the AI was performed by using 28000 images which were images (SSA/P 102 images, HP 425 images) out of total 1869 images immediately system showed sensitivity of 11.8%, specificity of 99.5%. PPV in high confidence Y. Maeda1, K. Ichimasa1, T. Ishigaki1, H. Nakamura1, N. Ogata1, T. Kudo1, A. Mori1
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2Showa University Koto-Tokyo Hospital, Digestive Disease Center, Tokyo, Japan

Results: The AI system automatically output the pathological prediction of 527 images (SSA/P 102 images, HP 425 images) resected between Sep. 2017 and Feb. 2018.

The main outcome measures were diagnostic sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of the AI system in identifying SSA/P in high confidence (probability > 90%).

Machine learning for the AI was performed by using 28000 images which were acquired from Jan. 2016 to Aug. 2017. In the lesion-based analysis, diagnosis of the target lesion was defined as SSA/P when the AI system showed at least one SSA/P output.

Results: The AI system automatically output the pathological prediction of 527 images (SSA/P 102 images, HP 425 images) out of total 1869 images immediately with high confidence (probability > 90%). In the image-based analysis, the AI system showed sensitivity of 11.8%, specificity of 99.5%, PPV in high confidence was 85.7% and NPV was 82.5%. However, in the lesion-based analysis AI system showed sensitivity of 27.8%, specificity of 95.9%.

**Pathology**

<table>
<thead>
<tr>
<th></th>
<th>SSA/P</th>
<th>Hyperplastic polyp</th>
</tr>
</thead>
<tbody>
<tr>
<td>AI output</td>
<td>SSA/P</td>
<td>12 2</td>
</tr>
<tr>
<td>(High confidence)</td>
<td>non-SSA/P</td>
<td>90 423</td>
</tr>
</tbody>
</table>

**Conclusion:** This study revealed AI system diagnosed SSA/P with high specificity, but low sensitivity in high confidence. However, further accumulation of endoscopic images for machine learning is required to make more robust model for diagnosing SSA/Ps.

Disclosure: Nothing to disclose

Reference

**P0782** A COMPARISON OF PERFORMANCE PARAMETERS FOR COLONOSCOPY FOR USING DIFFERENT ENDOSCOPY SYSTEMS: A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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2Rajratani Hospital, Bangkok, Thailand
3Shengjing Hospital, Dept. of Endoscopy, Shenyang, China
4Yaroslavl Clinical Oncology Hosp., Department of Endoscopy, Yaroslavl, Russian Federation
5University Medical Center Mainz, Interdisciplinary Endoscopy, Mainz, Germany

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Introduction: High-definition imaging should be the standard for diagnostic endoscopy and optimized patient care. However, many units still suffer from the high costs of these systems. Most recently, a novel brand offering high-definition imaging was introduced to the market which is significantly less expensive compared to most traditional endoscopy brands.

Aims and Methods: To investigate the performance parameters of colonoscopy between the new brand (Sonoscape) and established competitors (Pentax and Olympus). A prospective, multicentre, randomised controlled, parallel, non-inferiority trial conducted in 5 endoscopy units located in Germany, Italy, Thailand, China and Russia was conducted. Performance parameters assessed were cecal intubation time, withdrawal time, total examination time, number of polyps detected, and average size of polyps.

Results: A total of 252 patients were included. No significant differences were noted between the different groups regarding gender, age, previous surgery or bowel preparation. Cecal intubation time (Sonoscape 8 minutes vs. 7 (Pentax)/10 minutes (Olympus); p = NS) and withdrawal time (10.5 minutes vs. 8 (P)/9 minutes (O); p = NS) with the new brand was not significantly different to the others. Polyps were detected in 39% of patients with the new brand compared to 33% (P) and 43% (O) with the others (p = NS). Average size of the polyps detected was 5mm for the new brand and 6mm/5mm for the others (p = NS).

Conclusion: The performance of the new endoscopy brand is not inferior to that of the other brands studied. Therefore, future research should now focus on the image quality and the applicability for predicting histology. Major advantage of the new system is the low price which makes it even achievable for smaller sized endoscopy units.

Disclosure: Nothing to disclose

**P0783** DIAGNOSTIC ABILITY OF BLUE LIGHT IMAGING FOR PREDICTING DEEP SUBMUCOSAL INVASION IN COLORECTAL LESIONS

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Introduction: Blue Light Imaging (BLI) was recently introduced as a novel imaging technology allowing for enhanced visualization of the mucosal surface and vascular pattern morphology. Data regarding the applicability of BLI for prediction of deep submucosal invasion of colorectal lesions is missing.

Aims and Methods: Main study objective was to assess the potential of BLI for prediction of deep submucosal invasion of colorectal lesions. Consecutive patients undergoing screening or surveillance colonoscopy were prospectively evaluated using a high-definition endoscope with BLI capability. Circumscript lesions were examined with BLI before taking biopsy specimens or performing endoscopic resection. BLI images were graded according to surface and vascular pattern morphology and correlated with conventional histopathology in a prospective and blinded fashion.

Results: 120 cases were included. BLI yielded high-quality images in all cases. Based on pit pattern and vascular alterations BLI could predict the presence of deep submucosal invasion with high sensitivity (95%), specificity (91%) and accuracy (93%). Positive and negative predictive values of BLI for in vivo diagnosis of deep submucosal invasion were 88% and 95%, respectively.

Conclusion: BLI is a novel diagnostic tool allowing for real-time prediction of deep submucosal invasion of colorectal lesions with high accuracy. This becomes of crucial importance in clinical practice and could lead to an optimized and rapid diagnosis of neoplastic changes during ongoing endoscopy and an individualized management approach.

Disclosure: Nothing to disclose
Results: The location, size, and shape of the polyps were not statistically significant difference between the two groups. The CRR was not significantly different between the two groups. (Thin mini-snare group: 75.0% vs thick mini-snare group 89.4%, p = 0.068) There was no significant difference between the two groups in immediate bleeding (18.8% vs 6.4%), tissue retrieval (100% vs 100%), and tissue fly away (2.1% vs 0.0%, p = 0.32). Histopathologic features including specimen size, safety margin (996±0.160 mm vs 135±0.192 mm) and containing submucosal tissue in the resected specimen (6.3% vs 10.6%, p = 0.442) were not significant difference between the two groups. Regarding CRR related factors, experience of endoscopist was associated with CRR in univariate regression analysis. (odds ratio 4.037, p = 0.012). However, snare type, experience of endoscopists, size of polyp, shape of polyp, location of polyp and pathologic finding were not associated with CRR by multiple logistic regression analysis.

Conclusion: Cold snare polypectomy using thin wire mini-snare is considered to have no additional benefit compared to using thick wire mini-snare in small size (5–8 mm) colorectal polyps.

Disclosure: Nothing to disclose

P0786 COMPARISON OF THE CLINICAL EFFICACY OF THE COLD SNAKE POLYPECTOMY USING A THIN WIRE MINI-SNARE AND THICK WIRE MINI-SNARE FOR SMALL SIZE (5–8 MM) COLORECTAL POLYPS

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Introduction: Cold snare polypectomy (CSP) is established technique for the resection of colorectal polyps up to 10 mm in size without electrical current. However, there is a lack of comparative studies using a thin wire mini-snare (designed for CSP) and thick wire mini-snare during CSP. Thus, the aim of this study was to compare the clinical effectiveness of thin wire mini-snare and thick wire mini-snare during CSP in small colonic polyps.

Aims and Methods: This study was a prospective, randomized and controlled study. Between September and November 2017, a total of 113 neoplastic colorectal polyps were resected using CSP and included in this study. The primary outcome was complete resection rate by histopathologic features of resected specimens were carefully analyzed.

Results: A total of 113 eligible polyps were successfully resected using CSP (thin mini-snare group n=48) and thick mini-snare group (n=65) by 4 endoscopists.

Table 1. Demographic and procedural data pooled from six RCTs.

<table>
<thead>
<tr>
<th>Procedure outcomes and adverse events</th>
<th>Thin wire mini-snare group (n=48)</th>
<th>Thick wire mini-snare group (n=65)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete resection rate (%)</td>
<td>75.0% (36/48)</td>
<td>89.4% (42/47)</td>
<td>0.068</td>
</tr>
<tr>
<td>Retraction rate (%)</td>
<td>48 (100.0%)</td>
<td>47 (100.0%)</td>
<td></td>
</tr>
<tr>
<td>Fly away (%)</td>
<td>1 (2.1%)</td>
<td>0 (0.0)</td>
<td>0.320</td>
</tr>
<tr>
<td>Containing submucosa tissue in the resected specimen (%)</td>
<td>3 (6.3%)</td>
<td>5 (10.6%)</td>
<td>0.441</td>
</tr>
<tr>
<td>Size of specimen (μm, Mean ± SD)</td>
<td>8211.1 ± 504.93</td>
<td>8738.86 ± 716.71</td>
<td>0.585</td>
</tr>
<tr>
<td>Safety margin (mm, Mean ± SD)</td>
<td>996.08 ± 160.38</td>
<td>1358.89 ± 191.82</td>
<td>0.149</td>
</tr>
<tr>
<td>Depth Mucosa Submucosa</td>
<td>87 (91.6%)</td>
<td>45 (93.7%)</td>
<td>0.442</td>
</tr>
<tr>
<td>Depth (μm, Mean ± SD)</td>
<td>564.85 ± 304.92</td>
<td>454.96 ± 47.91</td>
<td>0.685</td>
</tr>
<tr>
<td>Complication (%) Immediate bleeding Delayed Bleeding Perforation</td>
<td>9 (18.8%)</td>
<td>3 (6.4%)</td>
<td>0.070</td>
</tr>
<tr>
<td>(primary outcome) (4.4% vs. 6.5%, p = 0.003)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0.970 -</td>
</tr>
</tbody>
</table>

Conclusion: To highlight the clinical relevance of WE, the hypothesis that we significantly increased ≥ 10 mm advanced ADR compared to air insufflation (AI) was tested. Data from six RCTs that compared AI to WE were pooled. The current primary outcome is based on previously unreported data.

Results: Table 1. Demographic and procedural data pooled from six RCTs. 5407 patients were randomized to AI (2699) or WE (2708): screening 35% and 32% (p = 0.003); surveillance 9% and 10%; positive fecal occult blood 50% and 50%; respective, WE showed significantly higher ≥ 10 mm advanced ADR (primary outcome) (4.4% vs. 6.5%, p = 0.001); higher overall ADR (20.9% vs. 27.4%, p = 0.001); higher all sizes advanced ADR (5.7% vs. 8.2%, p = 0.001);
Abstract No: P0787

Method (no. of patients) AI (n = 2699) WE (n = 2708) p
Age, year, mean (SD); 54 (12) 54 (12) 0.807
Male, n (%) 1476 (55) 1468 (54) 0.743
Insertion(Screening, n (%); [Surveillance, n (%)]; [FIT+ or FOBT+, n (%)]) 11350 (50); 11366 (50) 0.010; [0.102]; [0.999]
Cecal intubation (insertion) time, minutes, mean (SD); [Cecal intubation rate, n (%)]
Primary outcome: Combined ≥10 mm advanced ADR, n (%) 69 (5); 2614 (97) <0.001; [0.293]
Combined overall ADR, n (%) 120 (4.4) 176 (6.5) <0.001
Combined all sizes advanced ADR, n (%) 564 (20.9) 742 (27.4) 0.001
P values were obtained using t-test or Fisher's exact test, as appropriate. ADR, adenoma detection rate; AI, air insufflation; FIT, fecal immunochemical test; FOBT, fecal occult blood test; RCTs, randomized controlled trials; SD, standard deviation; WE, water exchange. Withdrawal time was > 8 minutes in both groups. RCTs included in pooled analysis: 1: Gastrointest Endosc 2010;72:693 (unsedated) NCT00747084. 2: J Interiv Gastroenterol 2013;3:7 (unsedated) NCT01383252. 3. Endoscopy 2014;46:212 (On demand minimal sedation) NCT01781850. 4. Am J Gastroenterol 2017;112:568 (Unsedated or propofol) NCT02135601. 5. Gastrointest Endosc 2017;49:456 (On demand minimal sedation) NCT02041507. 1 and 2 used non-split-dose; 3, 4, 5 & 6 used split-dose. In 1, 2, 3, 4, 5 & 6, WE bowel cleanliness during withdrawal was significantly better than AI. Total number of colonoscopists: 22. The longer cecal intubation time of WE was devoted to insertion salvage cleansing, and not a factor contributing to enhanced ADR. The trends of higher ≥10 mm advanced ADR, higher all sizes advanced ADR and higher overall ADR were present in all six RCTs (p < 0.5, sign test).

P0788 CAP-ASSISTED ENDOSCOPIC MUCOSAL RESECTION VERSUS ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL NEUROENDOCRINE TUMORS: A MULTICENTER RETROSPECTIVE STUDY FROM CHINA

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Introduction: Cap-assisted endoscopic mucosal resection (EMR-C) and endoscopic submucosal dissection (ESD) have been reported to be effective treatment methods for small rectal neuroendocrine tumor (NET) in limited studies. We aimed to compare the outcomes of EMR-C and ESD to determine which one is better for the treatment of rectal NET.

Aims and Methods: We retrospectively collected 702 patients diagnosed with primary rectal NET from January 2007 to September 2017 in eight tertiary medical centers from China. Clinicopathological characteristics, en bloc resection rate, operating time, estimated blood loss, complications, postoperative hospital days, recurrences were recorded and compared.

Results: Among the 702 patients, 279 meet the criteria and were enrolled in the study. 104 patients (37.28%) received EMR-C and 175 patients (62.72%) received ESD treatment. The demographic characteristics of the patients and the tumor size were well balanced. We did not observe significant difference concerning about en bloc resection rate (100% vs. 98.85%, p = 0.531) and pathologic R0 resection rate (97.11% vs. 94.28%, p = 0.382) between EMR-C group and ESD group, respectively. However, shorter operating time and less estimated blood loss were observed in EMR-C group (7.00 ± 4.79min vs. 21.73 ± 14.36min, p = 0.027; 4.17 ± 2.89ml vs. 6.75 ± 3.22ml, p = 0.039, respectively). There was also no significant difference concerning about complications and no serious adverse events were observed. Kaplan-Meier curves for non-recurrence survival and survival analysis showed that there were no significant differences between two groups.

Conclusion: EMR-C may be preferable for removal of small rectal NET (≤10 mm) with shorter operating time and postoperative hospital days, less blood loss and hospitalization cost compared with ESD. Prospective randomized controlled trials are further needed.

Disclosure: Nothing to disclose
Abstract No. P0789

P0789 IMPROVED ENDOSCOPIC RESSECTION OF LARGE FLAT LESIONS USING AN EXTERNAL ADDITIONAL WORKING CHANNEL (AWC)

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Introduction: En-bloc resection of lateral-spreading polyps, flat lesions larger than 2 cm in size, or early stages of cancer can be challenging. Endoscopic mucosal resection (EMR) offers the opportunity for resection in piece-meal technique, but completeness (R0) of the resection remains unclear. In contrast, standard endoscopic submucosal dissection (ESD) is complex, time consuming and associated with a significant rate of perforation. Furthermore for standard endoscopes no bi-manual tasks are possible. Additionally resection technique is faced by limited steer-ability and degrees of freedom. The two channel endoscopes are expensive, not available everywhere and have a small distance between the channels.

Aims and Methods: Here, we report our first experience using a new external additional working channel (AWC) (Ovesco, Tübingen, Germany). ESD and EMR with a modified grasp and snare technique was performed. The device can be fixed at the tip of a standard gastroscopy or pediatric colonoscope. The distance of the two working channels can be adjusted by the endoscopist. Via the AWC a second endoscopic tool can be inserted and used for bi-manual workflow.

Results: EMR with modified grasp and snare technique was performed successfully in 4 patients (1 upper GI tract, 3 lower GI tract). ESD was performed successfully in 4 patients (2 upper GI tract, 2 lower GI tract) (Table 1). Mean procedure time (scope-in to scope-out) was 68.5 min.

Conclusion: So far, based on our preliminary experience, we conclude that a new developed external additional working channel (AWC) enables endoscopic resec- tion of large lesions in the upper and lower GI tract. Potential benefits are its suitability for EMR and ESD, no need for dual-channel endoscope and an adjustable distance of working channels.

Disclosure: Nothing to disclose

Abstract No. P0790

P0790 CAN SERT SCORE PREDICT HISTOLOGICAL RECURRENCE IN PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION? COMPARATIVE STUDY WITH SMSA SCORE

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Introduction: Piecemeal endoscopic mucosal resection (pEMR) allows resection of larger non-invasive colorectal lesions. Histological recurrence (HR), deter- mined in surveillance colonoscopy after pEMR, is still a difficult to predict. SERT score (Sydney EMR-recurrence tool) predicts endoscopic recurrence (ER), nevertheless it has not been validated as a predictor of HR.

Aims and Methods: The present study aimed to validate SERT score as a pre-dictor of ER and HR and compare its predictive value to the SMSA score (size, morphology, site, access).

SERT and SMSA score were calculated for all lesions resected by pEMR between 2012-2018. At first surveillance colonoscopy, performed at 3-6 months, RE and RH were evaluated. In the absence of ER, biopsy of pEMR scar was performed in most cases. In patients with ER the removal of the residual lesion was attempted.

Results: 188 pEMR were considered. In the studied population, 61.7% were men and the mean age was 66.1 ± 9.8. Most lesions were located at the right colon (59.0%). The average size was 30.99 ± 13.8 mm. Considering Paris Classification, lesions 0-IIa + 0-IIb (42.0%) and 0-IIa + 0-IIb (39.4%) were more common. The overall HR rate was 23.4% (n = 44). ER occurred in 27.1% (n = 51), and in 72.5% of these cases (n = 37) HR was confirmed. In patients without ER, the HR rate was 4.9% (n = 7). There was a strong correlation between the SERT and SMSA scores (R2 = 0.61). There was a significant association between SMSA score and ER (p < 0.001) as well as HR (p < 0.001). A SERT ≥ 2 score was significantly associated with ER (p = 0.002) and HR (p = 0.015).

Conclusion: SERT score correlates with the SMSA score and both can be used to predict ER and HR in lesions removed by pEMR. SMSA score showed greater discriminative power for recurrent lesions. SERT score is less complex and allows predicting not only ER as RH.

Disclosure: Nothing to disclose

Abstract No. P0791

P0791 CLINICAL OUTCOMES AND PATIENTS’ SATISFACTION FOR NOVEL PATIENT REFERRAL SYSTEM CALLED ‘SAME-DAY POLYPECTOMY’

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Introduction: Substantial number of patients who diagnosed with polyps on screening colonoscopy undergo subsequent colon polypectomy on a separate day at referral hospital. We developed novel patient referral system called ‘Same-day polypectomy’ that performs colon polypectomy in tertiary hospital after same day referral from private clinics.

Aims and Methods: The aim of this study was to compare the clinical outcomes between conventional elective polypectomy and ‘Same-day polypectomy’ and to evaluate the patient’s satisfaction with this novel system.

Methods: Retrospectively reviewed prospectively enrolled colonoscopy database in a single referral center. A total of 122 patients were referred to Gangnam Severance hospital for polypectomy between July 2017 to December 2017. Among them, 57 patients received ‘same-day polypectomy’, and remaining 55 patients underwent conventional elective polypectomy. Polyp characteristics, complications, degree of bowel cleanliness using Boston Bowl Preparation Scale (BBPS) were compared between these two groups. Patients’ satisfaction for the ‘same-day polypectomy’ was assessed through questionnaires.

Results: There were no significant differences in the location and average number of resected polyps between two groups. However, the polyps in ‘same-day polypecto-my’ group were smaller in size than those of elective polypectomy group (6.3 ± 3.2 mm vs. 10.9 ± 8.7 mm, p < 0.001), and were more frequent in polypoid type. Moreover, mean total BBPS score was lower in ‘same-day polypectomy’ group than in elective polypectomy group (6.8 ± 1.6 vs. 8.4 ± 1.0, p < 0.001).

Conclusion: Our novel ‘same-day polypectomy’ is safe and acceptable patient referral system with high patients’ satisfaction.

Disclosure: Nothing to disclose
colonoscopy (as part of the endoscopic report, or added to the pathologic report, or handwritten on the pathologic report, or in a follow-up clinic visit report). After intervention, 62% of recommendations were written in the new electronic form, of which 79% were consistent with guidelines. When the electronic form wasn’t used, only 59% were consistent with the guidelines (p = 0.009).

Conclusion: Intervention, by guideline re-affirmation, and creation of a dedicated reporting form, significantly increases the number of well documented follow-up recommendations after polypectomy, and their consistency with societal guidelines.

Disclosure: Nothing to disclose

P0793 FACTORS INFLUENCING ACHIEVEMENT OF ADEQUATE BOWEL PREPARATION: ANALYSIS OF THE EUROPEAN COLONOSCOPY QUALITY INVESTIGATION GROUP (ECQI) PROCEDURAL QUESTIONNAIRE


Introduction: Assessment and rate of adequate bowel preparation are important quality measures for colonoscopy according to European Society of Gastrointestinal Endoscopy (ESGE) guidelines. We aimed to assess factors influencing the likelihood of adequate bowel preparation for colonoscopy.

Aims and Methods: The development of the European Colonoscopy Quality Investigation Group (ECQI) online questionnaire has been previously described. We analysed data collected between 2/6/16 and 31/1/18. A univariate logistic regression analysis was performed to assess which factors influence achievement of adequate bowel preparation, defined as a Boston Bowel Preparation Scale (BBPS) score ≥6.

Results: Data from 4447 completed questionnaires were analysed. 126 procedures were excluded due to insufficient information to establish adequacy of bowel cleanliness; of the remainder, 3726 (86%) procedures scored BBPS ≥6 and 195 (14%) BBPS < 6.

The achievement of adequate bowel cleansing was significantly affected by age (< 50 vs. ≥ 50 odds ratio (OR) 2.05, p < 0.001), gender (male vs. female OR 0.77, p = 0.004), inpatient status (inpatient vs. outpatient OR 0.42, p < 0.001), total quantity of fluid consumed (p < 0.001), dosing regimen (p < 0.001), the quantity of bowel preparation consumed (p < 0.001), and the duration between procedure and the last intake of bowel preparation (p < 0.001) (table 1). Reason for procedure also had a significant affect (p < 0.001), with screening due to familial risk increasing the likelihood of BBPS ≥ 6 (vs. clinical signs and symptoms OR 2.02, p = 0.004). Whether the patient followed instructions has a large influence on bowel clearance (yes vs. no OR 7.07, p < 0.001).

Conclusion: Adequacy of bowel preparation can be affected by age, gender and in/outpatient status. Indication can also influence adequacy of bowel clearance, along with both the total quantity of fluid and the quantity of bowel preparation consumed. In addition, using a split-dosing regimen with the last dose taken within 5 hours of the procedure appears to increase the likelihood of a BBPS ≥ 6. Ensuring good explanation of how to take the bowel preparation and stressing the importance of following instructions to the patient could also improve bowel clearance. Further information can be found at www.ecqigroup.eu

Disclosure: Amaro A, Agrawal A, Brink L, Hüniger M, Jover R, Ono A, Petruzziello L, Toth E; Consultancy and Advisory Board participant to Norgine: Spada C; Consultant fee from Norgine: Fischbach W; Consultancy and Advisory Board participant to Norgine; Speaking – Abbott, Bio Merieux, Falk, Merck Serono, Novartis, Nycoderm, Sanofi Aventis, Shire; Advisory speaking – AstraZeneca, Fresenius Biotech, Pfizer; Advisory – Boehringer Ingelheim, med update: Riemann JF in terms of ECQI, consultant to Norgine, otherwise no conflict of interest: Koulaouzidis A; No relevant conflict of interest: Kinnunen U; No conflict of interest: Patai A; No conflict of interest: Curran V; Employee of Norgine.

References

P0794 CLINICAL OUTCOME AFTER COLONSCOPIC POLYPECTOMY OF PATIENTS TAKING DIRECT ORAL ANTICOAGULANTS: COMPARISON WITH CLOPIDOGREL


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Introduction: Direct oral anticoagulants (DOACs) are increasingly used for the prevention of stroke in patients with atrial fibrillation and prevention and treatment of deep vein thrombosis or pulmonary embolism. However, little is known about the outcome after polypectomy of patients under DOACs medication.

Aims and Methods: We performed a retrospective study of patients who had colonoscopy polypectomy at Asan Medical Center from November 2010 to December 2017. We compared the frequency of delayed post-polypectomy bleeding (PPB) for the patients taking DOACs (DOAC group) with patients taking clopidogrel (clopidogrel group).

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Results: A total of 405 patients underwent polypectomy during the study period; 320 were on DOACs and 685 were on clopidogrel. The duration of drug discontinuation before colonoscopy was mean 2.9 ± 1.7 days in DOAC group and 5.9 ± 2.5 days in clopidogrel group, respectively. Patients in each group resumed taking DOACs on mean 1.9 ± 2.9 days and clopidogrel on mean 2.0 ± 1.5 days after polypectomy, respectively. Logistic regression analysis revealed no significant difference in frequency of PPB between DOAC users and clopidogrel users. (1.6% vs 1.6%, p = 0.988, unadjusted OR = 0.977, 95% CI 0.312–3.058).

Conclusion: The risk of post-polypectomy bleeding in patients taking DOACs seems not to be higher than the one of post-polypectomy bleeding in patients taking clopidogrel. Further studies are necessary to evaluate the risk of post-polypectomy bleeding related to DOACs.

<table>
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P0796 DEEP LEARNING FOR REAL-TIME AUTOMATED POLYP LOCALISATION IN COLONOSCOPY VIDEOS

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Introduction: Colonoscopic polypcetection can prevent colorectal cancer. Polyp detection varies considerably due to human error and missed adenomas may contribute to interval colorectal cancers. Automated polyp localisation using deep learning may avoid such problems. Previous work focused on realising the presence of polyps in individual frames captured from videos. Our aim in this pilot study was to extend this to polyp localisation within video sequences and to explore future-proofing by using algorithms trained on old image processors to locate polyps found using newer endoscopic technologies.

Aims and Methods: We trained and validated a Convolutional Neuronal Network (CNN) on 18517 frames created by merging research colonoscopy datasets from the Medical Image Computing & Computer Assisted Intervention Society challenges. 75% of frames contained polyps in both standard and high definition (HD) from older processors including Olympus Exera II (160-165 series) and Pentax EPKI 7000 (90i series). Our test set consisted of 11 HD videos featuring polyps in white light collected using the latest Olympus 290 endoscopes. Estimated median polyp size was 4mm (range 2-15) and morphology included (Paris Classification IIa = 4, Is = 6 and Ia+IIa LST-G = 1). Images were manually annotated by drawing bounding boxes around polyps and quality controlled by removing uninformative frames (e.g. blurred). A total of 2,611 polyp containing frames were included in the test set. Each positive case was scored if the computer-generated segmentation mask prediction overlapped with the bounding box. A false positive indicated a non-overlapping location (more than one can occur per frame).

Results: Our network operated at real-time video rate. F1 score accuracy was 92.5%. Sensitivity for polyp localisation was 98.5% and per-frame specificity 75.4%. Positive predictive value was 90.1%. Incorrect segmentation mask locations were predominantly limited to 3 videos and were generated by artefacts not represented during training.

Conclusion: We demonstrate through analysis of video frames that a CNN can locate polyps with high accuracy in real-time. The algorithm was trained using multiple endoscopic processors and worked with HD images from a new processor. Crucially the algorithm had not previously viewed or trained with any of the images from the new processor. This suggests that the CNN could remain useful as new endoscopic technologies are introduced. Further work will train our model on the larger datasets including complete colonoscopy procedures. This should improve accuracy further. Such a system could be used as a red flag technique to reduce missed adenomas during colonoscopy.

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Introduction: Endoscopic resection of all colonic adenomas improves the mortality caused by colon cancer. Cold polypectomy has been widely accepted for removal of small colorectal polyps on the basis of safety and technical ease. However, careful endoscopic diagnosis for identifying advanced neoplasia is essential at cold polypectomy because of its relative risk of incomplete resection and inappropriate histological evaluation.

Aims and Methods: Our aim is to investigate clinicopathological characteristics of colon polyps <10mm and assess the usefulness of Narrow-band imaging (NBI) magnifying endoscopy for diagnosis of advanced neoplasia. We retrospectively analised all colorectal lesions <10mm which were diagnosed by NBI magnifying endoscopy and resected endoscopically from March 2014 to February 2018. Various clinicopathological characteristics were analyzed. The diagnosis by NBI magnifying endoscopy was performed according to The Japan Narrow-band imaging Expert Team (JNBT) classification, which is a consensus classification...
P0798 THE DIAGNOSTIC ARTIFICIAL INTELLIGENCE (AI) SYSTEM FOR DETECTION OF COLON POLYPS WITH HIGH EFFICIENCY AND LEARNING
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Introduction: In the gastrointestinal endoscopy survey, the small neoplastic lesions are reported to be overlooked. Recently, artificial intelligence (AI) has been shown the remarkable progress in image recognition. The application of AI system for the endoscopic images are expected to be the favorable assistance. The recent AI progressions are primarily due to the availability of large-scale annotated datasets. But the high-quality images of gastrointestinal endoscopy are limited, especially with annotated and segmented datasets. The efficient machine learning system with lower-scale datasets of endoscopic images are needed.

Methods: The aim of this study was to develop the diagnostic AI model for colon polyp detection with efficient learning system. We indicated the single deep convolutional neural network (CNN) named single shot multibox detector (SSD) [1] and the pre-trained mode by the 4952 natural images of PASCAL VOC 2007 for developing the AI diagnostic model. Learning for fine tuning with the small number of non-magnified still images with annotation and segmentation data of protruded small colon polyps (≤10mm) with White Light Imaging, and additional learning by images of normal colon were conducted. The learning system was validated at each points of learning with additional images for learning as follows: (the number of colon polyps: 50, 100, 200, and 300 images, colon polyps and normal colon: 300+300 and 400+400 images) and diagnostic ability was obtained. The validation were conducted by using 200 number of small colon polyps (≤10mm) and 200 number of normal colon which were not used for learning. Additionally, the recognition test for video images by the diagnostic model learned 400 images of polyps and 400 images of normal colon are conducted.

Results: The sensitivity, specificity, accuracy for detecting the small colon polyps were improved as learned images of colon polyps was adding (60.0%, 94.3%, 82.5% by the 50 images learning, 85.0%, 98.1%, 89.5% by the 100 images learning, 90.5%, 93.5%, 92.5% by the 200 images learning, 93.0%, 92.8%, 92.8% by 300 images learning). Additional learning model with normal colon images show improvement of specificity, and the diagnostic model learned by 400 images of colony polyps and 400 images of normal colon show the sufficient diagnostic ability (95.0%, 98.5%, 97.3% by the 300 each images learning, 96.5%, 98.5%, 97.8% by the 400 each images learning). The pilot test by the video endoscopic images show the high frame rate detection for small colon polyps (frame rate > 25/sec).

Conclusion: This AI diagnostic model suggested that the machine learning by latest deep CNN with fine-tuning enables high efficiency of learning for detecting small colon polyps with limited number of teaching image datasets.

Disclosure: Nothing to disclose.

Reference

P0900 ENDOSCOPIC SUBMUCOSAL RESECTION (ESR) – INNOVATIVE METHOD AND INSTRUMENTS FOR RESECTION OF BIG LESIONS IN THE GIT
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Introduction: ESD is being the preferred method for big and complex lesions in the GIT, but some disadvantages of ESD are obvious: 1. Long and flat learning curve 2. Long-lasting and complex procedure 3. Relatively high rate of complications, bleeding and especially perforations 4. Uneven curve of resection 5. Hence, ESD is confined to expert endoscopists. Thus, a new method, called “Endoscopic Submucosal Resection (ESR)” incl. innovative instruments, called “Etal Adenoma Resection Instruments (FARIn)”, have been developed to overcome these drawbacks.

ESR consists like ESD of different steps. First a primary circumferential incision, but then followed by application of resection and with an innovative snare-like resection effector of a FARIn allowing vertically deep end even plan RF-surgical cutting close the muscularis propria without danger of perforation.

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Aims and Methods: First systematic clinical study in 22 patients with 15 big lesions. The location of the lesion was in the colon and one in the stomach. The lesions were bigger than 2 cm or had a high risk of perforation (e.g. submucosal lesion, because of location).

To evaluate safety and efficacy of ESR with FARIn especially the intended protection of the instrument against the wall of the GIT during RF-application to remove the specimen close at the muscularis propria.
In a step-up approach these first patients have been treated without circumferential incision as the first step.
Results: In 22 patients these lesions were removed successfully without relevant complications and without perforation. The rate of en-bloc resection or resection of one large piece with few small pieces was 15 of 22. Optimal cutting quality, no delay of cutting even in very big lesions, a completely even cutting plane close to the muscularis propria and very low thermal artifacts allowed a representative, high-quality histopathology. A pure resection time less than 30 seconds could be achieved in all cases.
The new method of ESR using FARIn proved to be promising, especially the possibility of vertical deep resection without risk of perforation, the high quality of cutting and specimen showed clear advantages compared to conventional snare-resection to ESD.
These findings and a short learning curve due to high ergonomics of the instrument justify further studies including circumcision of the lesion as a first step before application of the snare-like effector of a FARIn to evaluate, if ESR may become a superior alternative to EMR and ESD in therefore suitable cases.
Conclusion: ESR, a new method with innovative instruments for resection of big and complex lesions in the GIT showed in a first clinical assessment remarkably reasonable results in term of efficacy, safety ergonomics and procedure time.
Disclosure: Nothing to disclose

P0801 MELANOSIS COLI: A HELPFUL CONTRAST EFFECT OR A HARMFUL PIGMENTATION?
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Introduction: Melanosis coli is a brown or black discoloration of the colonic mucosa that results from accumulation of lipofuscin pigments in macrophages within the lamina propria. This condition has long been considered as a harmless pigmentation associated with, but not confined to, a long-term use of antihistamine- none laxatives. Several clinical and experimental studies, however, have provided some evidence of a possible relationship between long-term laxative use or melanosis and colorectal cancer risk. Other and more recent studies have shown no association with colorectal cancer. Essentially, the majority of these studies did not include matched controls and may be widely affected by confounders.

MC is usually reported to spare hyperplastic and adenomatous polyps. This enables enhanced visibility and improved observation of polyps in the dark background mucosa, probably linking melanosis coli with an increased polyp detection rate. With this association signifies also a causal relationship due to an oncogenic or toxic effect of melanosis on colonic mucosa is still unknown.

The possible mechanism behind this association is still unknown, but it is suggested that the increased Melanosis coli might be due to increased gut transit time.

The adherence to currently utilized quality indicators was assessed. Statistical analysis of one large piece with few small pieces was 15 of 22. Optimal cutting quality, no delay of cutting even in very big lesions, a completely even cutting plane close to the muscularis propria and very low thermal artifacts allowed a representative, high-quality histopathology. A pure resection time less than 30 seconds could be achieved in all cases.
The new method of ESR using FARIn proved to be promising, especially the possibility of vertical deep resection without risk of perforation, the high quality of cutting and specimen showed clear advantages compared to conventional snare-resection to ESD.
These findings and a short learning curve due to high ergonomics of the instrument justify further studies including circumcision of the lesion as a first step before application of the snare-like effector of a FARIn to evaluate, if ESR may become a superior alternative to EMR and ESD in therefore suitable cases.
Conclusion: ESR, a new method with innovative instruments for resection of big and complex lesions in the GIT showed in a first clinical assessment remarkably reasonable results in term of efficacy, safety ergonomy and procedure time.
Disclosure: Nothing to disclose

Reference

P0802 THE PRESENCE OF A GASTROENTEROLOGY TRAINEE DURING COLORECTAL CANCER SCREENING COLONOSCOPY IMPROVES ADHERENCE TO QUALITY INDICATORS
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Introduction: The effectiveness of colorectal cancer screening colonoscopy depends on increasing colorectal cancer incidence detection rate and on the detection of polyps and the quality of the procedure. Several key quality measures have been proposed to improve the effectiveness of screening colonoscopies [1].

Aims and Methods: We aimed at evaluating quality indicators of CRCSC in a tertiary teaching hospital with high colorectal cancer incidence rates and determine if the presence of trainees influences the quality of CRCSCs. A total of 2118 consecutive CRCSC reports were retrospectively evaluated over a 5 year period. The adherence to currently utilized quality indicators was assessed. Statistical analysis was performed with SPSSv23. A p value <0.05 was considered statistically significant.

Results: The mean age of the patients was 65.5±10.7 years and 56.9% (1205) were women. Sedation was performed in 77.1% (1634) CRCSCs. In 516 (24.4%) of the exams a gastroenterology trainee was present. Cecal intubation rate (CIR) was 86.5% (1833). Most common reasons for an incomplete CRCSC were: patient intolerance 46.3% (132); inadequate bowel preparation 20.4% (58) and technical difficulties with colorectal loop formation and adherences in 15.1% (43). Photodocumentation of cecal landmarks (PCL) was performed in 97.3% (1783) of the cases. Polyp detection rate (PDR) was 34.3% (726), out of which 13.4% (97) of the polyps were ≥1cm in diameter. The Boston Long-lasting Bowel Preparation Score (BBPS) for patients with adequate bowel preparation was 3.5% (530) of CRCSCs. Bowel preparation was considered good in 64.6% (1369) of the cases and fair in 19.7% (417) cases. In multivariate analysis (including gender, age, BBPS, PCL, CIR, PDR and sedation), the presence of a gastroenterology trainee was an independent predictor of compliance to CRCSCs quality indicators: use of BBPS score (OR 7.9, 95% CI 5.7–9.0, p <0.001), PCL (OR 2.8, 95% CI 1.1–6.9, p =0.025) and PDR (OR 1.5, 95% CI 1.2–1.8, p =0.001). The presence of a gastroenterology trainee during CRCSCs was the only independent predictor of a higher PDR (OR 1.6, 95% CI 1.3–2.0, p <0.001).

Conclusion: A suboptimal CIR were mostly due to intolerance and inadequate bowel preparation. The presence of a gastroenterology trainee improved adherence to quality indicators in CRCSCs, namely an adequate description of bowel preparation, the PCL and the CIR.

Disclosure: Nothing to disclose

Reference
higher adenoma detection. ADR was 50% for FUSE, 54% for SFV and 47% for Endocuff. ADR was not significantly different among the three colonoscopies (ARD test). ADR for FUSE vs l.2 in SFV vs 1 and Endocuff (ns). All polyps per colonoscopy (PPC) were 1.8, 1.9 and 1.5 respectively. 4% of all polyps in all groups were carcinomas. Time to ileum was with FUSE 5.4 min, with SFV 3.5 min, with Endocuff 6.3 min. Intervention time was for all groups 3.3 min (showing no difference in the handling of interventions). Withdrawal time was 16.3 min with FUSE, 18.1 min for SFV and 14.1 min for Endocuff (p = 0.04).

Conclusion: In a collective of 2849 patients randomly assigned to 3 different types of colonoscopies neither FUSE nor Endocuff could increase the ADR in a significant way. At present if ADR reaches around 50% no further benefit can be expected from new technology. Key factor for a high ADR seems to be long withdrawal times (e.g. 14 up to 18 min in SFV). FUSE and Endocuff show significantly shorter endoscopy times (FUSE little faster in ascent, Endocuff and FUSE faster in withdrawal), Endocuff even significantly less medication for sedation.

Disclosure: Nothing to disclose

P0804 THE OBJECTIVE EVALUATION USING EYE TRACKING FOR VISIBILITY OF COLORECTAL LESIONS

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Introduction: Recently, image-enhanced endoscopy (IEE) such as blue laser imaging (BLI-bright) and linked-color imaging (LCI) has been reported to improve detection and the miss rate of colorectal lesions. Improvements in visibility due to IEE have been assessed by according to endoscopists' visibility scores in many studies. However, such assessments are subjective, and objective assessments, such as quantifying the time required for endoscopists to detect lesions, are lacking. We have considered that one method of objectively measuring endoscopists' attention in real time, and thus determining the time they need to detect lesions, is eye tracking. Eye tracking uses a sensor to detect exactly where a participant’s eyes are focused. We aimed to objectively assess the detectability of BLI-bright, LCI and WLI in the colorectal lesions using eye tracking.

We recruited 11 endoscopists, 2 experts and 9 trainees, who were required to determine the most effective surveillance method after an endoscopic polypectomy: diminutive polypectomy and techniques for endoscopic imaging of large colorectal polyps. We aimed to objectively assess the detectability of BLI-bright, LCI and WLI in the colorectal lesions using eye tracking.

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P0805 DETERMINING THE MOST EFFECTIVE SURVEILLANCE SYSTEM AFTER AN ENDOSCOPIC POLYPECTOMY: A STUDY BASED ON THE LONG-TERM SURVEILLANCE OF 3,038 PATIENTS

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Introduction: Multiple evidence-based guidelines have been produced recently to address the question of how best to perform colonoscopy polypectomy.

Aims and Methods: We aimed to assess the adherence to these guidelines in 7 countries using an online survey, comparing responses to the standards presented in the 2017 ESGE Colon 1 polypectomy guideline. An institutional review board approved online survey was distributed to the members of gastroenterological and surgical societies of 7 countries via email during July 2017. The survey presented images of colorectal polyps and their colonic location and asked for the polypectomy technique respondents would use in their daily practice. A reminder email was sent after two weeks and the survey closed after 4 weeks.

Results: 19,467 endoscopic practitioners in 7 countries received the survey. Of 772 (4.0%) who responded, 707 (91.6%) fully completed the survey and their data was analysed. 162, 155, 131, 102, 60, 53 and 45 respondents were from Australia, USA, UK, Belgium, Canada, Israel and New Zealand respectively. 625/707 (88.6%) were surgeons and 131/707 (18.5%) were other gastroenterologists. Respondents had a median endoscopy practice duration of 18 years (IQR 10-27). Of two images of < 10 mm right sided colon polyps presented, 51.1% of respondents suggested they would perform cold snare polypectomy in line with guidance. In 45mm lesions, however, suggested cold biopsy forceps and 37.7% would have biopsied the 45mm lesion prior to referral. 9% suggested they would refer these lesions directly to a surgeon. Regarding an image of a large 80mm sigmoid lesion with an endoscopically visible demarcated area consistent with deep submucosal invasive cancer, 51.6% said they would refer to a surgeon in line with guidance whereas 27% suggested they would attempt EMR. 1.4% ESD and the remainder refer the case to another endoscopist.

Comparing the adherence to guidelines throughout all questions, surgeons (50%) were less adherent than physicians (65%), p < 0.001, consultants (63%) similar to trainees (67%), p = 0.122 and those who had undertaken an interventional endoscopy fellowship (63%) similar those who had not (64%), p = 0.450.

Conclusion: These data demonstrate encouraging adherence to international endoscopy guidelines. The work of international endoscopy societies should focus on developing a system of guidelines. The work of international endoscopy societies should focus on developing a system of guidelines. The work of international endoscopy societies should focus on developing a system of guidelines. The work of international endoscopy societies should focus on developing a system of guidelines.
Patients (n = 3,038) who adhered to this surveillance programme were enrolled in this study. There were 1,866 males (61%) and 1,172 females (39%). The mean age was 61.2 ± 10.9 years and the observation period was 3.1 years (maximum 11 years) on average.

The detection rate of cumulative adenoma and the cumulative detection rate of advanced neoplasia (AN) that includes carcinomas, high-grade adenomas, adenomas 10mm or more in size, and adenomas with villous components were analysed using the Kaplan-Meier method. All 3,038 patients were initially analysed and then divided into the AN group (n = 1,180) and the non-AN group (n = 1,858) for further analysis.

**Results:** The overall cumulative detection rates of adenomas were 16.4% at 1 year, 40.8% at 2 years, and 58.9% at 10 years. The cumulative detection rates in the AN group were significantly higher (p < 0.01) than the non-AN group. They were 18.5% at 1 year, 45.5% at 2 years, and 51.9% at 9 years, compared with 15.5% at 1 year, 38.1% at 2 years, and 58.9% at 10 years in the non-AN group. Moreover, AN was detected in 104 patients (57 in the AN group and 47 in the non-AN group). The overall cumulative detection rates of AN were 0.3%, 5.1%, and 8.4% at 1, 5, and 10 years, respectively. The cumulative detection rates of AN in the AN group were significantly higher (p < 0.01) than the non-AN group. They were 0.4% at 1 year, 7.4% at 5 years, and 9.9% at 9 years, compared with 0.3% at 1 year, 3.8% at 2 years, and 7.1% at 10 years in the non-AN group.

**Conclusion:** The cumulative detection rate of AN is significantly higher than that of non-AN when the primary lesion is AN and surveillance every 2 years is effective. However, further analysis is needed to determine whether the interval can be extended to 3 or more years. The findings of this study suggest that surveillance after 1 year is unnecessary.

**Disclosure:** Nothing to disclose

### P0807 A NEW MODIFIED ENDOSCOPY, SITE, ACCESS (SMSA) SCORE FOR IS A NOVEL RISK ASSESSMENT TOOL PREDICTING CRITICAL OUTCOMES OF ENDOSCOPIC MUCOSAL RESECTION (EMR)

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**Introduction:** Endoscopic mucosal resection (EMR) is now the standard of care for treatment of colorectal laterally spreading lesions (LSLs). The SMSA score is an effective tool in grading the difficulty of polypectomy but does not recognize EMR specific risk factors[1]. EMR specific risk assessment tools to predict procedural outcomes are currently lacking.

**Aims and Methods:** To develop and validate a new EMR specific endoscopic risk score (SMSA-EMR score) to predict technical success, adverse events and recurrence after EMR.

**Results:**

- **Low-Risk**
  - Total count, n (%): 634 (54.8)
  - Technical success of EMR, n (%): 624 (98.4)
  - IPB, n (%): 87 (13.7)
  - Surgical referral at 2 weeks, n (%): 22 (3.5)
  - EDR SC1, n (%)*: 44 (9.4)
  - EDR SC2, n (%)*: 13 (5.5)
  - SMSA-EMR Score: Total: 1157

- **High-Risk**
  - Total count, n (%): 523 (45.2)
  - Technical success of EMR, n (%): 487 (93.1)
  - IPB, n (%): 143 (27.3)
  - Surgical referral at 2 weeks, n (%): 53 (6.3)
  - EDR SC1, n (%)*: 89 (23.1)
  - EDR SC2, n (%)*: 22 (10.4)
  - SMSA-EMR Score: Total: 4.61 (2.3–9.4)

**Size:** <40mm:0-0.40mm=3

**Lesion lift:** Y.0 N-2

**Morphology:** Sesame-0 Flat-3

**Granularity:** Granular-0 Nongranular-1

**Total score:** Low-risk ≤2 Non-high-risk >2

**Disclosure:** Nothing to disclose

**Reference**
Results: (1) The location was the right colon in 15 cases, the left colon in 4 cases and rectum in 1 case. The macroscopic type was Ic in 16 cases and Isp in 4 cases. The mean tumour diameter was 39.8 mm (30–67). The mean procedure time was 55.9 minutes (16–120), the endoscopic en bloc resection rate was 96.7%, the pathological complete resection rate was 86.7% and fibrosis was noted in 12 cases. In terms of procedure-related adverse events, perforation was noted in 1 case and treatment had to be suspended in 1 case. (2) Findings positive for muscular-retracting sign were noted in 7 cases (23.3%). Amongst these cases, the invasion depth was adenoma in 2 cases, intramusosal carcinoma in 3 cases and submucosal invasive carcinoma in 2 cases. The endoscopic en bloc resection rate was 85.7%, the pathological total resection rate was 57.1% and procedure-related adverse events (perforation) was noted in 1 case. Although no significant difference was observed between the positive and negative cases in terms of lesion location or macroscopic type, mean tumour diameter and mean procedure time were significantly larger/larger in the positive group.

Conclusion: Our results suggested that treatment outcomes for ESD performed on large, protruding lesions of 3 cm or larger were favourable. It also appears that ESD could be used to treat even lesions accompanied by muscular-retracting sign. Some cases of adenomas also exhibit muscular-retracting sign and, if possible, endoscopic resection is optimal. However, as procedures in this investigation were performed by an experienced endoscopists, it is currently unclear as to whether ESD is unconditionally safe for such cases. It appears necessary to keep surgical resection in mind, and to judge one’s own skill level as well as the level of difficulty posed by the lesion preoperatively.

Disclosure: Nothing to disclose

P0809 THE TRACTION METHOD “CLIP WITH RUBBER BAND” CONTRIBUTES TO EFFECTIVE SUBMUCOSAL DISSECTION IN COLORECTAL ESD

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Introduction: In colorectal ESD, it is important to obtain sufficient traction for effective submucosal dissection. However, with gravity alone, it is often difficult to obtain sufficient traction for effective submucosal dissection. On the other hand, several traction methods have been developed and their usefulness have been reported. Although they are useful, some points remain in terms of complexity or cost, and so on. Here, we introduce another traction method using clip with rubber band, “rubber-clip-method (RCM)”. The advantages of RCM are simplicity, cost effectiveness and capability to change direction of traction.

Aims and Methods: We aimed to investigate the usefulness of RCM in colorectal ESD. A retrospective, single-center, observation study. Out of 145 consecutive patients of superficial colorectal neoplasms experienced in January 2014 – August 2017, 118 patients were included. 6 cases of NET-G1, 7 cases discontin-ued ESD due to severe fibrosis, 2 cases performed ESD with surgical treatment, and 12 cases used traction methods other than RCM were excluded. Of the included 118 cases, 51 cases were not used traction method (non-traction group), and 67 cases were used RCM (RCM group). Study 1: The comparison of the results of the ESD of the non-traction group and the RCM group. Study 2: We divided cases into 2 groups according by operation time, 88 cases of less than 1 hour and 30 cases of 1 hour or more. And we investigated the influence of using RCM or not of differences of background factors for long operation time of ESD with univariate and multivariate analysis.

Results: Study 1: Background factors such as age, male-female ratio, tumor location, and endoscopist experience and performance were comparible. The operation time of RCM group was significantly shorter than non-traction group (63 min vs 114 minutes, p<0.05). Overall resection rate was lower in particip-ants aged less than 60 years (57.8% vs 68.1%, p<0.001), males (61.3% vs 65.1%, p=0.05), and participants in small, non-public centre as compared to large, public centre (49.1% vs 64.5%, p<0.001). Free choice of feedback method significantly improved response rate in partici-pants aged less than 60 years (60.8% vs 54.7%, p=0.031), male (64.0% vs 58.6%, p=0.045) and in small non-public centre (56.2% vs 42.5%, p=0.043).

In the intervention arm, 1,168 participants (91.2%) answered the phone call concerning complications. Of them, 776 (66.4%) completed the automated ques-tionnaire. A total of 79 participants (6.2%) reported complications. When veri-fied, 46 reported complications (58.2%) were administrative errors. Another 25 complications (31.2%) involved clinically relevant complications. Finally, only 7 par-ticipants (0.2%) reported clinically relevant complications – one post-polypectomy bleeding requiring hospital admission and one appendicitis with appendectomy one day after screening colonoscopy. No complications were self-reported in the control group.

Conclusion: The overall response rate was not significantly improved with digital feedback, yet it yielded significant improvement in participants with baseline low resection rates. Our study demonstrated feasibility and efficacy of digital patient feedback on complications after colorectal ESD.

Disclosure: Nothing to disclose

Reference

P0810 EFFECTIVENESS OF DIGITAL HEALTH SERVICES FOR COLORECTAL CANCER – A RANDOMIZED HEALTH SERVICES STUDY

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Introduction: The European Society of Gastrointestinal Endoscopy guidelines (1) recommends measuring patient experience and patient reported complications after colonoscopy. We aimed to compare effectiveness of digital and paper-based feedback of patients experience and 30-day complications after screening colonoscopy.

Aims and Methods: We included all primary screening colonoscopies performed in two centres from September 2015 to December 2016. Consecutive patients were randomized in a 1:1 ratio either to intervention arm (choice of feedback method) or control arm (routine paper-based feedback). Participants in the inter-vention arm were asked on their preferred method of feedback (paper-based, automated telephone or online survey) and additionally were informed about the planned automated telephone contact 30 days after the procedure to assess complications. Participants in control group were not contacted, instead they could self-report complications in routine way. The primary endpoint was partici-pant’s response rate to feedback questionnaire. Secondary endpoint was partici-pant’s response to complications questionnaire. The study was registered as a randomised health services trial (HRS 408, 2015, year 1).

Results: We included a total of 2,541 participants, median age: 59.9 years, male/females ratio 1.05 (1.281 in intervention arm, 1.260 participants in control arm).

The response rate to feedback questionnaire for total study population was 65.16%. In the intervention arm, 155 (12.1%) participants chose online survey, 287 (22.4%) – automated telephone survey and 839 (65.5%) – paper-based survey. There was no significant difference in response rate between study groups (64.8% vs 61.5%, p=0.08). Overall response rate was lower in partici-pants aged less than 60 years (57.8% vs 68.1%, p<0.001), males (61.3% vs 65.1%, p=0.05), and participants in small, non-public centre as compared to large, public centre (49.1% vs 64.5%, p<0.001). Free choice of feedback method significantly improved response rate among participants with baseline lower response rate: younger than 60 years (60.8% vs 54.7%; p=0.031), male (64.0% vs 58.6%; p=0.045) and in small non-public centre (56.2% vs 42.5%; p=0.043).

In the intervention arm, 1,168 participants (91.2%) answered the phone call concerning complications. Of them, 776 (66.4%) completed the automated ques-tionnaire. A total of 79 participants (6.2%) reported complications. When veri-fied, 46 reported complications (58.2%) were administrative errors. Another 25 complications (31.2%) involved clinically relevant complications. Finally, only 7 par-ticipants (0.2%) reported clinically relevant complications – one post-polypectomy bleeding requiring hospital admission and one appendicitis with appendectomy one day after screening colonoscopy. No complications were self-reported in the control group.

Conclusion: The overall response rate was not significantly improved with digital feedback, yet it yielded significant improvement in participants with baseline low resection rates. Our study demonstrated feasibility and efficacy of digital patient feedback on complications after colorectal ESD.

Disclosure: Nothing to disclose

Reference

P0811 THE ROLE OF PAIN CATASTROPHIZING IN PAIN EXPERIENCE DURING ENDOSCOPIC PROCEDURES

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Introduction: Endoscopic procedures are unpleasant and in most cases painful. Identifying the factors that may contribute to their acceptance might be beneficial for the patient and helpful for the physician. Pain Catastrophizing (PC) has been associated with a number of pain-related outcomes, including chronic pain in IBD and experimentally induced pain but its role in the experience of pain during medical procedures has not yet being investigated.

Disclosure: Nothing to disclose
Aims and Methods: We investigated the role of PC and its relation to patient reported and clinician rated pain during endoscopic procedures. A total of 143 consecutive outpatients undergoing endoscopy from September to May 2017 were enrolled. Gender (57% females), age (M = 57.83; SD = 17.17), body mass index (M = 25.28; SD = 4.22) and previous endoscopic experiences (56%). During endoscopy, operators evaluated the patient using the Pain Assessment in Advanced Dementia (PAINAD) Scale. The Ramsay Sedation Scale (RSS) was used to assess patient’s level of consciousness and sedation effectiveness. After endoscopy and before discharge patients reported about pain and discomfort during the procedure. A total score for self-reported pain was derived through principal component analysis of visual-analogue, verbal, numerical and face scales. The Pain Catastrophizing Scale (PCS) was also administered to retrospectively assess patient’s aptitude for catastrophic pain. We carried out regression and mediation analyses to test study’s main hypotheses.

Results: Age, gender, BMI and previous endoscopic experiences were uncorrelated with clinician reported pain. As regards self reported pain, the analysis revealed marginally significant differences by gender (p < 0.05) and age (p < 0.05) with women and younger people reporting more pain. PC was significantly larger for women (p < 0.01). Clinician rated pain during the procedure predicted patient self reported pain (Beta = -0.664; p < 0.001; R2 = 0.41). PCS was also associated with self-reported pain (Beta = 0.384; p < 0.001; R2 = 0.34). Mediation analyses revealed that the relationship between clinician rated pain and self reported pain was accounted for by PCS (Indirect Effect of clinician rated pain on self reported pain through PCS = 0.101; [-0.142; 0.258]). Nevertheless, clinician-rated pain (Beta = -0.264; p < 0.001; R2 = 0.41) still was predictive of self-reported pain controlling for PCS. Mediation analyses results were robust controlling for gender, age and body mass index as well as for previous endoscopic experiences and types of endoscopic procedure.

Conclusion: PC was found to play a central role in the experience of pain during both upper and lower endoscopy in fact PC explains the association of clinician rated pain with patient reported pain. While similar findings have been reported in the context of other pain studies, this is the first study showing that catastrophizing is also important in the experience of pain during medical procedures. In order to make endoscopic procedures more acceptable and to facilitate the medical examination by the operator, non pharmacological interventions to reduce PC by a cognitive-behavioral therapy might disclose an avenue for future research and clinical practice.

Disclosure: Nothing to disclose

P0812 SAFETY AND EFFICACY OF THE FULL-THICKNESS RESSECTION DEVICE (FTRD) IN THE COLORECTUM: A POOLED ANALYSIS OF PUBLISHED RESULTS

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Introduction: The full-thickness resection device (FTRD) is approved for the resection of difficult adenoma and subepithelial tumors in the colorectum. Aims and Methods: The aim of this study was to analyse the safety and efficacy of the FTRD in the colorectum. A pooled analysis of data from published studies was performed. All studies that reported on the use of the FTRD in the colon and rectum were eligible for inclusion. A literature search was done to identify published studies and relevant congress abstract databases were searched.

Results: A total of 18 studies were included, 9 of them published as full-text and 9 proceedings were included. All studies assessed either primary or secondary endpoints. The major endpoints were the R0 resection rate and the proportion of patients in whom resection margins were reported. Technical problems were mostly related to the resection snare, which occurred in 34 cases. In most of these cases a successful resection however was achieved by use of a conventional resection snare following application with the FTRD. Complications included minor bleeding and postpolypectomy syndrome in 14 (2.6%) patients each. Severely bleeding was rare and occurred in 2 (0.4%) patients and perforations were reported in 13 (2.4%) patients. A surgical intervention due to a FTRD related complication was necessary in 9 (1.7%) patients.

Conclusion: The FTRD system provides high efficacy in the colorectum. The complication rate is low and most complications can be managed conservatively or endoscopically.

Disclosure: Nothing to disclose

P0813 DOES POLYP DETECTION RATE CORRELATE WITH MEAN ADENOMA PER COLONOSCOPY?

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Introduction: Adenoma detection rate (ADR) is the primary quality indicator for colonoscopy. Mean adenoma per colonoscopy (APC) reflects colon inspection better than ADR and is more appropriate to illustrate differences between individual endoscopists. Both these factors are rather difficult to obtain in terms of time and personnel. Polyp detection rate (PDR) is a user friendly alternative of ADR that can be easily evaluated from administrative data.

Aims and Methods: The aim of our study was to assess whether PDR and APC can be correlated and to determine conversion factor to predict APC from PDR in preventive (faecal occult blood test positive (FOBT+) and screening) colonoscopies. Retrospective study included asymptomatic individuals aged 45-75 who underwent preventive colonoscopy in 2012-2016 as part of Czech prospective multi-center study monitoring metabolic risk factors of colorectal cancer. Individuals with incomplete colonoscopy and endoscopists with less than 30 colonoscopies and/or no detected adenoma in the observed group were excluded from the study. Spearman’s correlation coefficient was used to assess the relation between individual PDR and APC. The resulting conversion factor to predict APC from PDR was obtained by linear regression.

Results: In total, the study included 1,614 preventive colonoscopies performed by 16 endoscopists. Correlation between PDR and APC in all preventive colonoscopies was high and statistically significant (Rs 0.70; p = 0.0027). There is a stronger correlation between PDR and APC in men (Rs 0.73; p = 0.0029) than in women (Rs 0.64; p = 0.0123 and 0.0189 for all preventive and screening colonoscopies respectively. In FOBT+ colonoscopies linear regression did not reflect the actual variability observed in data.

Conclusion: There is a strong correlation between PDR and APC. Because of better availability, PDR may replace ADR and APC in colonoscopy quality assessment. With some limitations, APC may be estimated from PDR using a conversion factor that varies based on colonoscopy indication and patient gender. With respect to the minimum ADR requested, i.e. 25% recommended by both ASCIE and ESGE, all colonoscopies should reach APC ≥ 0.4.

Disclosure: Nothing to disclose

P0814 IMPROVED COLORECTAL ADENOMA DETECTION RATE WITH LINKED COLOR IMAGING (LCI) TECHNOLOGY COMPARED TO WHITE-LIGHT HIGH-DEFINITION COLONOSCOPY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Linked Color Imaging (LCI) is a new endoscopic visualization technique which may increase colorectal adenoma detection rate by the improved endoscopic image enhancement combined with virtual chroemoendoscopy. However only limited data available in the literature on the effectiveness of this new technology.

Aims and Methods: We aimed to evaluate the effectiveness in the adenoma detection rate of LCI in patients referred to colonoscopy and compared to the results of the white-light colonoscopy technique.

We enrolled 1100 patients were randomized. 552 patients were enrolled in the LCI group and 548 patients into the WLC group. Adenoma detection rate (patients having at least one colorectal adenoma) was significantly higher in the LCI group (48.4%) compared to thecontrol WLC group 34.4% vs. 26.8%, respectively (p = 0.007). No significant differences were observed in the patient demographic characteristics, quality of colonoscopy preparation and withdrawal time between the two groups.

Conclusion: Based on our randomized controlled trial the LCI electronic chromoendoscopy enhancement of the Fujinon Eluxeo colonoscopy system was superior compared to the conventional HD-WLC in detecting of colorectal adenomas. This difference mainly explained by the more sensitive detection of minute adenomic colonoscopy.

Disclosure: Study was supported by ECT grant GINOP 2.1.1-15-2015-00128

P0815 IMPROVED COLORECTAL ADENOMA DETECTION RATE COMPARING WHITE-LIGHT HIGH-DEFINITION COLONOSCOPY: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Linked Color Imaging (LCI) is a new endoscopic visualization technique which may increase colorectal adenoma detection rate by the improved endoscopic image enhancement combined with virtual chroemoendoscopy. However only limited data available in the literature on the effectiveness of this new technology.

Aims and Methods: We aimed to evaluate the effectiveness in the adenoma detection rate of LCI in patients referred to colonoscopy and compared to the results of the white-light colonoscopy technique.

We enrolled 1100 patients were randomized. 552 patients were enrolled in the LCI group and 548 patients into the WLC group. Adenoma detection rate (patients having at least one colorectal adenoma) was significantly higher in the LCI group (48.4%) compared to the control WLC group 34.4% vs. 26.8%, respectively (p = 0.007). No significant differences were observed in the patient demographic characteristics, quality of colonoscopy preparation and withdrawal time between the two groups.

Conclusion: Based on our randomized controlled trial the LCI electronic chroemoendoscopy enhancement of the Fujinon Eluxeo colonoscopy system was superior compared to the conventional HD-WLC in detecting of colorectal adenomas. This difference mainly explained by the more sensitive detection of minute adenomas.

Disclosure: Study was supported by ECT grant GINOP 2.1.1-15-2015-00128
**P0915 ENDOSCOPIC AND MOLECULAR CHARACTERISTICS DURING THE DEVELOPMENT OF TRADITIONAL SERRATED ADENOMA**


Introduction: Colorectal serrated lesions (SLs) include hyperplastic polyp (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma/polyp (SSA/P). Our previous study shows that Type II-O pit pattern is highly specific to SSA/Ps, and that Type II-L plus Type III or Type IV are associated with malignant progression to SSA/P and with cytological dysplasia (CD) or high-grade dysplasia (HGD) (1). However, endoscopic features in TSA are not fully understood.

Aims and Methods: To study the病理ological and molecular features of SLs, we aimed to clarify the associations among the pathological, morphological and molecular characteristics of SLs. A total of 401 premalignant and malignant colorectal lesions were enrolled in this study.

Using magnifying colonoscopy, microsurface structures were assessed based on Kudo's pit pattern classification system, and the Type II pit pattern was subcategorized into classical Type-II, Type-II Open (Type II-O) and Type-II Long (Type II-L). Biopsy specimens were obtained from all lesions for genome DNA extraction, after which lesions were treated by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD).

Results: Pit patterns of the 383 colorectal lesions were as follows: Type II (n = 40), Type II-L (n = 9), Type II-O (n = 100), Type II plus III/IV (n = 21), Type II-L plus III/IV (n = 17), Type II-O plus III/IV (n = 40), Type II plus V (n = 4), Type II-O plus V (n = 12) and Type III/IV (n = 140). Type II-O was highly associated with sessile serrated adenoma/polyps (SSA/Ps) with BRAF mutation and CIMP-high. Most lesions with simple Type II or Type II-L were hyperplastic polyps (HPS), while mixtures of Type II or Type II-L plus more advanced pit patterns (III/IV) were characteristic of traditional serrated adenomas (TSA) (sensitivity, 73.7%; specificity, 92.1%). Type II-positive TSA frequently exhibited BRAF mutation and CIMP-low, while Type II-positive TSA were tightly associated with KRAS mutation, CIMP methylation and CIMP-low.

We next assessed the association between pit patterns, molecular features and HP. We found that Type II-L was more frequent in goblet cell rich type HP. These results suggest that Type II-L plus III/IV (n = 40), Type II-L plus III/IV (n = 17), Type II-O plus III/IV (n = 40), Type II plus V (n = 4), Type II-O plus V (n = 12) and Type III/IV (n = 140). Type II-O was highly associated with sessile serrated adenoma/polyps (SSA/Ps) with BRAF mutation and CIMP-high. Most lesions with simple Type II or Type II-L were hyperplastic polyps (HPS), while mixtures of Type II or Type II-L plus more advanced pit patterns (III/IV) were characteristic of traditional serrated adenomas (TSA) (sensitivity, 73.7%; specificity, 92.1%). Type II-positive TSA frequently exhibited BRAF mutation and CIMP-low, while Type II-positive TSA were tightly associated with KRAS mutation, CIMP methylation and CIMP-low.

Conclusion: Our results suggest that Type II subtypes may reflect distinct molecular subclasses in the serrated neoplasia pathway, and that Type II-L plus more advanced pit patterns could be useful hallmarks for identifying TSA at high risk of developing into CRC.

Disclosure: Nothing to disclose

References


**P0916 PREDICTIVE FACTORS FOR REPEATING COLONOSCOPY IN OUTPATIENTS WITH INADEQUATE BOWEL PREPARATION**


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Introduction: Inadequate bowel cleansing has been observed in 10–25% of all colonoscopies, and ‘bowel preparation directions’ are the identification of polyps, size (type, number) and cancer. The quality of bowel preparation was categorized as adequate or inadequate according to each endoscopist’s subjective impression. Multivariate analysis was performed in order to identify factors independently associated with repeat colonoscopy among patients with inadequate bowel cleansing.

Results: Of the 12,948 colonoscopies performed at 2 different sites, the quality of the bowel preparation was suboptimal (inadequate or poor) in 990 outpatients. Among these 990 individuals, colonoscopy was repeated within a 3-year period in 261 (26.3%). The mean time (standard deviation) interval between the index and the repeat colonoscopy was 2.78 (4.51) months. Despite the suboptimal preparation, caecum was intubated in 69.7% of the cases. Adenomas were identified in 130 cases while there were 113 cases of advanced neoplasia (65 advanced adenomas and 48 cancers).

Among the 261 repeated colonoscopies, the bowel preparation was adequate in 71.2% of the cases with 74 adenomas and 8 colorectal cancers seen only on the second examination, corresponding to an adenoma and cancer miss rate of 24% and 61.1% respectively.

Predictive factors for repeating colonoscopy were the “very poor” bowel preparation, the detection of polyps and of advanced adenomas on index colonoscopy as well as the positivity of the faecal occult blood screening test. Reaching the caecum during index colonoscopy was negatively associated with repeating colonoscopy in the reference period.

Disclosure: Nothing to disclose

References


**P0917 ENDOSCOPIC MUCOSAL RESECTION WITH ANCHORING OF THE SNARE TIP; MULTICENTER RETROSPECTIVE EVALUATION OF THE EFFECTIVENESS AND SAFETY**

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Introduction: Endoscopic mucosal resection (EMR) is the reference to resect colorectal neoplasia between 10 and 30 mm. Main objective of EMR is to resect completely the neoplastic tissue (complete resection) and if possible in only one piece (En Bloc) with safe margins on histological assessment (R0).

In case of R0 resection, the risk of local recurrence is 0% and control for local recurrence detection can be avoided. Conventional EMR lead to 65% of En Bloc resection for lesions under 20 mm. Anchoring the tip of the snare is a technical...
trick allowing to fix the snare tip into the submucosa in order to reduce snare slippage. The aim of the validation study was to evaluate the effectiveness and the safety of this anchoring-EMR (A-EMR).

Aims and Methods: We performed a retrospective analysis of A-EMR procedures performed consecutively in 4 French centers between May 2017 and January 2018. In those 4 centers, anchoring was systematically attempted for all EMR using Olympus® conventional snare (10 or 25 mm). All specimens were stretched on cork for pathology.

Results: 141 A-EMR were performed in 125 patients by 9 operators during the study period (mean size was 19.8 ± 40 mm). Anchoring was technically successful in 96.5% of cases. En bloc and R0 resection proportions were respectively 81.6% and 70.0%. R0 proportion significantly reduced with lesion size with respectively 82.6% in lesions ≤20 mm, 55.3% between 20 and 30 mm and 50.0% over 30 mm (p = 0.002). Complete perforations closed endoscopically occurred in 2.1% of cases and partial ones with target sign in 1.4% of cases.

Conclusion: Anchoring-EMR is effective to remove with margins (R0) the lesions between under 30 mm and safe with 2.1% of perforation closed endoscopically. This technique could improve R0 resection rate compared to conventional EMR but prospective randomized comparison is requested.

Disclosure: Nothing to disclose.

P0819 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL TUMORS ACCOMPANYED BY FIBROSIS IN THE SUBMUCOSAL LAYER

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Introduction: The possibility of complete curative en bloc resection is sometimes related to the presence and degree of fibrosis in the submucosal layer (SM), rather than tumor size and location. In this study, clinical outcomes of ESD for colorectal neoplasms accompanied by fibrosis were analyzed, to achieve exact diagnosis and safe treatment of such lesions.

Aims and Methods: The aim of this study was thus to establish a safe and curative ESD procedure for colorectal neoplasms showing fibrosis in the SM layer. ESD were performed for 1,512 colorectal neoplasms in 1,473 patients (783 female 6334, average 66.1 years old) from January 2003 to June 2017, and was completed for 1,497 lesions. Of these cases, 315 showed SM fibrosis. These cases were divided into three groups: absence of fibrosis (A), fibrosis due to benign causes (B), and fibrosis due to cancer invasion (C). Furthermore, cases were classified as mild (grade 1), moderate (grade 2), or severe (grade 3).

Clinical outcomes and pathological findings of the above-mentioned ESD cases were analyzed according to these endoscopic classifications to facilitate the safe achievement of ESD.

In addition, histological validation of endoscopic diagnosis was performed for the 240 of the 315 cases with fibrosis, to clarify for differential diagnosis between Type B and Type C.

Results: Of the 315 cases with fibrosis, 210 cases involved benign causes (Type B), and 115 cases were considered related to cancer invasion (Type C). As the results of the validation study (n = 240) for differential diagnosis between Types B and C as follows; sensitivity: 88.7%, specificity: 90.5%, accuracy: 89.2%, PPV: 96.3%, NPV: 74.0%.

In en bloc resection rate (n = 240), Type B (n = 215) were as follows: A: 97.3%, B: 96.9%, C: 96.5%. B: 88.5%; B: 63.5%; Type C: 100%; C: 96.3%; C: 61.1%. The en bloc resection rates for types B-3 and C-3 were significantly lower (p < 0.05) than that for Type A. There were no significant differences between Type A and Types B or C. However, C-2 lesions were Type B cases (0.5%) of perforation, 4 of which (Type B) required emergency surgery. From these results, tumors accompanied by mild to moderate fibrosis become the standard indication for ESD. The tumors accompanied by severe fibrosis should be indicated as relative indications for ESD and required high quality of ESD technique to avoid perforation.

Conclusion: Accurate diagnosis of fibrosis based on the peroperative endoscopic findings appears feasible and contributes to completing the ESD procedure safely and curatively.

Disclosure: Nothing to disclose.
scar was present. PPV for CR were 43.75% and 35.41% when adenomatous tissue or a flat ulcer were present. PPV for CR were 20.0% and 21.30% when an ulcer with irregular border or tumour mass were present. AUC, sensitivity and specificity for the prediction of a CR with endoscopy were 0.74 (95% CI 0.66–0.89), 69% and 79% for reader 1 and 0.81 (95% CI 0.71–0.92), 66% and 91% for reader 2. The interobserver agreement was substantial (quadratic weighted k = 0.68). In 30 patients, a biopsy was taken. The addition of biopsy results to endoscopic images did not improve the diagnostic performance for the selection of CR for both readers.

**Conclusion:** Endoscopy predicts complete response after a median time of 9 weeks with a sensitivity of 66–69% and specificity of 79–91%. The above mentioned endoscopic features can be used to select patients for an extended observation period to select for organ-saving treatment. Endoscopy should be used in combination with MRI to provide more detailed information on the response in the deeper layers of the bowel wall and the mesorectum.

**Disclosure:** Nothing to disclose

**References**


**P0823 ROLE OF FEACAL IMMUNOCHEMICAL TESTING IN THE DIAGNOSTIC WORKUP OF PATIENTS WITH IRON DEFICIENCY ANAEMIA**


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**Introduction:** Gastroscopy and colonoscopy are frequently included in the routine diagnostic workup of patients with iron deficiency anaemia (IDA). However, a high percentage of these examinations do not show any significant lesion. Fecal immunochromic testing (FIT) could be used to increase the efficiency of the IDA diagnostic workup due to its ability to detect intact globin from colorectal lesions.

**Aims and Methods:** We aimed to assess whether FIT may discriminate between significant colorectal or upper gastrointestinal lesions, saving unnecessary examinations in patients with IDA.

Methods: consecutive naive patients with moderate-severe IDA defined as Hb <11.9 g/dl in men and Hb <10.9 g/dl in women, and ferritin ≤ 30 g/dl, were enrolled from April 2016 to December 2017 in a prospective, observational study. All patients, patients with a history of inflammatory bowel disease, gastrointestinal cancer, gastrointestinal surgery, evidence of bleeding, gastroscopy and/or colonoscopy in the past 5 years, pregnancy or refusal to participate were excluded. Demographic data, comorbidity (Charlson’s Index), laboratory test results (cortisosteroids, NSAID, anticoagulants) and laboratory variables were collected. Faecal haemoglobin was measured using 1-Kit OC-Sensor®34, (FIT positive ≥ 10 mg/g, Proceed to endoscopic procedures. Gastroscopy with gastric and duodenum biopsies and colonoscopy were performed the same day the low iron status was detected. Two independent pathologists (35) interpreted the histological slides. The primary endpoint was the presence of one (PPV) or predictive value (NPV), the area under the curve (AUC) of FIT for SCL and CRC were calculated.

**Results:** 245 patients were included (66.1% female, mean age 71.4 ± 12.2 years, mean Hb 9.7 ± 3.5 g/dl). A significant gastrointestinal lesion was detected in 154 (62.8%) patients whereas the diagnosis was uncertain in the remaining 91 (37.2%) patients. The most frequent SCL were Helicobacter pylori gastritis (n=31) and angiodysplasia (n=11), whereas the most frequent SCL were...
advanced poly (n = 30), CRC (n = 28) and angiodysplasia (n = 19). Of 119 (48.8%) patients with a positive FIT result, 65 (54.6%) had SCL (PPV 54.6%) and 37 (31.0%) had SUGL (PPV 31.3%). Conversely, among 126 patients with a negative FIT result, 48 (38.1%) had SUGL and 20 (15.9%) SCL. Overall, 106 patients with a negative FIT result did not have any SCL at colonoscopy (NPV 98.8%). FIT detected 26 out 28 CRC Sensitivity (92.9%). Only 9.3% patients had SUGL and SCL simultaneously, having all of them a positive FIT result. The AUC of a positive FIT result for SCL and CCR was 0.78 and 0.87, respectively. In the multiple regression analysis, only non-use of NSAIDs and positive FIT were independently associated with SCL. If we had started the diagnostic workup performing colonoscopy in patients with a positive FIT result, gastroscopy in patients with negative FIT result or both examinations when the initial examination did not show any significant lesion, we would have saved 104 (21%) examinations and lost 2 cases of ECC-related death.

Conclusion: In patients with IDA, FIT may guide the sequence of endoscopic procedures, saving unnecessary examinations.

Disclosure: Nothing to disclose

P0825 EFFICACY OF ETOMIDATE- VERSUS PROPOFOL-BASED SEDATION FOR ADVANCED ENDOSCOPIC PROCEDURE : A PROSPECTIVE, RANDOMIZED, NON-INFERIORITY TRIAL

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Introduction: Propofol is widely used for endoscopic sedation in advanced therapeutic endoscopy, but concerns regarding cardiopulmonary adverse events have been raised. Etomidate has known little effect on the cardiovascular and respiratory systems. We aimed to compare the efficacy and safety of balanced etomidate and propofol sedation in therapeutic endoscopic procedure.

Aims and Methods: This study was a prospective, randomized non-inferiority trial that included patients who had been scheduled for advanced therapeutic endoscopy. All endoscopic procedures were performed at two institutions and patients were randomly assigned to either etomidate or propofol sedation. The main outcomes were satisfaction measured by VAS scale, with a difference of 0.30 points between groups.

Results: A total of 186 patients (propofol group: n = 94, etomidate group: n = 92) were evaluated. Etomidate group failed to prove the non-inferiority for overall satisfaction of patients measured by VAS score, with a difference of −0.35 (95% confidence interval [CI] = −0.21 to 0.24, p = 0.099). Among endoscopists and nurses, etomidate showed non-inferiority to propofol with differences of 0.06 (p = 0.08) and 0.07 respectively (etomidate: 95% CI = −0.55 to 0.66, p < 0.001; nurses: 95% CI = −0.57 to 0.73, p = 0.001) for a non-inferiority margin of −1. In terms of safety, overall cardiopulmonary adverse events occurred less commonly in etomidate group (27.7% vs. 14.1%, p = 0.023). Hypoxia occurred in 5.3% of cases in the propofol group and in 1.1% of cases in the etomidate group (p = 0.211). Cardiovascular adverse events tended to be more common in propofol group (3.4% vs. 1.2%, p = 0.078). Among endoscopists and nurses, etomidate showed non-inferiority to propofol with differences of 0.06 (p = 0.08) and 0.07 respectively (etomidate: 95% CI = −0.55 to 0.66, p < 0.001; nurses: 95% CI = −0.57 to 0.73, p = 0.001) for a non-inferiority margin of −1. In terms of safety, overall cardiopulmonary adverse events occurred less commonly in etomidate group (27.7% vs. 14.1%, p = 0.023). Hypoxia occurred in 5.3% of cases in the propofol group and in 1.1% of cases in the etomidate group (p = 0.211). Cardiovascular adverse events tended to be more common in propofol group (3.4% vs. 1.2%, p = 0.078). Among endoscopists and nurses, etomidate showed non-inferiority to propofol with differences of 0.06 (p = 0.08) and 0.07 respectively (etomidate: 95% CI = −0.55 to 0.66, p < 0.001; nurses: 95% CI = −0.57 to 0.73, p = 0.001) for a non-inferiority margin of −1. In terms of safety, overall cardiopulmonary adverse events occurred less commonly in etomidate group (27.7% vs. 14.1%, p = 0.023). Hypoxia occurred in 5.3% of cases in the propofol group and in 1.1% of cases in the etomidate group (p = 0.211). Cardiovascular adverse events tended to be more common in propofol group (3.4% vs. 1.2%, p = 0.078). Among endoscopists and nurses, etomidate showed non-inferiority to propofol with differences of 0.06 (p = 0.08) and 0.07 respectively (etomidate: 95% CI = −0.55 to 0.66, p < 0.001; nurses: 95% CI = −0.57 to 0.73, p = 0.001) for a non-inferiority margin of −1. In terms of safety, overall cardiopulmonary adverse events occurred less commonly in etomidate group (27.7% vs. 14.1%, p = 0.023). Hypoxia occurred in 5.3% of cases in the propofol group and in 1.1% of cases in the etomidate group (p = 0.211).

Conclusion: Etomidate-based sedation during advanced endoscopic procedures was found to have the same safety and efficacy as propofol sedation in patients with negative FIT result. However, etomidate-based sedation showed better safety in terms of cardiovascular adverse events and may be an alternative option for advanced endoscopic procedure, especially in patients with cardiopulmonary diseases.

Disclosure: Nothing to disclose

P0827 THE PERIAMPULLARY DIVERTICULUM: BOON OR BANE FOR THE ERCP ENDOCOPIST?

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Introduction: The prevalence of periampuillary diverticular disease (PAD) is relatively high (9% to 33%) in patients who undergo an endoscopic retrograde cholangio-pancreatography (ERC). It is currently unclear if the presence of PAD impacts the success, difficulty and complication rates of ERC.

Aims and Methods: The aim of the study is to investigate the success rate, procedure difficulty (ERC grade, cannulation difficulty, procedure time) and complication rate between patients with and without PAD. In addition, we sought to determine whether there is a difference in ERCP indication and size of CBD is not a predictive factor for choledocholithiasis between the groups. Patients with PAD were further analyzed according to ampulla location (within PAD, at the edge of PAD, near PAD) and size of PAD (small: <1.5cm, large: >1.5cm). A single-centre cross-sectional study was conducted. A total of 548 ERC procedures were performed at our endoscopy centre from January 2015 to December 2016. Patients with
P0828 UTILITY OF SPYGLASS® DS PERORAL CHOLANGIOSCOPY IN INDETERMINATE BILARY LESIONS
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Introduction: Accurate diagnosis of indeterminate biliary lesions is necessary for proper treatment plan. We aim to assess the diagnostic accuracy of SpyGlass visual assessment and Spybite biopsy in patients with indeterminate biliary lesions.

Aims and Methods: Between August 2016 and August 2017, we review a retrospective analysis of the patients with indeterminate biliary stricture who had an inconclusive results on the cross-sectional imaging or endoscopic retrograde cholangiopancreatography (ERCP) guided tissue sampling.

Results: A forty-eight patients (28 men, mean age 72.3 years) with indeterminate biliary stricture were enrolled. SpyGlass® DS peroral cholangioscopy (SDPC). The SDPC was technically successful in all of the case. The final diagnosed in 48 patients were malignant tumor in 17 patients, and benign lesions in 32 patients. The sensitivity, specificity, and overall accuracy of SpyGlass visual assessment and Spybite biopsy for the diagnosis of malignancy were 94.1% (16/17), 93.5% (29/31), 93.7% (45/48), 47% (8/17), 100% (31/31), 83.8% (40/48), respectively. There was no procedure related complication.

Conclusion: The SDPC demonstrated relative accurate rate of diagnosis for indeterminate biliary lesions with excellent safety profile and high technical success rate.

Disclosure: Nothing to disclose

P0829 COMPARISON OF ENDOSCOPIC SPHINCTEROTOMY, ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION AND ENDOSCOPIC SPHINCTEROTOMY PLUS ENDOCOPIC PAPILLARY LARGE BALLOON DILATION TREATMENT FOR REMOVAL OF LARGE BILE DUCT STONE
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Introduction: Large bile duct stones (> 15 mm in transverse diameter) appear to be more difficult to be removed with conventional methods such as endoscopic sphincterotomy (EST) and endoscopic papillary balloon dilation (EPBD). However, EPBD is limited to small stones of <10 mm in diameter because it dose not enlarge the bile duct orifice to the same extent as EST. Therefore, extraction of a large bile duct stone may require mechanical lithotripsy (ML) in addition to EST or EPBD. The main complication during ML is basket and stone impaction that could occur even during a routine stone extraction, and it could increase the risk of pancreatitis and cholangitis. We used EST, endoscopic papillary large balloon dilation (16–20 mm) dilation (EPBD) and limited EST plus EPBD to remove large bile duct stone in our patients.

Aims and Methods: We aimed to compare and evaluate the therapeutic outcome and complications of EST, EPBLBD and limited EST plus EPBLBD for large bile duct stone extraction.

Methods: A total of 185 patients with large bile duct stones (> 15 mm in transverse diameter), who received EST, EPBLBD and limited EST plus EPBLBD treatment between 1, January 2010 and 28, February 2018 at Kaohsiung Chang Gung Memorial Hospital, Taiwan, were recruited in this retrospective study. Patients were divided into three groups (31), EPBD (34), EST plus EPBLBD (58). The primary outcome variables are the success rate of complete stone removal and presence of complications after three endoscopic treatment.

Conclusion: Limited EST plus EPBLBD group resulted in similar outcomes in overall success rate of stone removal (93.8% vs. 93.5%) and EBLBD group (92.7%). Limited EST plus EPBLBD group had higher success rate of the first session treatment (93.8% compared to EST group (83.9%) and EPBD group (20.8%) (p=0.02). The second session treatment in EPBD group and 2(3.4%) limited EBLBD plus EPBLBD group, but they were not significant difference (p=0.215). Post-procedure bleeding occurred in EST group (9.7%) was higher than limited EST plus EPBLBD group (0%) and EPBD group (0%) (p=0.003). Multivariate logistic regression showed that age difference between the 2 groups in terms of cannulation difficulty, categorized in ascending order of difficulty—level 1 (31/31), level 2 (63.8%), level 2 (23.6% vs. 22.4%), level 3 (7.5% vs. 4.3%), and level 4 (6.2% vs. 9.5%). Similarly, there was no statistically significant difference in terms of ERCP grading, grouped in ascending order of difficulty—grade 1 (78.8% vs. 78.5%), grade 2 (17.8% vs. 19.8%), and grade 3 (3.3% vs 1.7%). Multivariate logistic regression showed that younger age was an independent predictor of cannulation success (p=0.023), while older age (p=0.010) and indication other than choledocholithiasis (p=0.038) were independent predictors of cannulation difficulty. Patients with PAD had a 3.3 times higher odds of having choledocholithiasis compared to those without (p=0.006).

Conclusion: ERCP in the presence of PAD is as successful, easy and safe as for patients without PAD. Older age and procedure indication other than choledocholithiasis may increase the difficulty of the procedure.

Disclosure: Nothing to disclose
P0832 INITIAL EXPERIENCES WITH TRANSPANCREATIC PRECUT SPHINCTEROTOMY IN PATIENTS 90 YEARS OF AGE AND OLDER

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Introduction: Needle knife papillotomy (NKP) and needle knife fistulotomy (NKF) are two major rescue techniques for facilitating biliary cannulation and are associated with post-ERCP complications. However, there are limited data, especially in the extremely elderly.

Aims and Methods: The aim of the current study was to evaluate the safety and efficacy of NKP and NKF in nonagenarians. Medical records of 184 patients with difficult biliary cannulation who underwent NKP and NKF from September 2000 and March 2018 were analyzed. Patients were divided into two groups: 90 years age and older (Group A: n = 26) and less than 90 years old (Group B: n = 158). Patient characteristics, indications for ERCP, technical success and complications were retrospectively evaluated. Success was defined as deep placement of a catheter into the common bile duct. A diagnosis and severity of ERCP complications was made according to Cottone’s classification.

Results: Mean age was 92.6 ± 2.7 (range 90–101) and 75.5 ± 9.9 (range 41–89) years old in Group A and Group B, respectively. Choledocholithiasis (51.8%) was the most frequent indication followed by malignant biliary obstruction (34.8%). Ten patients (38.4%) in Group A and 70 (44.3%) in Group B underwent prior placement of a pancreatic stent (p = 0.672). Periampullary diverticulum was found most often in patients of Group A (23.1%) than of Group B (10.8%, p = 0.105). The number of patients with American Society of Anesthesiologists (ASA) physical status class ≥ 3 was significantly larger in Group A than in Group B (53.8% vs 29.1%, p = 0.023). Threw was no significant difference in the success rates of cannulation in the first session (61.5% vs 65.8%, p = 0.839) and in the final session (96.2% vs 96.8%, p = 0.999) between Group A and Group B. Mean time to NKP/NKF and mean procedure durations were not significantly different between the two groups. Three complications (11.5%) occurred in Group A (pancreatitis in 1, perforation in 1, cholecystitis in 1) and 27 (17.1%) in Group B (pancreatitis in 15, bleeding in 4, perforation in 2, cholecystitis in 6). Complication rates were not significantly different. The use of a pancreatic stent was not related to complication rate. Early mortality rate was significantly higher in Group A than in Group B (19.2% vs 2.5%, p = 0.003). No ERCP-related deaths occurred in both groups.

Conclusion: With adequate timing and intervention, NKP and NKF can be regarded as safe and effective procedures in extreme elderly.

Disclosure: Nothing to disclose.

P0833 IS ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY MORE RISKY AND COMPLICATED FOR THE ELDERLY? A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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Introduction: Life expectancy is continually increasing, which is coming along with an increasing demand of endoscopic retrograde cholangiopancreatography (ERCP) in patients with advanced age. Few recent prospective studies have addressed the adverse events on the feasibility and safety of ERCP in elderly patient although technical advances and better operator experience in ERCP.

In this study, we compared the differences on success rates and adverse events of ERCP in patients older and younger than age 80.

Aims and Methods: From January 2015 to December 2015, we prospectively enrolled patients with naïve papilla who referred for ERCP at 6 centers of Daegu-Gyeongsang province. Patient and procedure related variables were compared according to the time of ERCP. Patients were divided into age 80 years old (group A) and patients < 80 years old (group B). Demographic data, success rate, outcome, complications, risk factors and mortality were compared between the groups.

Results: There were 1191 ERCPs performed (231 patients older than 80 years, 953 procedures in patients younger than 80 years). The median age was 70 years old and male/female ratio was 1.38:1. Mean age was 83.7 ± 8.7 years in the group A and 63.1 ± 9.8 years in the group B. The cannulation success rate was lower in group A (95.0% vs 97.1%, p = 0.107). There was no significant difference in the overall complication rates between group A and B (18.9% vs 20.9%, p = 0.500) and ERCP-related mortality (0.4% vs 0%, p = 0.200, respectively). Post-ERCP pancreatitis was found relatively often in patients of group A (9.2%) than of group B (4.1%, p = 0.05). All patients were treated with full recovery without surgical or medical treatment. There was no significant difference in the other complication rate such as bleeding, perforation, cholangitis and others between two groups.

Conclusion: ERCP in the patients aged 80 years or older is safe and has a high degree of success. However, post-ERCP pancreatitis must be carefully attended in older patients because of relatively high risk. The incidence of other adverse events of ERCP is similar in older patients compared with younger ones.

Disclosure: Nothing to disclose.

P0834 EFFICACY OF DOUBLE-BALLOON ENDOSCOPY FOR THERAPEUTIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) and its related procedures are difficult to perform in patients with surgically altered anatomy. Some studies have suggested that ERCP using a double-balloon endoscope (DB-ERCP) is useful for removing gallstones or remaining anastomotic constrictions in such patients. This procedure was first covered by the National Health Insurance of Japan in 2016, and it is expected that the demand for DB-ERCP will now increase. This study considered the efficacy and safety of DB-ERCP in patients with surgically altered anatomy.

Aims and Methods: This retrospective study included 29 patients (49 procedures, male/female: 24/5, average age: 76 [63–90] years) with surgically altered anatomy who underwent DB-ERCP between July 2015 and February 2018 at Kure Medical Center and Chugoku Cancer Center. Procedures were performed by two endoscopists, one experienced in ERCP, another in DB-ERCP. DB-ERCP was performed using EL-530BI or 580BT (FUJIFILM systems). The treatment results, adverse events, and clinical outcomes of DB-ERCP were evaluated.

Results: Endoscopic biliary treatment was attempted with the surgical reconstruction technique for 30 procedures in 15 gastrectomy patients (Roux-en-Y reconstruction in 22, jejuno-biliary anastomosis in 8, gastrojejunostomy in 8, gastrocolicostomy in 3, gastrostomies in 5 patients) and for 19 procedures in 14 choledochojejunostomy anastomosis patients (pancreatectomy: 14 procedures in 11 patients, and cholecystectomy/ bile duct resection: 5 procedures in 3 patients). The success rate of reaching the major papilla or target anastomosis was 91.8% (45/49), and the mean access time was 27 (5–84) min. The biliary cannulation success rate was 72.4% (21/29) in the first attempt. In 2 of the 8 unsuccessful cases, the percutaneous transhepatic cholangiography-drainage (PTCD) rendezvous technique was used, and biliary retrograde analysis with relatively small number of cases, further prospective evaluation was required to confirm the usefulness.

Disclosure: Nothing to disclose.
intubation was ultimately successful in 79.6% (39/49). In patients in whom the PTCD catheter could be reached, the biliary cannulation success rate was 86.7% (39/45). By the reconstruction technique, the success rates were 76.7% (23/30) for post-gastrectomy (Roux-en-Y reconstruction: 23/29 procedures, and gastro-jejunostomy: 0/1 procedure), 92.9% (13/14) for post-pancreatectomy, and 60% (3/5) for post-cholecystectomy/bile duct resection. The procedures included dilation in 34 procedures (endoscopic sphincterotomy (EST): 1 procedure, endoscopic papillary balloon dilation (EPBD): 16 procedures, and anastomosis site dilation: 13 procedures), drainage in 17 procedures (endoscopic drainage (ENBD)/endoscopic retrograde biliary drainage (ERBD): 15 procedures, and metallic stent placement: 2 procedures), and lithotomy in 24 procedures. The mean total procedure time was 95.3 (39–156) min. Procedural adverse events included guidewire-induced perforation in 1 patient and intra-abdominal deviation of the PTCD catheter in 1 patient, both were relieved with conservative therapy.

Conclusion: DB-ERCP for the intestinal tract with surgically altered anatomy is useful and can be performed with relatively minimal invasiveness. However, no standard procedure has yet been established. In some cases, examination duration is prolonged, and in some patients, biliary cannulation could be difficult even if the major papilla or target anastomosis was achieved. Thus, it is desirable to accumulate more cases to lead to further improvements in these endoscopes and devices.

Disclosure: Nothing to disclose

**P0835** NOVEL TECHNIQUE USING A LOOP-DEVICE FOR REPOSITIONING A NASOBILARY CATHETER FROM MOUTH TO NOSTRIL IN ERCP


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Introduction: Endoscopic nasobiliary drainage (ENBD) has been widely used for biliary drainage in patients with bile duct stones. However, it is difficult to reposition a nasobiliary catheter from mouth to nostril. We developed a new device for repositioning of ENBD catheter (Patient pending). The new device has a curved flexible loop and handle bar. The aim of this study was to evaluate the usefulness of new loop-device for helping the repositioning of an ENBD catheter from mouth to nostril.

Aims and Methods: Between January 2016 and December 2017, a prospective observational study was performed to evaluate the time for repositioning a nasobiliary catheter in ERCP. It was compared the result of ENBD procedure between new loop-device technique and conventional technique. In subgroup analysis, we evaluated the occurrence of oral cavity injury and time to ENBD catheter moving from mouth to nostril.

Results: A total of 206 ENBD procedures were performed using these two techniques. The mean time for repositioning a nasobiliary catheter was shorter in loop-device technique than conventional technique (39 sec vs. 361 sec, p = 0.001). Total success rate of new device technique was achieved in 98.1%. There was no complication such as oral cavity injury.

Conclusion: This technique using our new loop-device was useful for repositioning a nasobiliary catheter from mouth to nostril in ERCP. Outranking merit of new device is that it does not require the removal of mouthpiece before ENBD positioning. It can help to perform a rapid ENBD procedure and avoid the finger intubation was ultimately successful in 79.6% (39/49). In patients in whom the PTCD catheter could be reached, the biliary cannulation success rate was 86.7% (39/45). By the reconstruction technique, the success rates were 76.7% (23/30) for post-gastrectomy (Roux-en-Y reconstruction: 23/29 procedures, and gastro-jejunostomy: 0/1 procedure), 92.9% (13/14) for post-pancreatectomy, and 60% (3/5) for post-cholecystectomy/bile duct resection. The procedures included dilation in 34 procedures (endoscopic sphincterotomy (EST): 1 procedure, endoscopic papillary balloon dilation (EPBD): 16 procedures, and anastomosis site dilation: 13 procedures), drainage in 17 procedures (endoscopic drainage (ENBD)/endoscopic retrograde biliary drainage (ERBD): 15 procedures, and metallic stent placement: 2 procedures), and lithotomy in 24 procedures. The mean total procedure time was 95.3 (39–156) min. Procedural adverse events included guidewire-induced perforation in 1 patient and intra-abdominal deviation of the PTCD catheter in 1 patient, both were relieved with conservative therapy.

Conclusion: DB-ERCP for the intestinal tract with surgically altered anatomy is useful and can be performed with relatively minimal invasiveness. However, no standard procedure has yet been established. In some cases, examination duration is prolonged, and in some patients, biliary cannulation could be difficult even if the major papilla or target anastomosis was achieved. Thus, it is desirable to accumulate more cases to lead to further improvements in these endoscopes and devices.

Disclosure: Nothing to disclose

**P0836** APPROPRIATE THERAPEUTIC STRATEGY FOR INITIAL ENDOSCOPIC DRAINAGE IN OBSTRUCTIVE JAUNDICE

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Introduction: The first endoscopic bile duct drainage method used to treat obstructive jaundice differs according to the pathology and institutional policy. Although endoscopic nasal biliary drainage (ENBD) has advantages such as occlusion prevention by washing at bedside after indwelling, endoscopic bile duct drainage (EBD) with a plastic stent (PS) is often used owing to the complexity of ENBD. We investigated the influence of prior indwelling ENBD in obstructive jaundice on the patency of PS after EBD, endoscopic procedure frequency and hospitalisation period.

Aims and Methods: We enrolled 63 subjects with malignant distal bile ducts requiring drainage due to obstructive jaundice (34 with acute cholangitis) and 40 subjects with cholangitis due to common choledocholithiasis. The subjects were classified into prior ENBD (EBD with prior ENBD) and EBD (EBD without prior ENBD) groups.

Results: The median age was 70 (range, 54–93) and 77 (range, 55–92) years in patients with distal bile duct malignant stenosis and in those with cholangitis due to choledocholithiasis, respectively. The median PS survival was 29 (n = 24) and 43 (n = 39) days in the prior ENBD and EBD groups among patients with distal bile duct malignant stenosis and 29 (n = 13) and 37 (n = 21) days in the prior ENBD and EBD groups among those with cholangitis due to choledocholithiasis, respectively; the mean PS survival was not significant in the prior ENBD group. The serum bilirubin level before treatment was significantly higher than that in the EBD group (p = 0.04); however, there was no significant difference in the number of endoscopic procedures and hospitalisation period between the groups. No evidence for severe cholangitis exacerbations was observed in the initial EBD group. Conclusion: Currently, there are few studies that have compared ENBD and EBD as the initial endoscopic drainage procedures to treat obstructive jaundice. In this study, ENBD did not result in a prolonged follow-up period for PS or increased hospitalisation period and number of endoscopic procedures. However, considering the complexity of the procedure and suffering of the patient, EBD alone should be used even in cases of acute cholangitis.

Disclosure: Nothing to disclose

**P0837** IMPACT OF PERIAMPULLARY DIVERTICULUM ON ERCP PERFORMANCE: A MATCHED CASE-CONTROL STUDY

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Introduction: Periampullary diverticulum (PAD) is an outpouching within the ampulla that develops with aging and is usually found incidentally during endoscopic retrograde cholangiography (ERCP). PAD can interfere with biliary drainage and has been associated with the development of bile duct stones, gallstones and acute cholangitis. There is conflicting data on whether the presence of a PAD affects therapeutic success rates during ERCP.

Aims and Methods: We aimed to compare ERCP performance in patients with PAD with age and gender-matched controls using a U.S. national database. We retrieved ERCP recorded between 2000 and 2012 in the Clinical Outcome Research Initiative database.

ERCP cases in adults (≥18 years) with a periampullary diverticulum were included if the endoscopist reported a duodenal diverticulum in the CORI software. Patients were included if they had age, gender and description of major papilla visualization (achieved or not available). Patients with PAD were compared with age and gender-matched controls, selected randomly using a 1:3 fashion from all other ERCPs, regardless of the procedure indication. Demographic variables, procedure time (from scope insertion to withdrawal), endoscopic and fluoroscopic findings, and therapeutic success (e.g. stone extraction, determined by endoscopist) were compared. ERCP complications and medication use are not consistently recorded in CORI, and were not included in our study design.

Univariate regression was performed and a multivariate regression model was elaborated with variables considered significant (p < 0.05). Adjusted odds ratio were reported for each variable.

Results: Initial CORI database review revealed 28,271 ERCPs. PAD was reported in 1,325 (4.7%) cases (8.6% in patients ≥70 years old). We identified 1,089 PAD cases with complete information and selected 3,267 matched controls for comparison. Average age was 68.4 ± 14.3 years, and 2,400 (55.1%) were women. Patients with PAD had a significantly higher proportion of patients with PAD. Presence of a PAD increased the chance of a procedure being completed in 94.9% in PAD, 96.0% in controls (p = 0.2). The presence of a PAD did not decrease the visualization rates of the minor papilla (endoscopic view), the common bile duct or pancreatic duct (fluoroscopy).

There was no difference in ERCP therapeutic success between both groups (94.9% in PAD, 96.0% in controls [p = 0.2]). The presence of a PAD did not decrease the visualization rates of the minor papilla (endoscopic view), the common bile duct or pancreatic duct (fluoroscopy).

No significant difference was seen for ERCP performance in patients with PAD adjusting for hospital setting, procedure duration, use of sphincterotomy and two major indications (bile stone disease or stent-related procedures). Our results support literature showing that PAD should not be considered a barrier to ERCP success. This study also substantiates the hypothesis that PAD interferes with adequate biliary drainage and promotes bile stone formation.

Disclosure: Nothing to disclose
Disclosure: plications of the bilio-digestive anastomosis, in expert hands.

Results: We did not report any long-term complication (after 48 hours). Clinical success rate was 100%. Morbidity and mortality were respectively 4% and 0.81%, but mean time to re-intervention was significantly lower (74.9 ± 74.6 vs 765.6 ± 961.3 days; p < 0.0001). HR of ERCP repetition raised to 2.52 (95% CI 1.02–6.24; p = 0.03) if the analysis was therefore limited to the first 1000 days. The only factor associated to ERCP repetition risk was incomplete clearing.

Conclusion: Risk of re-intervention was significantly higher in the short-term after PF. Therefore, patients undergoing PF should undergo closer follow-up in the first years after ERCP.

Disclosure: Nothing to disclose

BILIARY METAL-STENTS IN PATIENTS WITH MALIGNANT JAUNDICE AND CBD STRUCURE: A RETROSPECTIVE COHORT STUDY COMPARING UNCOVERED, PARTIALLY COVERED AND FULLY COVERED STENTS

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Introduction: In Common Bile Duct (CBD) stones the access to CBD can be achieved through the papilla orifice followed by endoscopic sphincterotomy (ES), or through a precut fistulotomy (PF) in case of difficult cannulation; the two methods alter papilla anatomy differently, therefore intuitively leading to a different rate of stone recurrence. No data on stones recurrence in patients with CBD stones after PF has been published.

Aims and Methods: The aim was to evaluate CBD stone recurrence, re-intervention rate after PF versus ES. We performed a retrospective single-center cohort study including patients undergoing for the first time ERCP for CBD stones with PF in case of failed repeated cannulation attempts, matched for sex and age to ES patients randomly extracted from our database. T-test and Fisher’s tests were used for continuous and categorical variables comparison. Recurrence probability was calculated with Kaplan-Meier curve, and Cox analysis was employed to calculate hazard ratios (HR).

Results: 85 PF patients were included, with 85 matched controls (mean age 68.7 ± 12.9% years; 60% males). PF patients had the same overall recurrence rate (14.1% vs 12.9%) with a HR of 1.11 (95% CI 0.49–2.50; p = 0.81), but mean time to re-intervention was significantly lower (74.9 ± 74.6 vs 765.6 ± 961.3 days; p < 0.0001). HR of ERCP repetition raised to 2.52 (95% CI 1.02–6.24; p = 0.03) if the analysis was therefore limited to the first 1000 days. The only factor associated to ERCP repetition risk was incomplete clearing.

Conclusion: Risk of re-intervention was significantly higher in the short-term after PF. Therefore, patients undergoing PF should undergo closer follow-up in the first years after ERCP.

Disclosure: Nothing to disclose

NEEDLE-KNIFE FISTULOTOMY VERSUS STANDARD BILLARY SPHINCTEROTOMY FOR CHOLEDOCHOLITHIASIS: RECURRENCE OF COMMON BILE DUCT STONES

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Introduction: Endoscopic transpapillary biliary drainage is the treatment of choice for obstructive jaundice caused by malignant strictures. Different types of self-expanding metal stents (SEMS) are available: fully covered (FC), partially covered (PC) and uncovered (UC). The advantage of metal compared to plastic stents is the reduced risk of rehospitalization and complications expected in patients expected to survive for more than 3 months. However what is the most effective type of metal prosthesis is still debated.

Aims and Methods: The aim was to evaluate the re-intervention rate after positioning of SEMS versus PC versus UC SEMS. We performed a retrospective single-center cohort study including patients undergoing ERCP with positioning of SEMS for the first time for CBD malignant stenosis. A repeated ERCP was indicated in case of jaundice and/or choledocholithiasis. T-test and Fisher’s tests were used for continuous and categorical variables. Recurrence probability was calculated with Kaplan-Meier curve, and Cox analysis was employed to calculate hazard ratios (HR).

Results: 321 patients (63 FC, 55 PC, 203 UC) were included in this preliminary analysis, (mean age 69.2 ± 11.8 years, 52.6% males); 90.3% had pancreatic cancer, 3.7% cholangiocarcinoma, 6% had ampullary tumors or pancreatic neuroendocrine tumors. 29.3% patients were metastatic, 47% locally advanced, 23.7% were surgically resectable. Overall re-intervention rate for FC vs PC vs
UC SEMS was respectively 31.7% vs 12.7% vs 30%. Main reason for ERCP repetition due to stenosis and/or the diagnostic yield was related to stenosis in UC stenosis with obstruction due to stenosis and/or a stent in place. Patients with partially covered SEMS vs fully covered or uncovered SEMS had a HR of 0.49 (95% CI 0.27–0.88 p = 0.038) for repetition of ERCP.

Conclusion: To our knowledge, this is the first study comparing all three different types of SEMS to each other in terms of reintervention rate in patients with malignant jaundice. The 51% reduced risk of reintervention after PC SEMS positioning should encourage controlled studies to verify their higher benefit of this stent compared to UC SEMS.

Disclosure: Nothing to disclose

P0842 CLINICAL OUTCOME OF THE RESECTION MARGIN POSITIVE OR UNCERTAIN CASES AFTER ENDOPAPILLECTOMY FOR AMPULLARY NEOPLASMS
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Introduction: Endopapillectomy (EP) can be the first-line less-invasive treatment in patients with papillary adenoma without intraductal extension. However, the evaluation of resected margin was often difficult because of the burning effect caused by EP. This study investigated the clinical course of resection margin positive or uncertain cases after EP.

Aims and Methods: Between January 2007 and October 2017, 38 patients who performed EP for ampullary tumor were included in this study. Indication for EP was adenoma as determined by preoperative biopsy, without tumor spread into bile ducts. The resection margin at the vertical end was positive or uncertain in 13 patients (Group A), and at the horizontal end was positive or uncertain in 4 patients (Group B). In Group A, 1 patient was diagnosed as T2 (Du1) histopathologically, and received additional surgery. The resection margin at the vertical end was positive or uncertain in 13 patients (Group A), and at the horizontal end was positive or uncertain in 17 patients (44.7%). The resection margin at the vertical end was positive or uncertain in 13 patients (Group A), and at the horizontal end was positive or uncertain in 17 patients (44.7%). The resection margin was negative in 21 patients (55.3%), and positive or uncertain in 17 patients (44.7%).

Results: 23 patients were men, 15 were women. The mean age of the patients was 65 years old. 54 cases (89.5%) were carried out on block resection, and 4 patients (10.5%) were performed en bloc resection. Early complications occurred in 32% of all the patients (hemorrhage occurred in seven and pancreatitis occurred in eleven). 28 were diagnosed as adenoma, 10 were diagnosed as adenocarcinoma histopathologically. The resection margin was negative in 21 patients (55.3%), and positive or uncertain in 17 patients (44.7%). The resection margin at the vertical end was positive or uncertain in 13 patients (Group A), and at the horizontal end was positive or uncertain in 4 patients (Group B). In Group A, 1 patient was diagnosed as T2 (Du1) histopathologically, and received additional surgery. The resection margin at the vertical end was positive or uncertain in 13 patients (Group A), and at the horizontal end was positive or uncertain in 17 patients (44.7%).

Conclusion: Independently from tumor consistency, the low negative pressure suction generated by SP technique yields better quality smears. The lower bloodiness and decreased number of slides could make the pathological diagnosis faster and more cost-effective. In conclusion, the low negative pressure suction resulted in lower diagnostic yield, therefore we recommend the SP technique as the first method in the EUS-FNA sampling of soft tissues, such as lymph nodes and liver cancers.

Disclosure: Nothing to disclose

P0843 LOW PRESSURE NEGATIVE PRESSURE SUCTION YIELDS BETTER QUALITY SMEARS – PROSPECTIVE COMPARISON OF SLOW AND FASTER SUCTION TECHNIQUES OF ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION
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Introduction: Standard suction (SS) technique using a 10mL syringe is the recommended sampling technique of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in the diagnosis of pancreatic cancer, but it often leads to cell lysis with increased bloodiness with no improvement in diagnostic accuracy. However, mainly retrospective studies are available about the detailed sampling methods of cancers of other organs, and in these cases, there are no evidence-based recommendations. Aim of our prospective study is to compare the diagnostic yield and quality of cytological and/or histological samples obtained by slow-pull (SP) and SS techniques of EUS-FNA.

Aims and Methods: 378 EUS-FNAs were performed between January 2014 and December 2016 at the University of Szeged, 1st Department of Medicine. Histological and cytological samples were obtained from a total of 462 organs. In the prospective study we assessed the data of EUS-FNA samplings in which 22G needle and both techniques were applied. Patients with cystic lesions and EUS-FNA examinations with undocumented sampling technique were excluded from the study. We separately assessed and compared the efficiency of the two sampling techniques in soft, non-calcified (liver, lymph nodes, adrenal gland, etc.) and hard, fibrotic neoplasia (pancreatic cancer, submucosal neoplasia, etc.).

The quality of EUS-FNA samples was assessed based on the number of obtained and diagnostic smears, bloodiness, cellularity and diagnostic yield.

Results: 56 soft (39 lymph nodes, 9 primary or metastatic liver, 2 Klatskin, 2 paracaval and 3 mediastinal lesions) and 147 fibrotic (145 pancreatic and 2 abdominal) tumors were enrolled. In cases of hard, fibrotic tumors the diagnostic yield of the sampling (67.35% vs. 68.02%) and the cellularity of smears did not differ significantly between SP and SS groups (1.44 vs. 1.27), however it was substantially higher in case of soft tumors using SP technique of EUS-FNA (60.71% vs. 46.43% and 1.34 vs. 0.77; p < 0.001). The SS techniques resulted in significantly higher number of smear pairs both in soft, vascularized (1.74 vs. 3.19; p < 0.001) and fibrotic tumors (1.62 vs. 3.28; p < 0.001), but at the same time the proportion of diagnostic samples decreased (46.51% vs. 36.52% and 49.17% vs. 30.67%; p = 0.003). The SS technique substantially increases the bloodiness of smears independently from tumor (in soft tumors: 1.50 vs. 2.06 and in fibrotic tumors: 1.48 vs. 2.05). Histological samples were obtained in almost the same proportion of soft and fibrotic cancers (78.67% vs. 82.17%), and their diagnostic yield did not differ between subgroups (69.01% and 71.74%).

Conclusion: Independent from tumor consistency, the low negative pressure suction generated by SP technique yields better quality smears. The lower bloodiness and decreased number of slides could make the pathological diagnosis faster and more cost-effective. In conclusion, the low negative pressure suction resulted in lower diagnostic yield, therefore we recommend the SP technique as the first method in the EUS-FNA sampling of soft tissues, such as lymph nodes and liver cancers.

Disclosure: Nothing to disclose

P0844 CLINICAL UTILITY AND YIELD OF EUS IN PATIENTS WITH A PRIOR NON-DIAGNOSTIC MRCP; A TERTIARY CARE CENTER EXPERIENCE
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Introduction: The most effective investigation for suspected gallstones between MRCP and EUS is unclear. A 2015 Cochrane systematic review of their performance in common bile duct (CBD) stones concluded that the tests were of comparable accuracy. Conversely, a 2017 meta-analysis found EUS to be more sensitive. Any superiority of EUS may be due to better accuracy in detecting small stones. MRCP is routinely favoured as the 2nd line test following a non-diagnostic abdominal ultrasound and EUS subsequently performed as the 3rd line test when a suspicion remained. EUS is superior in the yield and clinical utility of EUS in this setting is unclear. The aim was to identify the yield of EUS in patients with prior non-diagnostic MRCP undergoing EUS in our tertiary centre.

Aims and Methods: All EUS reports from 2017 were reviewed along with the electronic patient records to identify cases with prior MRCP. Indication for the procedure, symptoms, liver blood tests and interval between MRCP and EUS were recorded. Findings of sludge, microcalculi (stones<0.2mm) and discrete stones were categorised together as stones. Subsequent ERCP or cholecystectomy was identified. Yield was defined as a finding that would lead to a change in management.

Results: A total of 1058 diagnostic EUS were screened of whom 253 (24%) had prior MRCP and formed the study group. Median age was 58 (16–88) years, 179 (71%) were female and 91 (36%) had a cholecystectomy. Median interval between EUS and MRCP was 5.2 (0.3–37) months. Indications for EUS were: n = 76 (30%) detailed CBD, n = 65 (26%) query CBD stones, n = 54 (21%) unexplained acute pancreatitis (AP), n = 23 (9%) right upper quadrant pain, n = 17 (6.7%) abnormal LFTs, n = 16 (6.3%) double duct sign and n = 2 (1%) dilated PD. There was a yield from EUS in 30 (12%) patients with no significant difference between those with (n = 11) or without cholecystectomy (n = 19). Stones were identified in 24 cases with median size of 4 mm (range 2–8) in: CBD (n = 16), cystic duct (n = 1) and GB (n = 7). Three had abnormal stones without stones (calcification CBD wall, thick walled CBD, polyp), 1 patient with possible stones (MRCP had no stone seen on EUS). I had a pancreatic mass, and I had chronic pancreatitis. All patients in whom EUS findings indicated an intervention (26/30) have been referred: ERCP in 13, cholecystectomy in 9, ERCP & cholecystectomy in 3 and chemotherapy in 1.

Conclusion: EUS following a non-diagnostic MRCP is a sizeable workload accounting for 24% of diagnostic activity in our unit with a clinically significant yield in 12% of predominantly small stones. Further prospective studies are required to ascertain the most cost-effective way to incorporate EUS into the investigations of suspected gallstone disease.

Disclosure: Nothing to disclose
P0845 PREDICTING MALIGNANCY RISK IN GASTROINTESTINAL STROMAL TUMOR WITH CONTRAST-ENHANCED HARMONIC ENDOSCOPIC ULTRASOUND USING A PERFORATION ANALYSIS SOFTWARE

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Introduction: A contrast-enhanced harmonic endoscopic ultrasound (CEH-EUS) is a promising imaging modality that can identify subepithelial tumors (SETs) by detecting the degree of enhancement. However, whether CEH-EUS alone can predict the malignancy risk of gastrointestinal stromal tumors (GISTs) remains unclear. This study aimed to evaluate the feasibility of CEH-EUS using a perforation analysis software for distinguishing among SETs and for predicting the malignancy risk of GISTs.

Aims and Methods: We retrospectively included patients with subepithelial lesions who underwent preoperative CEH-EUS. In total, 44 patients with histologically proven GISTs and benign SETs were enrolled in the study. Perfusion analysis was performed using a perfusion quantification software. Area under time intensity curve (AUC), peak enhancement (PE), wash-in rate (WiR), and wash-in perfusion index (WiPI) were calculated and compared between GISTs and SETs.

Results: When we allocated the enrolled patients into high- and low-grade malignancy, and benign groups, significant statistical differences of AUC (p < 0.001), PE (p < 0.001), WiR (p = 0.009), and WiPI (p < 0.001) were identified in the high-grade malignancy groups compared to benign groups.

Conclusion: CEH-EUS with a perfusion analysis using a perfusion analysis software could be a quantitative and independent method for predicting malignancy risk in gastrointestinal SETs.

Disclosure: Nothing to disclose

P0846 USEFULNESS OF PROCORE 20G NEEDLE FOR DIAGNOSIS OF PANCREATIC SOLID TUMOR

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Introduction: For pathological diagnosis of the pancreatic solid tumor, EUS-FNAB is known as a standard method that is minimally invasive and accurate. Many kinds of needles have been developed to improve diagnostic yield. EchoTip ProCore has the core tip at the side of needle for receiving core sample, the shape of the core tip is forward bevel in ProCore 20G (PC20) and reverse bevel in ProCore 22G (PC22). We compared the usefulness and safety with PC20 and PC22.

Aims and Methods: We conducted a retrospective study of EUS-FNAB with a PC20 or a PC22 for pancreatic solid tumor performed between April 2013 and March 2018 at Kyorin University hospital. The main outcome was to compare the usefulness and safety as well as cytological yield. The secondary outcome was the number of passes to obtain a diagnosis, the necessity of needle change and ratio of complications. First, we collected specimens by suction method, with two passes of puncturing. In cases with a lot of bleeding and cases with the small amount of specimens which was insufficient to examine, and cases when the needle was broken, we added more passes, changed to slow-pull method and other needles. Group 4.5 in histology and Class IV,V in cytology were diagnosed as malignant tumors.

Results: A total of 110 patients were enrolled this study. PC20 was used in 50 patients and PC22 was used in 60 patients. The final diagnosis were pancreatic ductal carcinoma in 94, metastasis pancreatic carcinoma in 3, neuroendocrine tumor in 2, autoimmune pancreatitis in 7, chronic pancreatitis in 3 and solid pseudopapillary neoplasm in 1. Maximum diameter of tumor, location of the pancreatic tumor, puncturing line, mean number of passes, and final diagnosis were not significant difference. Sensitivity, specificity and accuracy combining pathology and cytology were 97.4%, 100% and 97.6% in PC20, and 76.6%, 100% and 79.2% in PC22, there was significant difference at sensitivity and accuracy (p = 0.006 and 0.01). Even when comparing the pathological diagnosis of PC20 with the cytological diagnosis of PC22, sensitivity and accuracy were significant difference (sensitivity 97.9% vs 68.6% p = 0.001, accuracy 98.0% vs 73.3% p = 0.0004). The histological accuracy was achieved by the 1st, 2nd and after 3rd pass in 90.0%, 96.0% and 98.0% at using PC20, and 45.0%, 58.3% and 65.0% at using PC22 (p = 0.0001, 0.0001, 0.0001 respectively). The necessity of needle change was not significantly different between two needles. Mild pancreatitis occurred 1 patient in PC20, and hemorrhage occurred 1 patient in PC22, complication rate was not significant difference.

Conclusion: Our results showed that PC20 is more useful for diagnosis of pancreatic solid tumors with higher sensitivity and accuracy than those of PC22. In addition, it was suggested that the diagnosis could be obtained with fewer punctures on the PC20. As a limitation, we could not evaluate the involvement of needle shape and thickness.

Disclosure: Nothing to disclose

P0847 ENDOMETRIOSIS NODULE THICKNESS ON PRE-OPERATIVE RECTO-SIGMOID ENDOSCOPIC ULTRASONOGRAPHY PREDICTS THE NEED FOR BOWEL RESECTION VERSUS SHAVING TECHNIQUE

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Introduction: Recto-sigmoid endometriosis is an underdiagnosed disease responsible for non-specific digestive symptoms. Two surgical approach, recto-sigmoid bowel resection (segmental or patch) and shaving technique (intra-muscular layer dissection) are available. The aim of this study was to assess if pre-operative recto-sigmoid endoscopic ultrasonography (RS-EUS) findings might predict the need for bowel resection.

Aims and Methods: This retrospective study was conducted between January 2012 and March 2018 on patients with recto-sigmoid endometriosis evaluated by RS-EUS who underwent a curative surgical procedure in our tertiary center. Logistic multivariate regression model was used after univariate statistical analysis on nodules’ RS-EUS features (thickness, width, infiltration of the sub-mucosas, presence of a bump into the digestive lumen and presence of multiple recto-sigmoid localizations).

Results: 73/362 patients with recto-sigmoid endometriosis were evaluated by RS-EUS and underwent a recto-sigmoid surgery. After univariate analysis, thickness, width and infiltration of the submucosas were identified as potential predictive factors for bowel resection. In a multivariate logistic regression model, only thickness appeared to be a significant predictive factor for bowel resection (OR = 1.49, IC95% [1.04-2.12], p = 0.028). ROC analysis showed that a thickness over 5.20 mm might be used as cut-off value with a sensitivity of 76.0%, specificity of 92.6%, and an AUC of 0.82. Cut-off values for 100% sensitivity and 100% specificity were 0.90 mm and 10.00 mm respectively.

Conclusion: Presence of a recto-sigmoid nodule of endometriosis with more than 5.20 mm of thickness on RS-EUS predicts the need for nead new recto-sigmoid bowel resection versus shaving technique. Prospective studies are needed to confirm these results.

Disclosure: Nothing to disclose

P0848 ROLE OF CONTRAST-ENHANCED ENDOSCOPIC ULTRASOUND IN DIFFERENTIATION OF PANCREATIC CYSTS

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Introduction: It is a great challenge to differentiate between the type and the malignant potential of a newly diagnosed pancreatic cyst. Our aim was to assess the role of contrast-enhanced endoscopic ultrasonography (EUS) for increasing diagnostic accuracy.

Aims and Methods: The prospective study included 49 patients with pancreatic cysts. Inclusion criteria were: age over 18, presence of an undetermined pancreas cyst ≤ 10mm (CT, MRI), informed consent. Exclusion criteria were: severe chronic pancreatitis, cyst ≤ 10mm, platelet count ≤ 50,000/μm3, refuse of the patient to participate. We analyzed the cyst wall, the septae and the solid components of the pancreatic cyst with and without contrast enhancer (CE)(2,4/ml SonoVue,Bracco,Italy). The examinations were performed using an Olympus echoendoscope and Aloka ultrasound machine. The final diagnosis was based on fine needle aspiration result, surgery or follow-up.

Results: There were 49 patients (33 females, 16 males) included. Cyst size was between 10-90mm. The pancreatic location of the lesions were the head (n = 13), the uncinate process (n = 6), the neck (n = 11), the body (n = 11), and the tail (n = 8). The types of cysts were serous cystadenoma (n = 8); mucinous cystadenoma (n = 10); Intraductal Papillary Mucinous Neoplasm (IPMN) (n = 26); pseudocyst (n = 5). For the serous cystadenomas, a hyperenhancement of the cyst wall and septae with a slow wash-out and honeycomb aspect was observed in 7 of 8 patients. In case of mucinous cystadenomas hyperenhanced thick walls, septae and fast wash-out was characteristic (8/10). For IPMNs, the hyper-enhancement of the cyst wall and fast wash-out was found (24/26). All the pseudocyst presented hypoenhancement or no enhancement of cyst wall (5/5). Trough the enhancement pattern mucinous lesions could be differentiated from nonmucinous lesions (Se = 88%, Sp = 46%; p = 0.0139). From 18 pancreatic cysts with EUS, hyperenhanced mural nodules were present in 9 of them and malignancy was confirmed for all this cases (surgery n = 12; EUS-FNA n = 18).

Conclusion: The enhancing pattern was useful to differentiate malignant nodules from mucinous or debris and mucinous from nonmucinous pancreatic cystic lesions.

Disclosure: Nothing to disclose
P0849 ESOPHAGEAL ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION BIOPSY OF SUBEPITHELIAL GASTROINTESTINAL LESIONS – JUST WET-IT
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2University of Szeged, Department of Pathology, Szeged, Hungary
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Introduction: Endoscopic ultrasound guided fine-needle aspiration biopsy (EUS-FNA) is a well-established diagnostic tool in the upper gastrointestinal tract, but evidence is limited about its use in the rectum.

Aims and Methods: This retrospective analysis of a prospectively collected database aimed to evaluate the indications and diagnostic yield of EUS-FNA of rectal and perirectal subepithelial EUS-FNA examinations performed at the University of Szeged from 2015 were involved.

Results: A total of 15 rectal EUS-FNAs were performed between January 2015 and March 2018 (mean patient age: 53 years). Indication for rectal FNA was for: suspicion of lymph node metastasis (13 cases) and, with the only the former 3 cases, and with the latter in one case. Tissue sampling was possible in 12 cases (3 with stylet, 2 with vacuum, and 7 with both). Sampling was diagnostic in 6 cases (40%): endometriosis was confirmed in 1 case (25%), lymph node metastasis (from malignant melanoma and anal carcinoma) in 2 cases (40%), and tumor recurrence [two rectal and one ovarian] in 3 cases (60%). No adverse events were reported.

Conclusion: EUS-FNA may assist differential diagnosis of rectal and perirectal lesions by providing a safe sampling method of lesions that are often inaccessible for other modalities. It can be especially useful in confirming recurrence of malignancy and might also have additional value in the diagnosis of lymph node metastases and endometriosis that may occur as submucosal lesion endoscopically.

Disclosure: Nothing to disclose.

P0850 ESOPHAGEAL ULTRASOUND-GUIDED BIOPSY OF SUBEPITHELIAL GASTROINTESTINAL LESIONS – JUST WET-IT
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2Centro Hospitalar Covas da Beira, Gastroenterology, Covilhã, Portugal
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Introduction: Endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNAB) is the main method for acquisition of tissue from gastrointestinal subepithelial lesions (SELs). Despite the development of new needles, diagnostic yield remains low. The reason may be an ineffective transmission of negative pressure with the dry technique, as these lesions often have high cellular cohesion. A new method of aspiration has been described, where the needle is filled with saline solution (WST), with promising results in pancreatic lesions. This method hasn’t been tested in SELs.

Aims and Methods: Prospective single-centre study to assess the diagnostic yield of EUS-FNAB-WST in the diagnosis of SELs, without the use of rapid on-site evaluation (ROSE). Case group: patients who underwent rectal ultrasound, only when immunohistochemistry (IHC) could differentiate between gastrointestinal stromal tumour (GIST) and leiomyoma. The diagnostic yield of this prospective cohort between July 2015 and December 2017 was compared with a retrospective cohort using dry technique from the same institution.

Results: Seventy-one patients with SELs were included (49% male, mean age 66 years). Mean SEL size was 32 mm (min 10, max 120 mm), mean number of performed biopsies per patient was 2.42 (95% CI 1.82–2.99), 19 G in 8 (12%) and 25 G in 5 (7%). We obtained a conclusive cytological diagnosis in 60 cases (diagnostic yield of 85%) and IHC was performed in 58 cases (82%). The most frequent diagnoses were GIST (37%), leiomyoma (14%) and metastases (13%). When compared with a retrospective cohort of 56 cases, diagnostic yield was significantly higher (85% versus 25%, p < 0.001).

Conclusion: Wet suction technique allowed an excellent diagnostic yield in the diagnosis of rectal and perirectal lesions by providing a safe sampling method of lesions that are often inaccessible for other modalities. It can be especially useful in confirming recurrence of malignancy and might also have additional value in the diagnosis of lymph node metastases and endometriosis that may occur as submucosal lesion endoscopically.

Disclosure: Nothing to disclose.

P0851 EXAMINATION OF THE USEFULNESS OF ESOPHAGEAL ULTRASONOGRAPHY IN EARLY-STAGE STOMACH CANCERS
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Introduction: With the increasingly widespread use of endoscopic submucosal dissection (ESD) for early-stage stomach cancers, pre-surgical depth diagnosis for determining suitable treatment needs to be increasingly accurate. In normal experience, even if a diagnosis of intramuscular carcinoma is made, some lesions actually infiltrate the submucosa. Although there are various theories regarding the usefulness of endoscopic ultrasonography (EUS) in depth diagnosis, no fixed opinion has been arrived at. Therefore, the purpose of this study was to clarify the significance of performing EUS when diagnosing the depth of early-stage stomach cancers.

Aims and Methods: Of the cases that underwent ESD at our hospital between November 1, 2012 and October 31, 2017, subjects comprised 454 lesions in 393 cancers. Each detailed review of medical records was possible. Subjects were divided depending on whether they underwent preoperative EUS into an EUS group and a non-EUS group. We then retrospectively investigated accuracy rates for depth diagnosis (depths M-SM1 and SM2 or deeper) in each group. Results were then compared with accuracy rates for the tumor site (UML regions), histopathological differentiation (differentiable type/poor differentiation and undifferentiated type), the presence or absence of ulcerous complications, and differences in the degree of experience of the surgeon.

Results: Overall, the accuracy rates of depth diagnosis in pre-operative endoscopies was 90.7%, and between the EUS and non-EUS groups, accuracy was found to be low in the EUS group (79.6% vs. 94.4%; p < 0.001). In the EUS group, no differences were observed in diagnostic accuracy regarding different tumor sites (depths M-SM1 vs. SM2 or deeper: 92.0% vs. 90.5% and different histopathological differentiation (differentiable type/poor differentiation and undifferentiated type) 79.2% vs. 85.7%; p = 0.56). In the EUS group, the accuracy rate was significantly lower in cases with ulcerous complications than those without (ulcer presence/absence 72.2% vs. 90.5%; p = 0.03). In terms of surgeon experience, no differences were identified in accuracy rates between trainee and expert surgeons in either the EUS or non-EUS group (76.4% vs. 82.8%; p = 0.40) (91.3% vs. 92.3%; p = 0.68). Further, no difference was identified in the accuracy rates between trainee and expert surgeons in the EUS group depending on whether the lesion was endoscopically-treated (depth M-SM1) (85.4% vs. 92.0%; p = 0.24) or non-eligible (SM2 or deeper) (14.3% vs. 25.0%; p = 0.55).

In cases that were eligible for ESD, the significance of preoperative EUS was unclear. In cases of ulcerous complications in particular, EUS accurate rates were low, with difficulty discriminating between ulcer echo signals and invasive foci cited as the cause. In cases of ulcerous complications, it appears more important to diagnose depth using regular light imaging.

Disclosure: Nothing to disclose.

P0852 UTILITY OF LIVER AND SPLEEN EUS-ELASTOGRAPHY FOR PREDICTION OF LIVER CIRRHOSIS AND PORTAL HYPERTENSION: A PROSPECTIVE CASE-CONTROL STUDY
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Introduction: Liver Cirrhosis (LC) includes hepatic and splenic structural and functional changes, with subsequent Portal Hypertension (PH). Abdominal ultrasound, upper endoscopy and Transient Elastography (T-E) constitute LC and PH standard diagnostic workup, delaying it and increasing health care cost. EUS-Elastography (EUS-E) can be considered as a gold standard (G-S) diagnostic test (FibroScan®, EchoSens, Paris, France) findings. Control group: patients with no liver, biliary tract or spleen disease history, who after normal T-E, they underwent FibroScan® due to submucosal lesions workup. Liver and Spleen EUS-E were performed in each group by 2 gastroenterologists with expertise in EUS-E, using 3.8 mm working channel linear-array echoendoscope (ECG 3870UTK, Pentax Germany) with Hitachi AVIUS Ultrasound Console. LSM and SSM Strain Ratio (SR) and Strain Histogram (SH) were measured 10 times per patient. Azigos vein (Av) diameter (D), mean velocity (MV) and Blood Flow Volume Index (BFVI) were also measured once. The association between LSM and SSM-SH, reached AUC = 0.56). The accuracy rates were low, with difficulty discriminating between ulcer echo signals and invasive foci cited as the cause. In cases of ulcerous complications, it appears more important to diagnose depth using regular light imaging.

Disclosure: Nothing to disclose.
Abstract No: P0852

A. T-E and EUS-E results between study groups [median (minimum – maximum range)]

T-E Fibrosis [Elastography (kPa)]

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Median</th>
<th>Minimum – Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>21.30</td>
<td>(9.00–75.00)</td>
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<tr>
<td>Test</td>
<td>4.98</td>
<td>(1.00–7.50)</td>
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T-E Fibrosis variability (IQR/E)

<table>
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<th>Study Group</th>
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<th>Minimum – Maximum</th>
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<tr>
<td>Control</td>
<td>0.14</td>
<td>(0.00–0.32)</td>
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<tr>
<td>Test</td>
<td>0.12</td>
<td>(0.04–0.32)</td>
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LSM-Strain Ratio (SR)

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<tr>
<td>Control</td>
<td>12.10</td>
<td>(4.92–50.64)</td>
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<tr>
<td>Test</td>
<td>6.50</td>
<td>(2.34–18.40)</td>
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T-E Fibrosis variability (IQR/E)

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Median</th>
<th>Minimum – Maximum</th>
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<tbody>
<tr>
<td>Control</td>
<td>0.001</td>
<td>(0.00–0.32)</td>
</tr>
<tr>
<td>Test</td>
<td>0.001</td>
<td>(0.04–0.32)</td>
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LSM-Strain Ratio (SR)

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<th>Minimum – Maximum</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>7.53</td>
<td>(3.10–16.20)</td>
</tr>
<tr>
<td>Test</td>
<td>3.97</td>
<td>(2.01–8.85)</td>
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</table>

T-E Fibrosis variability (IQR/E)

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Median</th>
<th>Minimum – Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.001</td>
<td>(0.00–0.32)</td>
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<tr>
<td>Test</td>
<td>0.001</td>
<td>(0.04–0.32)</td>
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ULTRASOUND: DECISION TREE METHOD

Aims and Methods: We retrospectively analyzed gastric cancer patients who underwent EUS from September 2005 to February 2016. EUS T stage and pathologic T stage were classified as T1a, T1b, T2, or T3 and the accuracy of EUS T stage and factors affected over/underestimation were examined by using decision tree analysis-CHAID method.

Results: A total of 4818 patients were finally included in the study. The most significant factor affecting the accuracy of the EUS T stage was size. The rate of overestimation was higher in lesions > 3 cm, while the rate of underestimation was higher in lesions ≤ 3 cm.

Conclusion: In this hierarchical analysis, the most significant factor affecting the accuracy of EUS T stage was tumor size (3 cm). For the lesion larger than 3 cm, the rate of underestimation was more affected by differentiation, and for the lesion smaller than or equal to 3 cm, differentiation and tumor location were important.

Disclosure: Nothing to disclose

P0853 HIERARCHICAL ANALYSIS OF FACTORS ASSOCIATED WITH T STAGING OF GASTRIC CANCER BY ENDOSCOPIC ULTRASOUND: DECISION TREE METHOD

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Introduction: Precise prediction of the depth of tumor invasion (T stage) in gastric cancer is important for the decision of treatment modality and endoscopic ultrasound (EUS) is known to be the most reliable method for it. However, sometimes it can lead to overtreatment when EUS overestimates T stage or undertreatment when underestimates. Therefore, we examined what factors affect the T stage in patients with gastric cancer.

Aims and Methods: We retrospectively analyzed gastric cancer patients who underwent EUS from September 2005 to February 2016. EUS T stage and pathologic T stage were classified as T1a, T1b, T2, T3, and T4. Factors affecting over/underestimation were examined by using decision tree analysis-CHAID method.

Results: A total of 4818 patients were finally included in the study. The most significant factor affecting the accuracy of the EUS T stage was size. The rate of overestimation was higher in lesions > 3 cm, while the rate of underestimation was higher in lesions ≤ 3 cm. (37.2% vs 29.8% vs. 17.1%, p < 0.001)

Conclusion: In this hierarchical analysis, the most significant factor affecting the accuracy of EUS T stage was tumor size (3 cm). For the lesion larger than 3 cm, the rate of overestimation was more affected by differentiation, and for the lesion smaller than or equal to 3 cm, differentiation and tumor location were important.

Disclosure: Nothing to disclose

P0854 RANDOMIZED TRIAL COMPARING FNA AND FINE-NEEDLE BIOPSY FOR EUS-GUIDED SAMPLING OF SOLID TUMORS

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Introduction: The definitive diagnosis of solid tumors relies on immunohistochemical staining, which depends on enough tissue being submitted to the pathologist. Achieving adequate tissue acquisition from tumors by EUS-FNA remains a limitation. Advances in needle design, however, have improved tissue acquisition and therefore may improve the definitive diagnosis by EUS-FNA. Endoscopic ultrasound (EUS)-guided fine needle aspiration is used to collected aspirates for cytology analysis and biopsy samples for histologic analysis. We conducted a multicenter study to compare the accuracy of diagnosis via specimens collected with fine-needle biopsy (FNB) Vs. fine needle aspiration (FNA) for patients with solid tumors.

Aims and Methods: We performed a prospective single-blind study at 5 tertiary care institutions. A total of 4818 patients were finally included in the study. The most significant factor affecting the accuracy of EUS T stage was size. For the lesion larger than 3 cm, the rate of overestimation was more affected by differentiation, and for the lesion smaller than or equal to 3 cm, differentiation and tumor location were important.

Conclusion: In this hierarchical analysis, the most significant factor affecting the accuracy of EUS T stage was tumor size (3 cm). For the lesion larger than 3 cm, the rate of overestimation was more affected by differentiation, and for the lesion smaller than or equal to 3 cm, differentiation and tumor location were important.

Disclosure: Nothing to disclose

P0855 NOVEL EUS-GUIDED IRREVERSIBLE ELECTROTHERMAL ABLATION OF PANCREAS: AN EXPERIMENTAL STUDY

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Introduction: Endoscopic IRE can be performed using a flexible, thin, needle-shaped electrode for an endoscopic ultrasound (EUS)-guided procedure. This study aimed to evaluate the feasibility and efficacy of performing EUS-GUIDED IRE with endoscopic needle-electrode in porcine pancreas.

Aims and Methods: A 19-gauge (1.1 mm) endoscopic IRE electrode consisting of a flexible electrode covered with protective sheath, needle-shaped tip with two exposed electrode band, generator connectors, and electrode push handle. Experimental endoscopic IRE on the pancreas were performed by EUS-guided approach and compared with surgical approach. The animals were sacrificed after 24 h and their pancreases collected.

Results: IRE ablation using endoscopic needle-electrode was successful technically in EUS-guided approaches for the pancreas. Immediately following IRE, the ablated pancreatic tissue showed no gross change except focal hemorrhage. H&E staining showed a well-demarcated ablation site measuring 1.0–1.5 cm in diameter in the pancreas. TUNEL immunohistochemistry showed diffuse cell death along the puncture site 24 h after IRE. No complication was observed in pigs after endoscopic IRE ablation.

Conclusion: EUS-GUIDED IRE ablation was feasible and effective for pancreas using the newly developed device.

Disclosure: Nothing to disclose

P0856 THE VALIDATION OF STRING SIGN IN THE DIFFERENTIAL DIAGNOSIS OF PANCREATIC CYSTS

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Introduction: Pancreatic cystic lesions (PCL) are common. Mucinous PCL are considered to have malignant potential, albeit in a minority. Differentiating mucinous lesions from non-mucinous ones is, sometimes, challenging. We investigated the efficacy of string sign (SS), a very simple test, in this respect.

Aims and Methods: We performed a retrospective analysis reviewing the electronic medical records of the patients between October 2011 and March 2018

Analysis, or resolution of lesion. The primary objective was to compare EUS-FNA versus EUS-FNB for the cytological for histological diagnostic accuracy of malignancy using 22G EUS-FNA and the 22G EUS-FNB needles. The secondary outcome measures were rates of analysis yield (%) of malignancy on the first pass, technical failure, complications, and quality of histologic specimens.

Results: Accuracy of FNB analysis in malignancy is higher than all FNA cases (94.09% vs 91.53%), based on final patient diagnoses. Especially the findings from histologic analysis of FNBs were accurate for 93.55% of the cases, compared to 81.75% for FNAs (p < 0.001). In cytology analysis of malignant masses, samples collected by FNB accurately identified 89.78%, whereas samples collected by FNA accurately identified 85.71% (p = 0.046). Patients in whom diagnosis was established in first passes were 87.50% versus 79.17%, for FNA and FNB in the study. There was no significant difference in technical failure or complications between FNA and FN needles.

Conclusion: In the prospective study of patients with solid tumors, we found EUS-guided FNAs to produce more accurate diagnoses than samples collected by EUS-guided FNA samples.

References: Clinical Trials.gov no.: NCT02327065

Disclosure: Nothing to disclose
identifying the patients with PCL in whom string sign test was performed. This test was done by stretching fluid between fingertips or glass slide and fingertip. In case the stretch is equal or more than 5 mm, we consider it positive. A few drops of fluid is suffice. CEA and amylose measurement was done in case enough fluid was obtained. Cytologic examination was also done in most of the patients. Differential diagnosis of PCL was done by surgery or cytologic diagnosis. Immunohistochemical staining for MUC subtypes was performed in 10 cases, five from SS positives, five from SS negatives.

Results: A total of 587 patients with PCL were evaluated by EUS and samples were obtained by needle biopsy. Final diagnosis was available in 185 cases (97 pseudocysts, 38 IPMNs, 10 MCNs, 15 IPMN related adenocarcinoma, 12 adenocarcinoma, 3 ductal adenocarcinoma, 4 Serous cystic neoplasm (SCN), 4 neuroendocrine tumor (NET) and 2 Von Hippel Lindau related cystic lesions). SS testing was done in 172 patients. Fifty-six had histologically confirmed final diagnosis: 38 were mucinous (21 IPMNs, 7 MCNs, 10 IPMN related adenocarcinoma), while 18 were nonmucinous (7 pseudocysts, 3 NETs, 2 SCNs, 6 simple cysts). SS was tested in 22 IPMNs and 7 MCNs, while CEA could be measured in 11 IPMNs and 4 MCNs. There was only one patient with negative SS and high CEA value (818.3 ng/mL).

Table 1 represents the diagnostic validation of SS and CEA > 192 ng/mL in mucinous PCL.

<table>
<thead>
<tr>
<th>String</th>
<th>CEA &gt; 192 ng/mL</th>
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<tbody>
<tr>
<td>0.78</td>
<td>0.89</td>
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<tr>
<td>0.93</td>
<td>0.68</td>
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<td>0.80</td>
<td>0.73</td>
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</tbody>
</table>

Disclosure: Nothing to disclose

P0857 ENDOSCOPIC ULTRASOUND CORE BIOPSY ACQUISITION WITH A CENTER PROSPECTIVE STUDY

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Introduction: When on-site cytolgy is unavailable, European guidelines recommends performing two/three needle passes with a fine-needle biopsy (FNB), although the level of evidence is low. Core biopsy acquisition theoretically improves the diagnostic yield and it is optimal for tissue sampling for immunostaining and histologic diagnosis therefore it could potentially eliminate the use of ROSE.

Recently, a new Frasenne geometry needle has been developed to obtain a histologic sample for immunohistochemical staining, and histologic diagnosis. Although few studies are present in literature, previous observations proved that Frasenne biopsy needle yielded high-quality histology samples thus high diagnostic yield.

Aims and Methods: Primary aim is to evaluate the diagnostic accuracy of Frasenne geometry FNB in pancreatic (PL) and non-pancreatic lesions (NPL).

Secondary aim is to assess the rate of core tissue (preserved architecture specimens) obtained.

A single-center prospective cohort of patients who underwent EUS-FNB for solid lesions > 10 mm were evaluated (from June 2017 to January 2018) using 22 and 25 Gauge (G) Frasenne needles (Acquire, Boston Scientific needles).

For each needle pass, a different vial was used and numbered. At least three passes were required for cell-block evaluation.

The presence of core tissue was define as a sufficient material for adequate histologic interpretation.

Results: A total of 70 patients (mean age 69 years; range 87–40) were enrolled (33 females). Of the 58 PL, the most common final diagnosis was pancreatic cancer in 50. A median of 3.6 needle passes were performed (range 2–5; 22 G needle was used for 48 lesions. The diagnostic accuracy was 74.2% on the first pass (79.3% in PL vs 50% in NPL), 85.7% (93.1% vs 5.8%) at the second pass and reached 90% at 3rd needle pass (94% PL).

A tissue core biopsy was obtained in 56 lesions (79%) on the first pass and 85.7% after two passes (86.2% and 88.3% in PL respectively). Overall diagnostic accuracy was 92% (95.7% of PL) and a core tissue was achieved in 87.4%.

Conclusion: According to recent guidelines, 90% of diagnostic accuracy was obtained after three FNB passes. This accuracy seems to be even higher in the setting of PL (93% after two passes).

Frasenne geometry needles achieved a core tissue in 87% of lesions.

Disclosure: Nothing to disclose

P0858 SURVEILLANCE FOR ALLOGRAFT REJECTION AFTER INTESTINAL TRANSPLANTATION USING MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING

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Introduction: Acute cellular rejection (ACR), which is associated with graft failure, is one of the most important vexing problems after intestinal transplantation (IT). Whether endoscopic imaging could be used to predict ACR is not well determined.

Aims and Methods: We aimed to investigate the correlation of an endoscopic scoring system using a magnifying endoscopy under narrow-band imaging (ME-NBI) system with ACR after IT.

Method: Patients older than 18 years old who underwent IT from January 2011 to October 2018 were enrolled prospectively between June 2016 to March 2018. Endoscopic examinations were performed through ileostomy to anastomosis site with ME-NBI. The observed endoscopic findings were recorded by five components (V=E-N=C-H), each assessed in order of increasing severity from 0 to 3. A magnifying video scope (Olympus UCJ-10) was used.

The presence of core tissue was define as a sufficient material for adequate histologic interpretation.

1. ACR prediction and larger scale studies are warranted to validate these results.

Disclosure: Nothing to disclose

P0859 THE NEW INSERTION METHOD OF THE TRAN-NASAL ILEUS TUBE, THE ANTERIOR BALLOON METHOD, WAS APPLICABLE FOR THE SMALL BOWEL OBSTRUCTION: A RETROSPECTIVE CHART REVIEW

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3 Hamamatsu University, Center for Clinical Research, Hamamatsu, Japan

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Introduction: The gastrointestinal decompression is the initial and effective therapeutic approach for the patients with small bowel obstruction. Several recent studies showed that decomposition using the long trans-nasal tube achieved favorable clinical outcomes. Our previous pilot trail method using the newly developed trans-nasal ileus tube, the anterior balloon method, achieved effective decompression to the small bowel obstruction.

Aims and Methods: The present study was investigaged the effectiveness of the anterior balloon method for small bowel obstruction compared the ordinary insertion method.

The anterior balloon method used the ileus tube (CLINY double-balloon type; Create Medic Co., Ltd, Tokyo, Japan) of 300 cm length with two (anterior and posterior) balloons. After insertion of the tube into the duodenum, the anterior balloon was inflated and suctioned repeatedly with 10 mL of air using the 10 mL syringe until the ileus tube reached closely to the obstruction. A total of 126 patients with small bowel obstruction treated from January 2011 to October 2017 in Ureshino Medical center were retrospectively reviewed. The patients were divided into two groups: the patients treated by the anterior balloon method (44 patients: ABM group) and the patients treated by the ordinary insertion method (82 patients: OIM group). The patients’ characteristics including the causes of ileus, the treatment outcome, and the adverse events were compared between the two groups.

Results: The patients’ characteristics and symptoms on admission including fever, abdominal pain, abdominal distension, vomiting and defecation were not different. The patients’ characteristics and symptoms on admission including fever, abdominal pain, abdominal distension, vomiting and defecation were not different. The patients’ characteristics and symptoms on admission including fever, abdominal pain, abdominal distension, vomiting and defecation were not different. The patients’ characteristics and symptoms on admission including fever, abdominal pain, abdominal distension, vomiting and defecation were not different.

Disclosure: Nothing to disclose
Only 4 (1.67%; 2 females) patients developed pancreatitis, all prior to ileus tube insertion (8.3%).

### Discussion

Nothing to disclose

### Reference


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**P0860 HYPERAMYLASAEMIA POST ANTEGRADE DOUBLE BALLOON ENTEROSCOPY – DOES INDOMETHACIN MAKE A DIFFERENCE?**

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**Introduction:** High amylase does not always signify acute pancreatitis and it can occur due to focal areas of ischaemia in the pancreas due to mechanical stress during double balloon enteroscopy (DBE). The use of rectal NSAIAs to prevent post DBE pancreatitis has never been explored unlike in ERCP where patients receiving rectal NSAIAs have a lower incidence of pancreatitis.

**Aims and Methods:** Patients who received rectal indomethacin (100mg) 30 minutes prior to antegrade DBE were compared to a control group who did not receive indomethacin before the above protocol was implemented. Serum amylase and CRP 3 hours before and after DBE were compared.

**Results:** 240 patients (56 indomethacin, 184 controls; 50% males; mean age 58.5 ± SD 14.0) were included.

Indications included: IIDA (37.5%), obscure overt gastrointestinal bleeding (17.1%), suspected Crohn’s disease and strictures (17.9%), complication of coeliac disease (1.3%), small bowel (SB) tumours / polyps (17.9%), others (8.3%).

Patients had a median of 13.0 ± SD 13.0 passes, 65.0 ± SD 25.0 minutes, 170 ± SD 52.0 cm of SB examined. 36.3% underwent a therapeutic procedure during DBE: APC/adrenaline/clips (27.5%), foreign body removal (0.4%), polypectomy (8.3%).

Only 4 (1.67%; 2 females) patients developed pancreatitis, all prior to implementation of indomethacin in the local protocol. They had a median age of 47.0 ± SD 14.0 years, 9/10 had positive withdrawal time (adenomas detected), 86.7 ± SD 29.4 passes, 90 ± SD 52.0 minutes, 150cm ± SD 64.2 cm of SB examined and median hospital stay of 14 ± SD 5.2 days. 3 had polypectomies. 2 episodes occurred in the same patient. All had evidence of pancreatitis on CT scan. None of the patients received indomethacin before DBE.

Mean amylase (51.6 ± SD 22.7 vs 143.0 ± SD 143.9 U/L p = 0.0001) and CRP (13.0 ± SD 64.1 vs 17.3 ± SD 71.7 mg/L p = 0.0001) after the procedure were significantly higher than before the procedure. Females had a significantly higher amylase than males post procedure (155.2 ± 130.7 U/L I p = 0.017). Mean amylase 3 hours after DBE was significantly lower in patients who received indomethacin (114 vs 152) (p = 0.044). 83.9% had a rise in amylase in the indomethacin group compared to 92.2% controls. (p = 0.064).

Whilst there was no correlation between post-procedure amylase (p = 0.552), CRP (p = 0.058) and duration of the procedure, there was a significant association between amylase post procedure and length of SB examined. (Spearman’s rho 0.186; p = 0.005).

**Conclusion:** This study identifies a role for rectal indomethacin in patients undergoing antegrade DBE. We have demonstrated that rectal indomethacin reduces amylase post DBE and no patients given indomethacin experienced pancreatitis. Larger studies are required to assess if this also transforms into lowering risk or severity of pancreatitis.

Nothing to disclose

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**P0861 NEED FOR ENTEROSCOPY IN LIVER TRANSPLANTED PATIENTS**

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**Introduction:** The management of liver transplanted (LT) patients is often complex and requires a multidisciplinary approach. Anaemia due to obscure or overt gastrointestinal bleeding and bile duct complications can occur in LT patients, thus, the need for enteroscopy (capsule enteroscopy (CE), double-balloon enteroscopy (DBE)) or a double-balloon cholangiopancreatography (DB-ERCPC), can be present also in LT subjects. Nowadays few data about the diagnostic success and safety of these procedures in LT patients are present. Use of DBE is increasing for the management of post-transplant biliary strictures while anecdotal case-reports are available about CE after LT.

We aimed to evaluate the need for enteroscopy after LT and to estimate the success rate and the safety of these procedures.

**Aims and Methods:** We analysed retrospectively 468 patients, underwent orthotopic LT (OLT), followed in our Liver Transplant Unit in the last 5 years (from January 2013 to January 2018). We collected those who performed an enteroscopy including CE, DBE and DB-ERCPC. We collected data about the clinical and demographic characteristics of the patients (i.e. age, sex, year and reason of OLT, current medical therapy and previous LT), the diagnostic yield/success rate of the procedures and incidence of complications. We also valued the enteroscopic success (achievement of biliary anastomosis) and the therapeutic success for DB-ERCPC.

**Results:** 21 patients (4.5%) underwent one or more enteroscopies (26 procedures). We collect 9 CE (one of that followed by anterograde DBE), 14 DBE-ERCPC for 10 patients and 2 retrograde DBE. Medical indications to perform CE were iron deficiency (7/9) and chronic diarrhoea (2/9). DB-ERCPC was performed primarily for stenosis of the biliary anastomosis, with recurrence cholangitis (4/10) or with asymptomatic cholestasis (1/10). Less frequent indications were gallstones (3/10), PSC-related biliary tract stenosis (1/10) and biliary fistula (1/10).

The diagnostic yield for CE was 55% (5/9) and the most frequent cause of bleeding was jejunal angioectasia (4/9), followed by duodenal ulcer and ileal erosions. The enteroscopic success of DBE-ERCPC was 50% (7/14), the first cause of failure was the impossibility to find the biliary anastomosis. The diagnostic success was 50% (7/14).

One patient performed an anterograde DBE for treating a jejunal angiodysplasia, previously found on CE. Two retrograde DBE was performed in patients with suspected thickening of distal jejunal, with one diagnosis of intestinal localization of Large B-cell lymphoma and a normal findings in the other patient.

No procedural complications in the long and short term were observed with all the procedures.

**Conclusion:** A significant number of the liver transplanted patients can have the necessity to perform a small bowel endoscopy. All the analysed procedures were safe and with a good diagnostic yield/success. We suggest that Liver Transplantation Units should have the possibility to perform enteroscopy to improve the management of LT patients.

Nothing to disclose
rectosigmoid colon were respectively 6.2%, 5.2%, 6.1% and 17.3%. While all of these positive withdrawal times were longer than negative withdrawal time (67.3 ± 18.62 vs 51.11 ± 17.86, t = 10.729, 87.94 ± 29.51 vs 60.66 ± 22.27, t = 12.983; 86.12 ± 28.42 vs 58.77 ± 22.82, t = 13.830; 74.88 ± 25.67 vs 53.62 ± 20.46, t = 18.392; p < 0.001 respectively). The positive withdrawal time in ascending colon was respectively shorter than that in transverse colon and descending colon (67.31 ± 18.62 vs 87.94 ± 29.51, 86.12 ± 28.42 vs 74.88 ± 25.67, p < 0.001). However, there were no statistical differences between them in ADR (6.2% vs 5.2%, 6.1%, p > 0.05). The positive withdrawal time in transverse colon and descending colon was all longer than that in rectosigmoid colon (87.94 ± 29.51, 86.12 ± 28.42 vs 74.88 ± 25.67, p < 0.001). While the ADR in rectosigmoid colon was obviously higher than that in other three segments of colon (17.3% vs 6.2%, 5.2%, 6.1%, p < 0.001).

Conclusion: ADR and withdrawal time are all various in different colon segments. During the operation of colonoscopy, withdrawal time in ascending colon may be shortened appropriately. The adenomas in rectosigmoid colon are more likely to be detected and do not take longer withdrawal times.

Disclosure: Nothing to disclose.

P0863 YIELD OF CAPSULE ENDOSCOPY IN OBSCURE GI BLEEDING: A COMPARATIVE STUDY BETWEEN PREMENOPAUSAL AND MENOPAUSAL WOMEN
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Introduction: Premenopausal women (PMW) often have a complete study of the gastrointestinal tract without findings justifying anemia/blood loss often motivating investigation of other causes.

Aims and Methods: The present study aimed to evaluate adequacy of findings in capsule endoscopy (CE) performed in the setting of obscure gastrointestinal bleeding (OGB) in women (PMW and menopausal women (MW)). Retrospective, single-center study, including female patients submitted to CE in the setting of OGB between May 2011 and December 2016. Patients were divided into 2 groups according to age, considering fertile age as ≤55 years and menopause as ≥55 years. The diagnostic yield (DY), the bleeding rate and the time to rebleed were evaluated and compared between groups. Rebleeding was defined as drop of Hb ≥2g/dL or need for transfusional support or presence of melena/hematochezia.

Results: A hundred and eighty three female patients underwent CE for OGB, of whom 30.6% (n = 56) were PMW and 69.4% (n = 127) were MW. DY was 35.4% in PMW and 12.5% in MW. The most common findings were angiodysplasias in both groups (PMW:38.8%, MW:62.7%). In PMW, only 1.8% required therapeutic endoscopic treatment. In 18.1% of MW CE findings led to additional endoscopic treatment. Rebleeding at 1, 3 and 5 years in PMW was respectively 4.6%, 10.2% and 35.4% and 12.5% in MW. The most common findings were angiodysplasias.

Conclusion: Rebleeding at 1, 3 and 5 years in PMW was significantly lower than in MW and postmenopausal age as risk factors present could lower the mortality of gastric cancer.

Disclosure: Nothing to disclose.

P0864 IS PAN-ENTERIC VIDEO CAPSULE ENDOSCOPY A COST-EFFECTIVE OPTION FOR OPTIMIZATION OF CROHN'S DISEASE THERAPY IN ENGLAND?
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Introduction: The treatment paradigm for Crohn's disease (CD) is changing with the 95% level was calculated using probabilistic sensitivity analysis.

Aims and Methods: This study aims to identify whether the pan-enteric standard use of VCE in the CD care pathway would be cost effective in England. A patient-level, care pathway model specific to CD management in England was developed. Specifically, NICE guidance for CD management was supplemented by consensus opinion of a sample of physicians with CD and VCE expertise. The model included local pricing, NHS tariffs, incidence rates, step-up treatment, and the use of faecal calprotectin testing (FCT) to inform the need for endoscopic monitoring practices: colonoscopy or VCE, respectively. Provision of drug therapy influenced the onset, progression, or remission of CD flares, fistulae, and abscesses. Data for VCE were derived from a pan-intestinal small bowel and colon capsule, which provides pan-enteric assessment VCE (pVCE). Outcomes for 4,000 simulated patients over 20 years were assessed. Cost of care and patient quality of life (QoL) were compared between monitoring options (pVCE or colonoscopy). The willingness to pay threshold was taken as a conservative £10,000 per quality-adjusted life year (QALY) gained. Significance of results at the 95% level was calculated using probabilistic sensitivity analysis.

Results: All experts agreed that the CD care pathway had to be individualised to patient profile. However, consensus was sufficient to develop a protocolised pathway to model. Step-up treatment started with glucocorticosteroid and progressed to biologics (± azathioprine). High-risk patients (≥3 risk factors present) could initiate treatment with biologics directly. Need for endoscopy was informed by FCT, that is performed at least once per year. The 20-year care costs were £69,745 (£3,487 per year) with colonoscopy and £67,806 (£3,390 per year) with pVCE. pVCE was associated with increased patient QoL, with patients accruing a mean of 7.8 QALYs compared with 7.3 QALYs with colonoscopy. The simulation showed that the use of pVCE for monitoring is beneficial in England, saving £1,941 per QALY gained. Tests showed that pVCE would be considered cost-effective in 96.9% of 2,000 bootstrapped simulations. The 95% credible interval extended to £10,913 per QALY gained.

Key outcome drivers in the simulation were the need for surgical procedures (25% of costs) and the use of biologic therapies (24%). Use of pVCE resulted in earlier detection of inflammation and initiation of biologics, which increased care costs in the short term. In some patients, earlier treatment resulted in optimised outcomes with earlier abcess drainage preventing subsequent resection. As lower-cost biosimilars become available, the cost-effectiveness of pVCE may increase.

Conclusion: Use of pVCE for monitoring of CD activity is likely to be cost-effective in England over 20 years. Improved patient outcomes, including reduced need for bowel resection, are additional benefits.

Disclosure: RS is the owner and RTT and MB are employees of Coreva Scientific, which received consultancy fees for this work. NVL and CL are employees of Medtronic. AL and MM have previously provided medical advice to Medtronic for which they received honorarium in line with fair market value.
**P0866 SMALL BOWEL CAPSULE ENDOSCOPY (SBCE) IN THE ELDERLY, A MULTICENTRE PROSPECTIVE STUDY IN LORDANBY REGION**

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**Introduction:** Data on SBCE performance and yield in the elderly are scant and conflicting. Our aim was to compare SBCE performance and yield in old and very old patients with their younger, adult counterpart in a large, prospective, multicentre study.

**Aims and Methods:** From October 2011 to December 2013, data of 2294 consecutive patients undergoing SBCE in 30 Centres of Lordanby Region, were prospectively collected in a dedicated database. For the purpose of this study, we included 2260 adult patients (≥18 years old). Patients were stratified by three age-related groups, namely: A (18–64 years old, n = 898), B (65–79, n = 935), C (≥80, n = 336). Diagnostic yield (DY) was defined as any small bowel (SB) abnormality, and clinical significant findings (CSF) as SB P2 lesions, in accordance to Saurin’s classification. CSF were classified in five categories using a modified Capsule Endoscopy Structured Terminology (Cest): (i) stenosis, (ii) luminal blood, (iii) inflammatory (erosion, ulcers), (iv) neoplastic (polyp, mass), (v) vascular. Chi-square for independent proportions was used to compare the three groups for the following outstanding characteristics: indication, gender, outpatient status, completion rate, retention rate, DY, CSF, and category of findings. p value<0.05 was considered statistically significant.

**Results:** Suspect small bowel bleeding was the leading indication to SBCE (75.3%), without differences between groups. Males were under represented in group C (45% vs 51.6 and 56% in group A and B, respectively), without statistical significance (p = 0.28). As shown in table 1, we did not find any difference among the three groups in the frequencies of the above-mentioned variables of interest.

**Conclusion:** In this large prospective series, in the elderly, SBCE performed as well as adults, without difference in terms of outpatient status, diagnostic yield, completion rate, retention rate, and findings.

**Disclosure:** Nothing to disclose

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**P0867 DEVELOPMENTAL INNOVATIONS WHILE PRODUCING A NOVEL CAPSULE**

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**Introduction:** Small bowel capsule endoscopy (CE) has made tremendous technological progress, due to its superior patient acceptability and safety profile. However, CE of the colon is held back by the need for a prep as good as or better than an average colonoscopy. C-Scan is a novel capsule which obviates the need for any cathartic or laxatives (Check Cap Ltd, Mount Carmel, Isfiya, Israel) (1). The X-ray imaging capsule overcomes the requirement for bowel preparation, a major deterrent for CRC screening. No prep, diet restrictions or medications are applied. The device records for 100 hours. Developing this new capsule required numerous innovations, herein described, which are spinoffs with major side-benefits. Such benefits are in addition to helping achieve the primary goals of producing an efficient, safe capsule requiring no prep, which successfully identifies polyps, screens the colon, prevents cancer and thus saves lives.

**Aims and Methods:** A capsule has been produced and trials performed in over 200 humans. This capsule, in addition to identifying polyps, delivers novel information on motility, with pressure measurements and thermal measurements, and advances physiologic concepts and knowledge regarding native colonic functions in health and disease states. The CE- (Certificate European) approved capsule, used in over 200 humans to screen for polyps, has presented challenges and led to a series of exciting technological innovations, herein described.

**Results:** The three-point online monitor, embedded in a tracking unit attached to the back of the patient, has delivered patterns of capsule movement in a prep-less normal colon, leading to real-life tracks of how colonic contents move. The performance of the 3D colon was examined in a uniquely designed mechanical phantom model of the colon and a high correlation between behavior in humans and the phantom was demonstrated. Accuracy of the capsule tracking by triangulation from the 3 sensors on the back of the patient is +/-5mm, including when patients (except morbidly obese) are in motion. This allows clinicians to localize findings correctly, facilitating the planning of subsequent interventions.

Two examples illustrate the accuracy of the system during clinical procedures: The new algorithms developed for the C-Scan detect the minute motion of the small bowel peristalsis and colon movements caused by ventilation. The pressure monitors on the C-Scan Capsule deliver real-life measurements of the relative pressures throughout the segments of the colon, opening a path to reflecting on interventions which target specific sites within the colon.

**Conclusion:** The development of the C-Scan capsule has stimulated the above five technologic innovations which may all continue to deliver new physiologic information allowing us to deliver better health.

**Disclosure:** Prof Lachter works as a paid consultant for Checkcap

**Reference**

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**P0868 SMALL BOWEL NEOPLASIA DETECTION IN LYNCH SYNDROME USING VIDEO CAPSULE ENDOSCOPY**


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**Introduction:** Lifetime risk of developing small-bowel cancer in patients with Lynch syndrome (LS) is estimated to be around 4%, which is more than 100 times the risk of the general population. This risk is almost similar to the lifetime risk of colorectal cancer in the general population, for which screening is generally recommended. Screening for small-bowel cancer in Lynch syndrome has, until now, not been included in guidelines for surveillance of families with Lynch syndrome. In 2016 Mallorca group gave the advise small bowel screening interventions often end in a different place than they initially envisioned. The development of the C-Scan capsule has stimulated the above five technologic innovations which may all continue to deliver new physiologic information allowing us to deliver better health.

**Disclosure**

**Table 1**

<table>
<thead>
<tr>
<th>Group</th>
<th>N Patients</th>
<th>Outpatient (%)</th>
<th>Completion (%)</th>
<th>Retention (%)</th>
<th>DY (%)</th>
<th>CSF (%)</th>
<th>Stenosis (%)</th>
<th>Luminal blood (%)</th>
<th>Inflammatory (%)</th>
<th>Neoplastic (%)</th>
<th>Vascular (%)</th>
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<tbody>
<tr>
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<td>649 (65.6)</td>
<td>891 (90)</td>
<td>10 (1)</td>
<td>604</td>
<td>509 (51.4)</td>
<td>13/509 (2.56)</td>
<td>51/509 (10)</td>
<td>137/509 (26.9)</td>
<td>93/509 (18.2)</td>
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<td>Outpatient (%)</td>
<td>935</td>
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<td>836 (89.4)</td>
<td>4 (0.4)</td>
<td>529</td>
<td>477 (51.4)</td>
<td>12/477 (2.5)</td>
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<td>120/477 (25.1)</td>
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<tr>
<td>Completion (%)</td>
<td>336</td>
<td>202 (60)</td>
<td>310 (92.2)</td>
<td>3 (0.8)</td>
<td>190</td>
<td>164 (48.8)</td>
<td>1/164 (0.6)</td>
<td>21/164 (12.8)</td>
<td>43/164 (26.2)</td>
<td>77/164 (47.6)</td>
<td>174/164 (58.5)</td>
</tr>
</tbody>
</table>

**[Transit time measurement for C-Scan capsule]**

A capsule has been produced and trials performed in over 200 humans. This capsule, in addition to identifying polyps, delivers novel information on motility, with pressure measurements and thermal measurements, and advances physiologic concepts and knowledge regarding native colonic functions in health and disease states. The CE- (Certificate European) approved capsule, used in over 200 humans to screen for polyps, has presented challenges and led to a series of exciting technological innovations, herein described.

**Results:** The three-point online monitor, embedded in a tracking unit attached to the back of the patient, has delivered patterns of capsule movement in a prep-less normal colon, leading to real-life tracks of how colonic contents move. The performance of the 3D colon was examined in a uniquely designed mechanical phantom model of the colon and a high correlation between behavior in humans and the phantom was demonstrated. Accuracy of the capsule tracking by triangulation from the 3 sensors on the back of the patient is +/-5mm, including when patients (except morbidly obese) are in motion. This allows clinicians to localize findings correctly, facilitating the planning of subsequent interventions.

Two examples illustrate the accuracy of the system during clinical procedures: The new algorithms developed for the C-Scan detect the minute motion of the small bowel peristalsis and colon movements caused by ventilation. The pressure monitors on the C-Scan Capsule deliver real-life measurements of the relative pressures throughout the segments of the colon, opening a path to reflecting on interventions which target specific sites within the colon.

**Conclusion:** The development of the C-Scan capsule has stimulated the above five technologic innovations which may all continue to deliver new physiologic information allowing us to deliver better health.

**Disclosure:** Prof Lachter works as a paid consultant for Checkcap

**Reference**
In 91.5% of the procedures, caecal visualization was achieved. Small-bowel neoplasia was detected in two LS patients and three OBS patients (p = 0.06). The two groups have a significant statistically different mean age (SD): 41.3 ± 14.0 vs 62.9 ± 17.2 years in OBS group (Table 1). Besides small bowel adenocarcinoma, LS patients and OBS patients have statistically significant difference in incidence of vascular lesion, angiectasia and minute polyps (Table 1).

Conclusion: The prevalence of small-bowel neoplasia in asymptomatic patients with LS was 8% vs 1.1%. Although the incidence of small bowel adenocarcinoma did not reach statistical significance difference, a trend through statistically significantly significant difference was observed and this suggests further multicentric studies are needed.

Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lynch Group</th>
<th>Obscure Bleeding</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>12 (48.0%)</td>
<td>163 (58.2%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>13 (52%)</td>
<td>117 (41.8%)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), years</td>
<td>41.3 (14.0)</td>
<td>62.9 (17.2)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Adenoma Small Bowel, n</td>
<td>2 (8.0%)</td>
<td>3 (1.1%)</td>
<td>0.06</td>
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<tr>
<td>Normal examination, n</td>
<td>4 (16.0%)</td>
<td>53 (18.9%)</td>
<td>1.0</td>
</tr>
<tr>
<td>No caecal visualisation, n</td>
<td>1 (4.0%)</td>
<td>25 (8.9%)</td>
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</tr>
<tr>
<td>Vascular lesion, n</td>
<td>4 (16.0%)</td>
<td>118 (42.1%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Emangioma/varice, n</td>
<td>0 (0%)</td>
<td>21 (7.5%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Angiectasia, n (%)</td>
<td>3 (12.0%)</td>
<td>114 (40.7%)</td>
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</tr>
<tr>
<td>Lymphangiectasia, n (%)</td>
<td>4 (16.0%)</td>
<td>42 (15.0%)</td>
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<tr>
<td>Submucosal lesion, n (%)</td>
<td>1 (4.0%)</td>
<td>29 (10.4%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Minute polyps, n (%)</td>
<td>10 (40%)</td>
<td>35 (12.5%)</td>
<td>0.001</td>
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<tr>
<td>Red spot, n (%)</td>
<td>4 (16.0%)</td>
<td>53 (18.9%)</td>
<td>1.0</td>
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<tr>
<td>Erosion/ulcer, n (%)</td>
<td>5 (20%)</td>
<td>78 (27.9%)</td>
<td>0.5</td>
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<tr>
<td>Substenosis, n (%)</td>
<td>1 (4.0%)</td>
<td>10 (3.6%)</td>
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</tbody>
</table>

[Small bowel neoplasia detection in Lynch syndrome using video capsule endoscopy: Results]

Disclosure: Nothing to disclose

P08809 THE DIAGNOSTIC YIELD OF SMALL BOWEL CAPSULE ENDOSCOPY IN POSTSURGICAL CROHN'S DISEASE

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Introduction: Post-operative endoscopic recurrence (POER) of Crohn’s disease (CD) is frequent and unpredictable. In clinical practice, colonoscopy is recommended 6–12 months after surgery, in order to detect early POER and guide management. The aim of our study was to determine the diagnostic yield of small bowel capsule endoscopy (SBCE) in this setting.

Aims and Methods: We reviewed the records of 5471 patients subjected to SBCE in our department from March 2003 to March 2017 (males/females: 2693/2778, mean age ± SD: 50.5 ± 28.4 years). Among these patients, we identified 677 with known CD, of whom 41 had undergone SBCE 6–12 months following ileocolonic resection. Any lesions detected in the proximal small bowel were also recorded. All these patients had also undergone ileocolonoscopy at the same time to assess for POER using the Rutgeerts score. The findings of the two tests were compared to examine whether SBCE can detect more proximal lesions in patients who did not exhibit POER (that is a Rutgeerts score ≤ 1) during ileocolonoscopy.

Results: POER was detected in 16/41 (39%) patients by ileocolonoscopy. SBCE detected lesions in the neoterminal ileum in 15 of these 16 patients (overall rate 36.6%) as in one patient the capsule did not reach the neo-terminal ileum during the battery’s life span. Concurrent lesions in the neo-terminal ileum and more proximally were detected by SBCE in 9/15 patients; however, two patients with an ileocolonic Rutgeerts score of 0 had more proximal lesions during SBCE.

Conclusion: SBCE is not cost-effective and cannot be recommended as an adjuvant to ileocolonoscopy to identify more proximal lesions post-operatively in CD patients. However, it may substitute for ileocolonoscopy considering local cost, disease characteristics and patient preferences.

Disclosure: Nothing to disclose

P0870 DEVELOPMENT OF QUALITY MEASURES FOR CAPSULE ENDOSCOPY REQUIRES A NOVEL APPROACH BASED ON A PERFORMANCE REVIEW OF A LARGE SINGLE CENTRE SERVICE

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Introduction: Capsule Endoscopy (CE) is a popular non-invasive technology to provide diagnostic imaging of the small bowel. As with all endoscopic techniques, quality of CE procedures will affect patient outcomes. Unlike upper and lower gastrointestinal endoscopy there is little in the literature on CE quality control, and there is a paucity of data. We present a novel approach to CE quality assurance initiatives.

Aims and Methods: To perform an analysis of our CE service with reference to procedure quality and patient outcomes. A retrospective review of CE procedures performed in our institution from 2010 through 2015 when CE was undertaken. CE procedures were identified from a database. Rapid Reader and other hospital electronic patient information software was used to extract essential information. Recorded data covered Pre-Procedural, Procedural and Post-Procedural domains and included patient demographics, indication, preparation quality, caecal visualisation, findings, complications, and CE reader. Data was grouped according to outcome or potential KPI and compared using a chi² test, p < 0.05 was considered significant.

Results: In all 1,227 CEs have been included and analysed; 50% (n = 615) female, median age 56 years (range 13–93). The overall diagnostic yield (DY) was 39% (n = 477). Only 85% (73%) CEs were performed for non ESGE approved indications including abnormal radiology (n = 41). The DY was similar for ESGE and non-ESGE recognised indications 34% (n = 390) and 35% (n = 30) respectively, p = 0.92. However CEs performed to assess known disease had a higher DY than screening CE; known CD (65.1%) vs suspected CD (38%) (p = 0.001), OR2.9. Overall 8% (n = 98) of CEs were incomplete. Surprisingly DY was significantly higher for incomplete, 56% (n = 55) versus complete studies 37% (n = 422), p = 0.004, likely reflecting the pathology encountered. Similarly, DY was higher in the 38% (n = 459) of CEs with a poor-quality bowel preparation; 55% (n = 244) vs 40% (n = 302), p = 0.001. Only 2/1272 (0.1%) experienced true capsule retention.

Conclusion: Our study suggests development of quality measures for CE will require a novel approach and further research. As expected KPIs based on standard endoscopy experience have yielded contradictory results. Incomplete studies and poor preparation quality were both associated with lower diagnostic yields, which is not that surprising as bleeding is a major indication and significant findings can inhibit or slow capsule passage. In addition, the diagnostic yield for CEs is higher for disease assessment compared to screening tests. Our data also suggests that other indications including abnormal radiology can be an appropriate indication for CE. Finally, our data supports a structured approach to CE training.

Disclosure: Nothing to disclose

References


P0871 LONG-TERM OUTCOME OF ENDOSCOPIC TREATMENT OF BILIARY STRIATURE FOLLOWING LIVING DONOR LIVER TRANSPLANTATION

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Introduction: Biliary strictures remain one of the most challenging aspects after living donor liver transplantation (LDLT). Endoscopic procedures are the initial treatment in LDLT. One thousand four hundred forty one patients underwent LDLT from May 1995 to May 2014. Biliary strictures developed in among 145 patients who were successfully managed with endoscopic drainage, biliary stent could be removed in 94 patients. After for 12 months
follow up after removal of endoscopic retrograde biliary drainage (ERBD), 69 patients with recurrent biliary obstruction and 20 patients (33.3%) showed recurrent biliary stricture. We compared the risk factors between no recurrent biliary stricture and recurrent biliary stricture group. Younger donor age was associated with lower recurrence rate, and non-B, non-C liver cirrhosis was associated with increased recurrence rate of biliary stricture.

Conclusion: Long-term outcome of the endoscopic treatment of biliary stricture occurring after LDLT was relatively fine, but the clinician should be careful of ERBD removal and following up in the case with factors associated with recurrent biliary stricture.

Disclosure: Nothing to disclose

P0872 EUS-ANTEGRADE BILIARY STENTING VERSUS PTBD FOR DISTAL MALIGNANT BILIARY OBSTRUCTION IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

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Introduction: Distal malignant biliary obstruction (DMBO) in patients with surgically altered anatomy (SAA) is traditionally managed with PTBD, since anatomical features complicate endoscopic approach to the biliary orifice. Recently, enteroscopy and EUS assisted approaches have emerged as alternative treatments; however, limited data comparing between the procedures has been available so far.

Aims and Methods: The aims of this study were to compare EUS-antegrade treatment (AG) with PTBD for DMBO in patients with SAA. Patients who underwent EUS-AG or PTBD as management of DMBO and had history of upper intestinal surgery at 2 tertiary centers between 4/2007 and 1/2018 were evaluated retrospectively. In EUS-AG, the bile duct was punctured under EUS-guidance, followed by guidewire placement through the obstruction, dilatation of the fistula, and metallic stent placement cross DMBO. Naso-biliary drainage was placed though the fistula only if there might be any chance of stent dysfunction or active cholangitis. PTBD typically had 3 steps approach: Firstly, the bile duct was punctured under ultrasound guidance followed by external drainage tube placement. In the 2nd session, a metallic stent was deployed cross DMBO with removing the external drainage. In the 3rd session, the external drain was removed after confirmation of good bile flow through the stent. The study outcomes were the technical and clinical success rates and the adverse event rate. Technical success and clinical success were defined as successful interventional procedure of serum total bilirubin level to 50% reduction of the initial level. Survival duration was analyzed with Kaplan-Meier method between the groups. Possible factors which can affect the survival duration were also analyzed with multivariable analysis. Continuous valuables were described with median (interquartile range).

Results: A total of 53 patients were enrolled. Among them, 24 patients underwent EUS-AG and 29 had PTBD. Basic characteristics (EUS-AG/PTBD) were the same except the procedural time. Continuous valuables were described with median (range 5–38).

- Technical success and clinical success were defined as successful interventional procedure of serum total bilirubin level to 50% reduction of the initial level.
- Survival duration was analyzed with Kaplan-Meier method between the groups.
- Possible factors which can affect the survival duration were also analyzed with multivariable analysis. Continuous valuables were described with median (interquartile range).

Conclusion: There were no significant differences in safety and efficacy between EUS-AG and PTBD for DMBO in patients with SAA. EUS-AG might be a treatment of choice for management of DMBO in SAA patients same as PTBD.

Disclosure: Nothing to disclose

P0873 THE USEFULNESS OF NEWLY MODIFIED NON-FLARED FULLY COVERED METAL STENT OF 12 MM-DIAMETER COMPARED WITH CONVENTIONAL STENT FOR PERIAMPUTAL MALIGNANT BILIARY STRUCTURES

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Introduction: Endoscopic ultrasonography guided choledochoduodenostomy (EUS-CD) using a lumen apposing metal stent (LAMS) has been recently reported as an alternative approach to the management of patients with malignant obstructive jaundice and failed endoscopic retrograde cholangiopancreatography (ERC). Aims and Methods: The aim of this study was to analyze the safety, technical and clinical efficacy of EUS-CD in this setting of patients. Retrospective analysis of a prospectively maintained data base of consecutive patients with unresectable malignant distal bile duct obstruction who, between 10/2015 and 12/2017, underwent EUS-CD using the study device (Electrocuttery enhanced (EC)-AXIOS, Boston Scientific Corp., Marlborough,Massachusetts, USA) after unsuccessful ERCP in a single tertiary-care academic medical center. Technical success was defined as accurate positioning of the stent. Clinical success was defined as resolution of biliary obstructive symptoms with a decrease in the total bilirubin level to 50% reduction of the initial level.

Results: Forty-six patients (47.8% female; median age 73.1 ± 12.6) underwent direct EUS-CD using the biliary EC-AXIOS(6x8mm in 21(45.7%); 8x10mm in 18(41.3%); 10x10mm in 6 (13%)). ERCP failure was due to inability to get deep biliary cannulation in 30 patients (65.2%) and to duodenal obstruction in the remaining 16(34.8%) patients. The procedure was technically successful in 43/46 (93.5%) patients, with a mean procedural time of 14.7 min (range 5–38).

Disclosure: Nothing to disclose

P0874 DEVELOPMENT OF A NOVEL INTERNAL FISTULA TUBE FOR ENDOSCOPIC TRANSMURAL BILIARY DRAINAGE

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1Saitama Medical University International Medical Center, Hidaka city, Saitama, Japan
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Introduction: We developed a biliary internal fistula tube (BIFT) which has been constructed with a conventional biliary stent tube and a bioabsorbable polymer seat (BAPS) for a transmural biliary drainage. In this study we attempted to compare the difference between the BIFT and conventional tube (CT) in biliary-enteric fistula formation.

Aims and Methods: The BIFT is a conventional biliary tube wrapped with the BAPS, which is 0.5mm thickness. The BAPS is an ideal scaffold for tissue regeneration which allows easy penetration of cells. BIFT group (n = 6): The pigs were laparatomized to expose the extraperitoneal bile duct (EHBD). The 5cm BIFT was placed between gallbladder (GB) and duodenum (DU). CT group (n = 6): The 5cm CT was placed between GB and DU in a similar manner of the BIFT group. In both group these pigs were sacrificed and re-laparatomized at 4 weeks after the placement.

Results: BIFT group: At 4 weeks after the placement, the distance between GB and DU was shortened. A biliary-enteric fistula, which had 1.5cm bower diameter was constructed between GB and DU. CT group: At 4 weeks after the placement, the CT became surrounded by connective tissue, and the distance between GB and DU came closer to each other. However, the connective tissue between GB and DU was fragile and easy to be divided. The lumens of the CT has biliary sludge and almost became obstructed.

Conclusion: The placement of the BIFT between GB and DU induced rapid and good fistulization, and has the potential for application as a novel device for transmural biliary drainage avoiding the need for exchange of tubes.

Disclosure: Nothing to disclose

P0875 EUS-GUIDED CHOLEDOCHODUODENOSTOMY USING A LUMEN APPOSING METAL STENT FOR MALIGNANT DISTAL BILIARY OBSTRUCTION: A PROSPECTIVE ANALYSIS OF A SINGLE CENTER EXPERIENCE

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1Humanitas Research Hospital, Digestive Endoscopy Unit, Division of Gastroenterology, Rozzano (MI), Italy
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Introduction: Endoscopic ultrasonography guided choledochoduodenostomy (EUS-CD) using a lumen apposing metal stent (LAMS) has been recently reported as an alternative approach to the management of patients with malignant obstructive jaundice and failed endoscopic retrograde cholangiopancreatography (ERC). Aims and Methods: The aim of this study was to analyze the safety, technical and clinical efficacy of EUS-CD in this setting of patients. Retrospective analysis of a prospectively maintained data base of consecutive patients with unresectable malignant distal bile duct obstruction who, between 10/2015 and 12/2017, underwent EUS-CD using the study device (Electrocuttery enhanced (EC)-AXIOS, Boston Scientific Corp., Marlborough,Massachusetts, USA) after unsuccessful ERCP in a single tertiary-care academic medical center. Technical success was defined as accurate positioning of the stent. Clinical success was defined as resolution of biliary obstructive symptoms with a decrease in the total bilirubin level to 50% reduction of the initial level.

Results: Forty-six patients (47.8% female; median age 73.1 ± 12.6) underwent direct EUS-CD using the biliary EC-AXIOS(6x8mm in 21(45.7%); 8x10mm in 18(41.3%); 10x10mm in 6 (13%)). ERCP failure was due to inability to get deep biliary cannulation in 30 patients (65.2%) and to duodenal obstruction in the remaining 16(34.8%) patients. The procedure was technically successful in 43/46 (93.5%) patients, with a mean procedural time of 14.7 min (range 5–38).
Clinical success was achieved in 45/46 (97.7%) patients with a reduction in the rate of complications including acute pancreatitis which occurred in 13.3% vs. 3.5% (p < 0.01). The recurrence rate (13.3% vs. 3.5%) was also higher in the ETGBD group than in the P-GBD group respectively. After adjustment of inverse-probability-of-treatment-weighted method, adverse event rate was not statistical different between two groups. However, for late adverse events including migration of stent or dislodgement of drainage tube, stent or tube obstruction, tracts in the liver, and recurrence of cholecystitis it is shown that EUS-GBD is significantly higher odds ratio compared to EUS-GPD (odds ratio 3.38 (95% CI 1.08 to 10.54)). P-GBD also showed a higher risk of additional intervention compared to EUS-GPD (odds ratio 3.60 (95% CI 1.26 to 10.32)). Moreover, logistic regression analysis showed that P-GBD was significantly associated with re-intervention (odds ratio 3.68, 95% CI 1.43 to 9.47, p = 0.007). Conclusion: EUS-GBD and P-GBD were both effective means of achieving gallbladder drainage. However, EUS-GPD might be beneficial than P-GBD in long term management for the patients with acute cholecystitis who are not suitable for cholecystectomy. Disclosure: Nothing to disclose

P0877 LONG-TERM OUTCOME OF EUS-GUIDED GALLBLADDER DRAINAGE VS. PERCUTANEOUS GALLBLADDER DRAINAGE IN PATIENTS WHO ARE UNFIT FOR CHOLECYSTECTOMY: WHICH IS BETTER?

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Introduction: EUS guided gall-bladder drainage (EUS-GBD) has become increasingly used to treat patients with acute cholecystitis who are not eligible for surgery. However, there are limited data comparing long-term outcomes of EUS-GBD and conventional percutaneous cholecystostomy (P-GBD). We therefore performed a retrospective study to compare the efficacy and safety of EUS-GBD and P-GBD in patients with acute cholecystitis.

Aims and Methods: We studied 182 patients who required gallbladder drainage for acute cholecystitis from February 2010 to November 2014. We used propensity-score weighting to adjust for differences in all covariates (age, sex, comorbid diseases, previous drugs) between EUS-GBD and P-GBD groups, and compared early and late adverse events needed for re-intervention in each group.

Results: A total of 182 patients (75 in EUS-GBD group and 107 in P-GBD group) were enrolled in this study. The technical/clinical success rate was 98.7%/100% (74/75, 74/74) in EUS-GBD and 99.1%/98.1% (106/107, 104/106) in P-GBD group respectively. After adjustment of inverse-probability-of-treatment-weighted method, early adverse event rate was not statistical different between two groups. However, for late adverse events including migration of stent or dislodgement of drainage tube, stent or tube obstruction, tracts in the liver, and recurrence of cholecystitis it is shown that EUS-GBD is significantly higher odds ratio compared to EUS-GPD (odds ratio 3.38 (95% CI 1.08 to 10.54)). P-GBD also showed a higher risk of additional intervention compared to EUS-GPD (odds ratio 3.60 (95% CI 1.26 to 10.32)). Moreover, logistic regression analysis showed that P-GBD was significantly associated with re-intervention (odds ratio 3.68, 95% CI 1.43 to 9.47, p = 0.007).

Conclusion: EUS-GBD and P-GBD were both effective means of achieving gallbladder drainage. However, EUS-GBD might be beneficial than P-GBD in long term management for the patients with acute cholecystitis who are not suitable for cholecystectomy. Disclosure: Nothing to disclose
TUESDAY, OCTOBER 23, 2018
09:00–17:00
Surgery II – Hall X1

P0879 THE THREE-YEAR EXPERIENCE OF ENDOSCOPIC TREATMENT OF THE ZENKER’S DIVERTICULUM
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Introduction: Current surgical guidelines of Zenker’s diverticulum treatment recommend incising the intersection of the criopharyngeal muscle (criopharyngeal myotomy) and performing a diverticulectomy. The working hypothesis of our scientific research assumes that the results of tunnel endoscopic cryo-pharyngeal myotomy will exceed the results of standard endoscopic treatment with respect to the effectiveness of clinical development of diseases and reducing the number of their relapses.

Aims and Methods: We report the results of a comparative study of the endoscopic treatment of Zenker’s diverticulum. In the period from July 2014 to March 2018 67 patients were included in our research. At the initial stage (until March 2017), all operations were performed according to the traditional method. Later, after the introduction of the new tunneling technique, it was given priority in application due to a number of advantages. The standard protocol for preoperative examination included the transnasal endoscopy and X-ray examination. In the presence of signs of diverticulitis, conservative treatment was performed before the reduction of inflammatory changes in the mucosa. The average age of the patients was 66 (from 34 to 86) years.

Results: According to the traditional method, 36 patients (group I) were operated on. In group II, 31 operations were performed using the tunnel technique. No technical or clinical difficulties associated with the myotomy or the mucosal defect closure were noted. The average time of the surgical intervention was 56±7 in the first group is 60±4 minutes in the second.

Conclusion: Tunnel surgery is a pathogenetically justified method of treating Zenker’s diverticulum as a neuromuscular disease. We suppose that today the tunnel technique stands to be the preferable treatment option of the Zenker’s diverticulum.

Disclosure: Nothing to disclose

References

P0880 PREVALENCE OF PRECANCEROUS CONDITIONS AND LESIONS OF THE STOMACH IN CANDIDATES FOR BARIATRIC SURGERY

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Introduction: Intestinal type gastric adenocarcinoma is preceded by a long lasting malignant preneoplastic process. Patients with chronic atrophic gastritis and/or intestinal metaplasia are at higher risk for gastric adenocarcinoma. Endoscopic surveillance is recommended to patients with extensive atrophic and/or intestinal metaplasia [1]. Obesity is a worldwide health problem. Surgical treatment has been shown to be the effective treatment for severe obesity and also for its complications. Roux-en-Y gastric bypass (RYGB) is one of the most commonly performed bariatric procedures. Although gastric cancer in the excluded stomach has been shown to be the most effective treatment for severe obesity and also for its advantages. The standard protocol for preoperative examination included the transnasal endoscopy and X-ray examination. In the presence of signs of diverticulitis, conservative treatment was performed before the reduction of inflammatory changes in the mucosa. The average age of the patients was 66 (from 34 to 86) years.

Results: According to the traditional method, 36 patients (group I) were operated on. In group II, 31 operations were performed using the tunnel technique. No technical or clinical difficulties associated with the myotomy or the mucosal defect closure were noted. The average time of the surgical intervention was 56±7 in the first group is 60±4 minutes in the second.

Conclusion: Tunnel surgery is a pathogenetically justified method of treating Zenker’s diverticulum as a neuromuscular disease. We suppose that today the tunnel technique stands to be the preferable treatment option of the Zenker’s diverticulum.

Disclosure: Nothing to disclose

References

P0881 GASTRIC PRESSURE AND ESOPHAGEAL REFLUX EXPOSURE SUGGEST THAT OMEGA-LOOP BYPASS IS DIFFERENT FROM BILLROTH II

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Introduction: Obesity is a global epidemic and consequently bariatric surgery is increasingly performed. More recently, omega-loop gastric bypass (OGB), consisting primarily of a long lesser-curvature gastric tube with a terminolateral gastro-enterostomy at 180–200 cm distal to the ligament of Treitz, was introduced. Thousands of these procedures have now been performed globally, being considered a safe and effective option for morbid obese patients. Despite positive effect in terms of weight loss and improvement of obesity-related comorbidities, there are concerns about symptomatic biliary reflux gastritis and esophagitis requiring revision. Concerns have also been expressed due to chronic biliary reflux, because of a similarity with old Billroth II (BII) procedure that exposed patients to the risk of gastric cancer. However, scarce data are available on the physiopathological effect of these two procedures on gastro-esophageal function.

Aims and Methods: Since gastric and esophageal reflux can depend from proximal gastric pressure, we aimed at assessing the esophagogastric junction (EGJ) function, esophageal peristalsis and reflux exposure using high-resolution manometry (HRM) and impedance-pH monitoring (MII-pH) after OGB and BII.

Methods: Obese (body mass index, BMI, > 35) patients underwent symptomatic questionnaires (GerDQ), endoscopy, HRM and MII-pH before and one year after surgery. We enrolled obese patients without dysmotility or any evidence of GERD. Intragastric pressures (IGP) and gastroesophageal pressure gradient (GEPG) were calculated. Esophageal motor function and EGJ were classified according to the Chicago Classification V. 3. EGJ contractile integral (EGJ-CI) was also calculated. Total acid exposure time (AET %), total number of refluxes and symptom association probability (SAP) were assessed. A group of patients who underwent BII, referred for follow-up, was studied with the same protocol to serve as the control population.

Results: We enrolled 22 OGB patients and 12 BII subjects. After surgery, none of the patients reported de novo heartburn or regurgitation. At endoscopic follow-up 1 year after surgery, esophagitis was absent in all patients and no biliary gastritis or presence of bile was recorded. Manometric features and patterns did not vary significantly after surgery, whereas IGP and GEGP statistically diminished (from a median of 15 to 9.5, p < 0.01, and from 10.3 to 6.4, p < 0.01, respectively) after OGB. BII subjects had significant lower values in IGP and GEGP (median of 4.2, p < 0.001, and similar GEGP 4.3, p = n.s.). LES pressure as well as EGJ-CI were significantly lower in BII subjects than OGB ones (13 vs 22 mmHg, p < 0.05, and 11 vs 21.5 mmHg/cm, p < 0.05, respectively). A dramatic decrease in the number of reflux events (from a median of 41 to 7; p = 0.01) was observed after OGB, whereas BII patients had a statistically significant higher values in esophageal acid exposure and number of reflux episodes (57 vs 7; p < 0.001), in particular in weakly alkaline reflux (38 vs 0; p < 0.001).

Conclusion: In contrast to BII, OGB did not expose to gastroesophageal reflux disease, but was a potential indicator to weakly alkaline reflux. Also the difference in IGP and in GEGP as assessed by HRiM suggests that gastric bile reflux can occur more easily in BII than in OGB and that these two techniques share more differences than analogies.

Disclosure: Nothing to disclose

References
Introduction: Laparoscopic distal gastrectomy is widely performed for managing gastric submucosal tumors (SMTs) that measure ≤5 cm in diameter. Laparoscopy and Endoscopy Cooperative Surgery (LECS) is performed to ensure a sufficient margin while avoiding deformation or stenosis.

Aims and Methods: We conducted a retrospective review of the data of 83 patients who underwent LECS for SMTs or early gastric cancers at our institution between April 2012 and February 2018. While Non-exposed Endoscopic Wall-inversion Surgery (NEWS) and classical LECS predominantly were performed for small SMTs, for early gastric cancers, we adopted the combination of laparoscopic approaches to neoplasia with non-exposure technique (CLEAN-NET).

Results: The patient age range was 58.3 ± 14.2 years old. The male:female ratio was 44:39. The serum levels of C-reactive protein on POD1 and POD3 were 3.3 mg/dl, respectively.

The surgical procedure consisted of classical LECS/CLEAN-NET/NEWS in 14/17/48 cases; all early gastric cancers were treated by NEWS. Postoperative complications were anastomotic stenosis (n = 1), delayed gastric emptying (n = 5), exacerbation of GERD (> Grade II by the Clavien-Dindo classification) (n = 4).

The postoperative complications were anastomotic stenosis (n = 1), delayed gastric emptying (n = 5), exacerbation of GERD (> Grade II by the Clavien-Dindo classification) (n = 4).

Conclusion: Use of minimally invasive surgical procedures such as LECS could allow deformation, stenosis and extent of resection to be minimized in resection of gastric tumors. LECS including NEWS and CLEAN-NET are feasible and effective for gastric surgery.

Disclosure: Nothing to disclose

Conclusion: Laparoscopic distal gastrectomy for early gastric cancer is a safe, effective, and minimally invasive surgical procedure for elderly patients.

Disclosure: Nothing to disclose
P0886 BILE DUCT INJURY AFTER CHOLECYSTECTOMY: NEW CLASSIFICATION AND NOVEL APPROACH FOR THE MANAGEMENT IN EMERGENCY SITUATIONS. DATA OF 178 CASES

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Introduction: We have analysed our data on managing bile duct injury and have proposed a new classification more relevant in our clinical practice.

Aims and Methods: From October 2010 to May 2017, total 178 patients of mean age 51 (range 30–74) years were referred to our unit with bile duct injury following or during laparoscopic cholecystectomy. Laparoscopic cholecystectomy was described as ‘uneventful’ in 45% and ‘difficult’ in 55% patients; 19 injuries were recognised at operation. Rest patients were transferred on 7th post operative day on an average. Exploration and complete diversion of bile was done in initial 12 patients along with feeding jejunal (for bile refeeding) of type II & III. Later on all patients were internally drained irrespective of type II / type III, and feeding jejunal was not done. Average time for hepatico jejunostomy – day 62 following initial surgery. Out of 74 patients of type II and III only 39 patient required Hepatico jejunostomy with feeding jejunostomy (for bile refeeding) of type II & III. Later on all patients were internally drained irrespective of type II / type III, and feeding jejunal was not done. Average time for hepatico jejunostomy – day 62 following initial surgery. Out of 74 patients of type II and III only 39 patient required Hepatico jejunostomy (52.7%), one needing surgery was lost to follow up, rest 34 (45.9%) were managed successfully with endobiliary repeat/multiple stenting. All patient with type I injury were subjected to ERC-papillotomy and stenting of common bile duct was done successfully. Out of 102, 91 patients had drains kept during surgery and was draining bile, 11 patients had Bioma which was drained with pigtail catheter percutaneously. Two patients died, one was referred on day 11, after redo laparoscopy which was done on post of day 6, patient was in sepsis, ARDS & MODS. Was operated for biliary peritonitis but could not be saved. Another patient was referred on post operative day 12 with biliary fistula from drain and peritonitis with liver failure. On exploration found to have type III Bile duct injury with portal vein clipping and complete thrombosis with ischomic liver. This patient died of liver failure with sepsis post operatively.

Results: We propose new classification for bile duct injury according to its prevalence in our region and our management recommendations.

TYPE I: Cystic duct stump blow out...

TYPE II: Partial clip on CBD with or without cystic duct stump blow out or lateral injury.

TYPE III: a. Segment loss of CBD <2cm.
b. CBD / CHD > 2 cm extending upto hilum.
c. Hilar injury with separate sectoral ducts.  
d. Any of above with ligation of right hepatic artery.

TYPE IV: Isolated sectoral duct injury.

Distribution of our cases according to types.

Number of patients: Type I = 102, Type II – 34, Type IIIA – 19, Type IIIB – 15, Type IIC – 4, Type IID – 2, Type IV – 2

Conclusion: Bile duct injury following laparoscopic cholecystectomy is a complex management problem and results in significant postoperative morbidity.

Bile duct injury recognized intraoperatively always does better irrespective of severity of injury.

More complex injuries are better drained first and then later date reconstruction is advisable. We propose a use of endobiliary plastic stents (routinely used following ERC) for internal drainage and repair of bile duct over stent without use of conventional T tube and if required later date hepaticojejunostomy can be done.

ERC is used in type I and II injury and use of multiple stents after a salvage segment of ductimal stents.

In presence of biliary sepsis and peritonitis, surgical lavage and endobiliary stenting is advisable before subjecting patients to ERC.

Disclosure: Nothing to disclose

P0888 PREVENTION OF POSTOPERATIVE BILE-LEAKAGE BY A NEWLY DESIGNED TISSUE SEALANT PATCH

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Introduction: Up to 10–15% of patients develop a bile-leakage after liver surgery, which increases the length of hospital stay as well as overall mortality and morbidity. However, with no effective preventive measure at hand, the surgical community is forced to accept bile-leakage as an unavoidable post-surgery complication.

Aims and Methods: To overcome the clinical challenge of post-operative bile leakage we developed a new tissue sealant patch to prevent this complication. The tissue sealant patch was designed in a multi angle approach including in-vitro comparison on tensile, burst pressure measurements and testing in a liver perfusion model with clinically relevant competitors. For in-vivo evaluation a porcine bile-leakage model was established and the tissue sealant patch was investigated in a prospective randomized animal trial with a suturing group and Veriset®/C213 HemoPatch as controls.

Results: More than 30 different prototypes were screened in-vitro. The final selected sealant prototype showed superiority compared to clinical used competitors Tachosil®, Hemopatch® and Veriset® in tensile and burst pressure testing (p < 0.05 each). Moreover, the newly developed patch reduced the leakage rate significantly in the liver perfusion model (p < 0.05). The pre-clinical performance of the sealant patch was confirmed in a porcine bile-leakage model. 21 animals were included in the study and randomized for treatment with the sealant, Veriset® or suturing (n = 7 each). After 7 days incidence of bile leakage was significantly lower in the sealant group compared to the Veriset® group (p < 0.05) and comparable to the suturing control group. These promising results were supported by strong bile containment and the formation of a smooth fibrous capsule by the sealant within one week. This was parallel to the formation of neo bile ducts. Furthermore, no systemic or local side effects (e.g. biloma) were seen.

Conclusion: The new designed sealant was as effective as suturing in preventing bile-leakage in our animal model. This was due to strong bile containment and formation of a fibrous capsule by the sealant within one week. The efficacy of the sealant was also histologically proven, as formation of neo bile ducts – which indicates a biliary obstruction – was detected. More importantly, no clinical relevant side effect of the sealant became evident. To our knowledge, this is the first report of a randomized trial showing the efficacy of a tissue sealant device for preventing postoperative bile leakage.

Disclosure: Nothing to disclose

P0887 BRAUN ENTEROENTEROSTOMY AFTER PARTIAL PANCREATECOOUDENOECTOMY AND CHILD RECONSTRUCTION DECREASES MORBIDITY, CLINICALLY RELEVANT DGE, AND BILE LEAKS – A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Due to its high rates of postoperative mortality and morbidity, resections of the pancreas remain a high-risk operation. Since its first description by Kausch et al. and Whipple et al., several surgical reconstruction techniques have been introduced to minimize the risk for postoperative mortality and morbidity after pancreatoenduxeontomy/ PD. These reconstruction techniques include the standard Child reconstruction defined as pancreaticojunostomy/PJ followed by hepaticojunostomy/HJ and the gastrojejunostomy/GJ (s-Child), the s-Child reconstruction with an additional Braun enterenterostomy (BE-Child), and the isolated Roux-en-Y-pancreatoenterostomy (ISRY), in which the pancreas anastomosis is reconstructed in a separate loop after the GJ. Yet, no comparative systematic review with meta-analysis has been performed to assess the impact of these most commonly used reconstruction techniques on the postoperative course of patients undergoing PD.

Aims and Methods: This systematic review with meta-analysis aims to compare the effect of different reconstruction techniques on the postoperative course of patients after PD.

For this purpose, the Preferred-Reporting-Items-For-Systematic-review-and-Meta-Analysis/PRISMA-guidelines were used to conduct a systematic review with meta-analysis. Databases of PubMed/Medline, Scopus, Cochrane Library and Web-of-Science were screened for relevant articles meeting predefined inclusion/exclusion criteria. A total of 3675 publications were extracted and 3653 were excluded. Those remaining publications were thematically reviewed and a total of 18 studies were included. Finally, a total of 18 studies comparing the postoperative outcome of single vs. multiple techniques on the postoperative course of patients undergoing PD.

Disclosure: Nothing to disclose
PO889 SHORT-TERM SURGICAL MORTALITY AND Morbidity of Distal Pancreatectomy Performed for Benign vs Malignant Diseases: A NSQIP Analysis

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Introduction: Distal pancreatectomy (DP) accounts for 25% of all pancreatic resections. Complications following DP occur in around 40% of the cases.

Aims and Methods: Few studies compared the clinical outcomes of distal pancreatectomy in benign versus malignant diseases.

We studied all patients undergoing DP from the National Surgery Quality Improvement Program (NSQIP) pancreatectomy participant user data specific file from 2014-2016. NSQIP includes prospective validated outcomes and anonymized data for patients' demographics, functional statuses, preoperative risk factors, laboratory data, and 30-day postoperative outcomes for patients undergoing major surgery in more than 500 hospitals. The primary outcome in this study was short term surgical morbidity and mortality. The patients were divided into 2 groups, those who underwent DP for benign diseases (DP-B) and those who underwent DP for malignant diseases (DP-M). We used the chi square test or Fisher's exact (when one or more cells had an expected frequency lower than 5) to compare categorical variables between the 2 groups. We used the independent t-test for continuous variables. We performed multivariable logistic regression to evaluate the association between benign or malignant distal pancreatectomies and 30-day postoperative outcomes. We included confounders into the models based on both clinical and statistical significance.

Results: Over the specified period, 1685 (47%) patients underwent DP-B and 1894 (53%) patients underwent DP-M. DP-M patients were significantly older, had significant longer operation time and hospital stay. The most common indications of DP-B and DP-M were mucinous cystic neoplasm (26.4%) and pancreatic adenocarcinoma (75%), respectively. Open DP was the most performed type of surgery for both benign (39%) and malignant (60%) lesions while laparoscopic DP was performed at a higher rate for benign indications (29%) compared to malignant ones (15%). Thirty-day mortality occurred in 0.4% of DP-B compared to 1.3% of DP-M. Pancreatic fistula occurred in 20% of DP-B compared to 18% of DP-M. Moreover, composite morbidity (including thromboembolism, sepsis, wound infection, cardiac, respiratory, and urinary complications) were significantly higher in DP-M. On multivariate analysis, bleeding (p = 0.002) and composite morbidity (p = 0.01) were significantly higher in the DP-M group. Among composite morbidities, thromboembolism was shown to be significantly associated with DP-M (OR = 2.1, p = 0.0004).

Conclusion: Our study showed that DP-M is significantly associated with higher composite morbidity, sepsis, and thromboembolism. However, no significant difference in mortality was found between DP-B and DP-M groups.

Disclosure: Nothing to disclose.

PO8890 VALIDATION OF DAY 1 DRAIN FLUID AMYLASE LEVEL FOR PREDICTION OF CLINICALLY RELEVANT FISTULA FOLLOWING DISTAL PANCREATECTOMY USING THE NSQIP DATABASE

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Introduction: In a previous multicenter study, post-operative day 1 drain fluid amylase level (DFA-1) level of 2000 was found to be most predictive of the development of clinically relevant post-operative pancreatic fistula (CR-POPF).

Abstract No: P08890

<table>
<thead>
<tr>
<th>Benign (n = 1,685)</th>
<th>Malignant (n = 1,894)</th>
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<tbody>
<tr>
<td>Mortality</td>
<td>7 (0.4)</td>
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<tr>
<td>Bleeding</td>
<td>180 (10.7)</td>
</tr>
<tr>
<td>Return to Operation Room</td>
<td>49 (2.9)</td>
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<tr>
<td>Composite morbidity</td>
<td>282 (16.7)</td>
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<tr>
<td>Thromboembolism</td>
<td>33 (2.0)</td>
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<tr>
<td>Sepsis</td>
<td>97 (5.8)</td>
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Unadjusted OR (95% CI) | p-value | Adjusted OR (95% CI) | p-value

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<tbody>
<tr>
<td>Mortality</td>
<td>2.13 (1.13–1.69)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>2.13 (1.13–1.69)</td>
<td>0.002</td>
<td></td>
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<tr>
<td>Return to Operation Room</td>
<td>1.45 (1.01–2.09)</td>
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<tr>
<td>Composite morbidity</td>
<td>1.32 (1.11–1.56)</td>
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<tr>
<td>Thromboembolism</td>
<td>2.12 (1.40–3.21)</td>
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<tr>
<td>Sepsis</td>
<td>1.21 (0.92–1.58)</td>
<td>0.17</td>
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[Table comparing outcomes between benign and malignant distal pancreatectomies, before and after adjusting for clinically confounding variables]

Aims and Methods: We aimed to validate the previously established cut-off level for DFA-1 after distal pancreatectomy using the NSQIP database.

Methods: Patients undergoing distal pancreatectomy from the National Surgery Quality Improvement Program (NSQIP) pancreatectomy specific PUF file from 2014-2016 were studied. We applied the DFA-1 of 2000 cut off to compare clinical outcomes in both groups. In order to validate the previously defined DFA-1 level, we performed a receiving operating characteristic (ROC) curve to independently determine the optimal cut-off value of DFA1.

Results: 1012 patients underwent DP. CR-POPF occurred in 206 (20.4%). Patients with DFA1 levels ≥ 2000 U/L were more likely to develop CR-POPF (32.5% vs. 11.3%, p < 0.0001), to have a higher mean number of days before drain removal (8.86 versus 5.59, p < 0.0001), to have a drain 30-days post-operatively (12.7% versus 6.3%, p < 0.0001) and to undergo percutaneous drainage (13.8% vs. 9.7%, p = 0.04). Application of maximal Youden index calculated the DFA-1 level value at 2000 U/L with a sensitivity of 64.85% and a specificity of 63.65% for CR-POPF, with PPV and NPV of 32.49% and 88.75%, respectively and a Youden index of 0.32.

Using a different population of patients and a different data set as well as an independent analysis, we successfully validated a DFA1 of 2000 as striking the best balance of sensitivity and specificity for the detection of CR-POPF. The identified cut-off might be employed in the design of a trial of early drain removal in patients undergoing distal pancreatectomy.

Disclosure: Nothing to disclose.
Surgical resection is generally accepted in patients with advanced neoplasia (AN) (high-grade dysplasia (HG) or malignancy). Currently, the main challenge is to determine the risk of progression to AN in patients with PCNs. It is unclear whether the revised 2018 European guideline is more accurate for identifying AN in IPMN preoperatively. Of these, 44 patients with IPMN separately: receiver operating characteristic (ROC) curves were calculated and compared to measure diagnostic value. Results: Of the 2018 European guideline criteria and 2017 IAP guideline criteria in identifying AN in IPMN. Conclusion: The revised 2018 European guideline criteria were superior to the 2013 European guideline criteria and 2017 IAP guideline criteria in identifying AN in IPMN in this retrospective analysis.


P0893GUT INFLAMMATION DEMONSTRATES A CIRCADIAN RHYTHM AND THE CLOCK IS DISRUPTED IN A MURINE MODEL OF COLITIS
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Introduction: The circadian clock oscillates over a 24-hour (or circadian) cycle and is entrained to external stimuli such as light and food availability. At the molecular level, these circadian oscillations are generated by transcriptional- translational feedback loops. Tissue cells show circadian rhythms in gene expression and consequently the symptoms of many inflammatory diseases are diurnal. Phytopathologically, patients with IBD do not have diurnal symptoms, but there is emerging evidence of circadian dysrhythmia at a cellular level in the gut and gastrointestinal conditions are more prevalent in shift workers.2,3 The interplay between gut inflammation and circadian biology requires further investigation.

Aims and Methods: The aim of this study was to examine circadian variation in inflammation within the colonic lamina propria, using a mouse model of colitis.

Methods: C57BL/6 mice were given 2% (w/v) DSS in drinking water ad libitum for 4 days, followed by 4 days of water. Contact mice drank water throughout. Mice were sacrificed at 4 different times across the circadian day: Zeitgeber Time (ZT)0 (lights on); ZT6 (mid-light); ZT12 (lights off) or ZT18 (mid-dark). Samples of colonic tissue were taken for histological staining and analysis of clock and inflammatory gene expression. Faece isolates were isolated for calprotectin staining by ELISA. Colonic lamina propria immune cells were isolated from inflamed and naive mice by enzymatic digestion and immune cell populations were quantified using flow cytometry.

Results: Mice administered DSS developed colitis, demonstrated by an average weight loss of 15% body weight (compared with +5% weight gain in controls), significantly greater spleen weight and reduced colon length. Furthermore, histological analysis confirmed inflammation within the colon. Flow cytometry revealed increased populations of neutrophils, monocytes, macrophages and dendritic cells within the lamina propria following DSS treatment.

Conclusion: Gene expression of pro-inflammatory cytokines (IL-1β, IL-6, IL-17A) and iNOS was significantly elevated in mice with DSS compared with controls at all time points. However, a subset of cytokines (IL-10, TNFα and IFNγ) showed dramatically enhanced expression during the night (ZT18) compared to the day (ZT6), with up to a 4-fold increase in ZT18.

This localised inflammation was accompanied by dampening of the diurnal variation in the expression of inflammation, most notably retinoids in the colon. Of interest, attenuated expression of retinoids was also noted in the liver of DSS treated mice. Our data suggest circadian variation in inflammation responses in a murine model of colitis, which coincides with dampening of rhythms in colitis gene expression. This early work suggests colitis is a circadian disease and opens the possibility of identifying the circadian clock mechanism as a potential therapeutic target.

Disclosure: Nothing to disclose

References:


P0894 ADMINISTRATION OF IMM-124E AMELIORATES COLITIS
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Introduction: Inflammatory bowel disease (IBD) is exacerbated by lesions in the epithelial barrier, which allow translocation of bacterial products from the gut lumen to the host’s circulation. Systemic exposure to bacterial products, including lipopolysaccharide (LPS) elicits strong immune responses, and thereby contributes to the pathogenesis and perpetuation of IBD. LPS exposure in...
particular, promotes production of pro-inflammatory cytokines, and affects immune system by activating high levels of inflammatory markers, such as neutrophils and monocytes. Glutathione peroxidase 4 (GPx4) activity and expression is diminished, compared to healthy controls. In line with this, CD patients exhibited increased LPO levels, which are inversely correlated with GPx4 activity and expression. The increased LPO levels are associated with the activation of the innate immune system and the inability of inhibitors to prevent cell death. The increased LPO levels may also be due to the activation of the pro-inflammatory cytokine expression in the intestinal epithelial cells. This study highlights the potential role of GPx4 in the pathogenesis of Crohn's disease and suggests a novel therapeutic strategy targeting GPx4 to ameliorate symptoms of intestinal inflammation.

Aims and Methods: In this study, we analyzed the expression of GPx4 and LPO in intestinal epithelial cells of patients with inflammatory bowel disease and healthy controls. We performed microarray analysis and qPCR to identify the genes upregulated or downregulated in the active lesion-derived organoids. The expression of selected genes was compared between the organoids generated from active and inactive lesion of colon in the same patient with UC (DDW 2018). We aimed to identify lesion-specific epithelial cell function in UC to compare the gene expression between the organoids generated from active and inactive lesion of small intestine in same patient with CD. Human small intestinal organoids were generated from both active and inactive lesion of the small intestinal tissue surgically resected from an identical patient with CD. Both organoids were cultured for a month to remove the effect of LPS on epithelial cell function after stimulation.

Introduction: Patients with inflammatory bowel disease (IBD) mainly present with ulcerative colitis (UC) or Crohn's disease (CD). Recently, it has been recommended that mucosal healing is therapeutic goal of IBD because dysregulation of epithelial cells might cause frequent relapse. However, the pathogenesis of epithelial cells in IBD remains unknown. Especially, although skip lesions in small intestine are often observed in the patients with CD, the mechanism to develop ulcer and stenosis at a certain part in entire small intestine remains unknown. We have previously identified the lesion-specific epithelial cell function in UC to compare the gene expression between organoids generated from active and inactive lesion of colon in the same patient with UC (DDW 2018).

Aims and Methods: We therefore aimed to identify lesion-specific genes to compare the gene expression between the organoids generated from active and inactive lesion of small intestine in same patient with CD. Human small intestinal organoids were generated from both active and inactive lesion of the small intestinal tissue surgically resected from an identical patient with CD. Both organoids were cultured for a month to remove the effect of LPS on epithelial cell function after stimulation. Comprehensive gene expression profiles in the organoids were assessed by microarray analysis. The expression of genes upregulated or downregulated (≥2 fold change) between active and inactive lesion-derived organoids were selected. The expression of selected genes was confirmed by RT-PCR using three pairs of small intestinal organoids in addition to another two patients with CD. This study was approved by the ethics committee.

Results: We have established both small intestinal organoids generated from active and inactive lesion of same CD patient. The configuration and growth patterns of organoids from active lesion were the same as the organoids from non-active lesion. There was no significant difference of phenotypes such as stem cell and differentiation markers in the organoids. In spite of no significant difference of phenotypes, microarray analysis identified 7 upregulated genes in the organoids from active lesion more than 2 times compared to the organoids from inactive lesion. 3 downregulated genes in the organoids from active lesion less than half were also identified. 3 of 7 upregulated genes and all downregulated genes were preserved in the organoids from another patient but not all three genes were preserved in the organoids from another patient.

Conclusion: Comparison of gene expression between organoids from active and inactive lesion of same patient might reveal the fundamental pathogenesis in intestinal epithelial cells of CD. The identification of lesion specific genes might also be useful for the modulation of molecular mechanism and therapeutic target for mucosal healing in CD.

Disclosure: Nothing to disclose

References:

Disclosure: Nothing to disclose

References:
**P0898 THE EFFECT OF NEW HERBAL PRESCRIPTION DERIVED FROM BOJANGGUNBI-TANG ON INFLAMMATORY BOWEL DISEASE**

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**Introduction:** Bojanggunbi-tang (BGT) is one of the most frequently used herbal prescription in Western colon diseases and their pharmacological activities of BGT on digestive system are well-documented. However, BGT consists of 16 herbs, which makes it difficult to standardize and quality-control due to high cost in industrial manufacture.

**Aims and Methods:** The purpose of the current study is to develop a new simple and effective prescription derived from original prescription. We developed the essence of BGT (BGT-E) by mixing three herbs of BGT. Two herbs are Lonicer japonica Thunb. and Alisma orientalis, known as the most effective herbs in BGT. The other herb is Atractylodes macrocephala selected by literature review and screening test of total 16 kinds of components in BGT. Colitis mouse model was induced by 5% Dextran Sulfate Sodium (DSS) and body weight, histological damage, clinical score, gross anatomical score and pathological damage in the model. In addition, BGT-E showed dose-dependent decrease of pro-inflammatory cytokines including IL-1β, TNF-α, and IL-17.

**Conclusion:** BGT-E could be a substitute prescription of BGT in clinical practice and a new candidate for alternative medicine for inflammatory bowel disease.

**Disclosure:** Nothing to disclose

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**P0899 UPON AIEC INFECTION, CROHN'S DISEASE-ASSOCIATED CIRCULATING miRNAs ARE TRANSPORTED BETWEEN HUMAN MACROPHAGES VIA THE EXOSOMAL SHUTTLE**

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**Introduction:** The intestinal mucosa of CD patients is abnormally colonized with adherent-invasive E. coli (AIEC) strains, which are able to adhere to and invade intestinal epithelial cells, to survive and replicate within macrophages and to induce a strong pro-inflammatory response. AIEC, small extracellular vesicles of 30-100 nm, play a role in cell-to-cell communication by transferring their content from a donor cell to a recipient cell. We recently reported that upon AIEC infection, human macrophages secrete exosomes that induce a pro-inflammatory response and enhance the intracellular replication of AIEC bacteria in recipient cells.

**Aims and Methods:** This study aimed at investigating whether exosomes can transfer the microRNA (miRNA, miR) content between human macrophages during AIEC infection, and whether these miRNAs may contribute to the increased inflammation and AIEC replication observed in exosome-receiving cells. Exosomes released by human THP-1 macrophages uninfected (Exo-uninfected) or infected with the AIEC LF2 strain (Exo-AIEC) or the commensal E. coli HS strain (Exo-HS) were purified using the ExoQuick reagent and used to incubate with naïve THP-1 macrophages. The levels of the previously reported AIEC markers were analyzed by qRT-PCR. In silico analysis was performed to predict the biological processes in which these miRNAs are potentially involved.

**Results:** Most of the CD-associated circulating miRNAs were detected in the purified exosomes. The levels of some miRNAs were increased in Exo-AIEC compared to Exo-uninfected or Exo-HS. The levels of these dysregulated exosomal miRNAs were also increased in THP-1 macrophages incubated with Exo-AIEC compared to those incubated with Exo-uninfected or Exo-HS. This suggests an efficient microRNA transfer via exosomes. In silico analysis revealed that the dysregulated exosomal miRNAs might be implicated in inflammatory responses and autophagy, which is required to restrain AIEC intracellular replication, among other biological processes.

**Conclusion:** Although functional studies are required to investigate the role of the exosomal miRNAs, our study suggests that during AIEC infection, miRNAs can be transferred between human macrophages via the exosomal shuttle to mediate their role as regulators of innate immune responses.

**Disclosure:** Nothing to disclose

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**P0900 CY6R1 EXPRESSION IN INFLAMMATORY BOWEL DISEASE**

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**Introduction:** The pro-angiogenic cytokine-rich protein 61 (CY6r1) is a novel proinflammatory factor. Whether CY6r1 is involved in the development of inflammatory bowel disease (IBD) remains unknown. The purpose of this study is to investigate the expression of CY6r1 in patients with IBD.

**Aims and Methods:** We achieved the colonic mucosa from 23 patients with IBD who had undergone colonoscopy. We measured the expression of CY6r1 and inflammatory markers in the biopsy specimens using the real-time PCR. And, we determined the expression of CY6r1 in LPS (Lipopolysaccharide) -treated colonic epithelial cells (Caco-2 and HCT 116).

**Results:** Expression of CY6r1 in the inflamed mucosa was 2.5 times higher than that of the non-inflamed mucosa (p = 0.002). Expression of TNFα receptor (C6r1) and TLR(10-like-receptor)-4 increased significantly in inflamed mucosa than that of the non-inflamed mucosa (all p < 0.05). Time-dependent increase in CY6r1 expression was observed in Caco-2 and HCT 116 after the treatment with LPS.

**Conclusion:** Our results reveal a novel mechanism suggesting the role of CY6r1 and therapies targeting CY6r1 in patients with IBD.

**Disclosure:** Nothing to disclose

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**P0901 SUCINATE INDUCES EMT THROUGH SUCNR1**

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**Introduction:** Epithelial-to-mesenchymal transition (EMT) is a process which allows a switch of the phenotype from epithelial cells towards a fibrotic behavior. This process has been widely associated with the development of fistulas, a complication in IBD patients associated with an activation of the inflammation. Under inflammatory conditions, the metabolite succinate is accumulated and its receptor, called SUCNR1, mediates profibrotic responses in hepatic stellate cells; however, there is no study analyzing its role specifically in epithelial cells and in EMT.

**Aims and Methods:** We aim to analyze the role of succinate and its receptor in EMT. HT-29 intestinal epithelial cells were treated with different concentrations of succinate (0, 0.1, 0.5, 1, 5mM) or TGF-β (5ng/ml) during 48 hours. In some experiments, HT-29 cells were transfected with a specific SUCNR1 siRNA or with a negative control siRNA using Lipofectamine. The expression of EMT markers (Snail1, Snail2, Vimentin and E-Cadherin) was analyzed by qPCR and Western blot. Intestinal fibrosis was induced in vivo using the heterotopic transplant model. Briefly, one intestinal graft from WT or KO mice was transplanted into the neck of a recipient mouse for 7 days. The expression of EMT markers was analyzed by qPCR. Intestinal resections from CD patients were obtained and the expression of SUCNR1, Snail1, Snail2 and E-Cadherin was analyzed by qPCR. Results are expressed by mean ± SEM (n=5). Statistical analysis was performed with one-way ANOVA followed by Newman-Keuls test.

**Results:** In HT-29 cells, succinate induces in a dose-dependent manner: a) a significant increase in both mRNA and protein levels of SUCNR1; b) a significant increase in the mRNA expression of Vimentin, Snail1 and Snail2 and c) a significant reduction in the mRNA and protein expression of E-Cadherin. In HT-29 cells transduced with SUCNR1-specific siRNAs, the mRNA expression of Vimentin, Snail1 and Snail2 induced by succinate was significantly lower than that detected in HT-29 transfected with negative control siRNA (1.12 ± 0.12 vs 1.87 ± 0.09, 1.00 ± 0.09 vs 1.85 ± 0.18, 1.07 ± 0.26 vs 2.57 ± 0.19, respectively). In murine intestinal fibrotic tissue from WT mice we detected, seven days after transplantation a significant increase in the mRNA expression of Vimentin (3.50 ± 0.48), Snail1 (4.87 ± 0.79) and Snail2 (2.45 ± 0.25) and a significant reduction in the expression of E-Cadherin (0.60 ± 0.06) compared with that detected at day 0 (1.01 ± 0.07, 1.06 ± 0.13, 1.04 ± 0.10, 1.00 ± 0.04 respectively). In intestinal tissue from SUCNR1-/- mice, 7 days after transplantation we detected no significant changes in the expression of Vimentin, Snail1, Snail2 and E-Cadherin in KO-grafts at day 0 and levels of these markers were significantly lower than those detected in WT mice at day 7. Finally, SUCNR1 expression positively and significantly correlates with the expression of Snail1 (r Spearman = 0.6925, p < 0.001, n = 36) and Snail2 (r Spearman = 0.6305, p < 0.0001, n = 36) in intestinal resections from CD patients.

**Conclusion:** Succinate activates EMT in intestinal epithelial cells through its receptor SUCNR1, which identifies a new molecular mechanism involved in EMT and points to a new possible target for fistula-treatment.

**Disclosure:** Nothing to disclose
P0902  ECTOPIC EXPRESSION OF REG3A IN THE MICE DISTAL COLON INFLUENCING INTERACTIONS BETWEEN NOTCH AND IL-22 SIGNALING PATHWAYS, AND PROMOTES TISSUE REPAIR BY THE AUGMENTATION OF EGF SIGNALING

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Introduction: Members of the Reg gene family share common upstream regulatory motifs and protein structures. Each member gene shows a distinct region-specific expression pattern in the colon. For example, REG3A is exclusively expressed in the intestinal epithelial cells (IECs) of the mouse proximal colon. In contrast, disease-active ulcerative colitis or Crohn’s disease patients show ectopic expression of REG3A in rat IECs. Those ectopically expressed REG3A may contribute to initiating tissue repair partly through its ROS scavenger activity. In our previous study, we have demonstrated the importance of Notch signaling in colorectal tissue repair, and also its dominant role in IL-22-induced Reg gene family expression. However, the precise role of Notch signaling in “ectopic” expression of REG3A, or the comprehensive functional role of REG3A in the inflamed colorectal environment is poorly understood.

Aims and Methods: The role of Notch signaling in REG3A expression was examined by immunohistochemical analysis of REG3A and HES1 in Villin-cre1 mice. Ectopic expression of REG3A in rat IECs. Those ectopically expressed REG3A may contribute to initiating tissue repair partly through its ROS scavenger activity. In our previous study, we have demonstrated the importance of Notch signaling in colorectal tissue repair, and also its dominant role in IL-22-induced Reg gene family expression. However, the precise role of Notch signaling in “ectopic” expression of REG3A, or the comprehensive functional role of REG3A in the inflamed colorectal environment is poorly understood.

Results: Under homeostatic condition, REG3A was specifically expressed in the proximal colon of WT mice. However in RBP-Jκ/mice, IEC-specific deletion of RBP-Jκ resulted in complete loss of both Hes1 and REG3A expression in the proximal colon. In DSS-colitis mice, REG3A was ectopically expressed by rat IECs during the mucosal regeneration phase. In vitro analysis using distal colon-derived organoids confirmed IL-22-induced REG3A expression via STAT3 phosphorylation, which was completely cancelled by DIZ-mediated blockade of Notch signaling. Immunoprecipitation assay further revealed the direct interaction between STAT3 and HES1 in distal colon-derived organoids, in regards to priming IL-22 stimulation or Notch Signaling activity. To evaluate the direct effect of REG3A on IECs, organoid re-construction assay was performed under the presence of recombinant mouse REG3A. Those REG3A-treated organoids were subjected to microarray analysis and immunoblotting to identify the IEC-intrinsic molecular pathway (s) regulated by REG3A.

Conclusion: REG3A expression was augmented by IL-22 stimulation in intestinal epithelial cells efficiently rescues the organoid re-construction defect. The results indicate that IL-22 enhances EGF signaling pathway by REG3A, which was confirmed by immunoblotting analysis demonstrating increased phosphorylation of EGFR and ERK1/2. Furthermore, addition of REG3A significantly upregulated IL-22 expression, indicating EGF-Notch axis in maintaining functional intercellular communication in the intestinal epithelium.

Disclosure: Nothing to disclose

P0903  3.25-(OH)2D3 STIMULATES NHE3 EXPRESSION VIA ERK1/2 SIGNALING PATHWAY IN DSS COLITIS MICE

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Introduction: Vitamin D (VitD) and vitamin D receptor (VDR) have been regarded as protective factors for colonic mucosa in ulcerative colitis (UC) patients. Recent epidemiological studies have suggested that UC patients commonly suffered from low VitD deficiency. However, the potential molecular mechanisms by which VitD/VDR protects colonic mucosa in UC remain poorly understood. Sodium/hydrogen exchanger 8 (NHE8) is reported to play a protective role in colitis, and in recent years, it has been found that NHE8 expression could ameliorate mucosal injury caused by VitD deficiency. 1,25(OH)2D3 supplementation could ameliorate DSS colitis via VDR-ERK1/2-NHE8 pathway.

Aims and Methods: A total of 136 IBD patients (98 Crohn’s disease and 38 ulcerative colitis) from the First Affiliated Hospital of Nanjing Medical University were evaluated. Demographic data and clinical characteristics were collected. HRV in IBD patients was compared with those in the healthy control. HRV parameters the power of high-frequency (HF) and the ratio of HF and low frequency (LF), reflects vagal/sympathetic balance were assessed.

Results: The power of HF component was significantly decreased in CD (n = 98), UC (n = 38) and IBD (n = 136) patients respectively, compared with healthy control (n = 136) patients. Patients with UC or CD in state of different disease activity had significantly lower levels of HF compared with health control. However, there was no significant differences of HF levels in mild CD, moderate and severe CD patients. UC patients also had the same alterations at stage of different disease activity.

Conclusion: Altered HRV were found in both CD and UC patients, implicated impaired autonomic function in patients with IBD.

Disclosure: Nothing to disclose

P0904  ASSESSMENT OF AUTONOMIC FUNCTION IN INFANTILY BOWEL DISEASE BY HEART RATE SPECTRAL ANALYSIS: MICROSPORIDIA AND INFLAMMATORY BOWEL DISEASE

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Introduction: Heart rate variability (HRV) are used to evaluate of autonomic dysfunction in various clinical disorders. In this study, we examined HRV in patients with inflammatory bowel disease (IBD) to evaluate autonomic function.

Aims and Methods: The role of Notch signaling in REG3A expression was examined by immunohistochemical analysis of REG3A and HES1 in Villin-cre1 mice. Ectopic expression of REG3A in rat IECs. Those ectopically expressed REG3A may contribute to initiating tissue repair partly through its ROS scavenger activity. In our previous study, we have demonstrated the importance of Notch signaling in colorectal tissue repair, and also its dominant role in IL-22-induced Reg gene family expression. However, the precise role of Notch signaling in “ectopic” expression of REG3A, or the comprehensive functional role of REG3A in the inflamed colorectal environment is poorly understood.

Results: Ectopic expression of REG3A in the inflamed distal colon is mediated by the interaction between IL-22-STAT3 and Notch-Hes1 pathway. Ectopically secreted REG3A functions as a positive regulator of IEC-intrinsic EGF signaling, and thereby contribute to the repaired of the inflamed colorectal epithelium.

Disclosure: Nothing to disclose

P0905  CLASS-I HISTONE DESACetylASES AS A NEW THERAPEUTIC TARGET FOR THE CONTROL OF ADHERENT-INVASIVE E. COLI-INDUCED INTESTINAL INFLAMMATION

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Introduction: Crohn’s disease (CD) is a chronic inflammatory bowel disease with a complex etiology including genetic, environmental, infectious, and also epigenetic factors. Adherent-invasive E. coli (AIEC) are chronic colonizers, which in triggering and maintaining ileal CD. AIEC bacteria adhere to the enterocytes through high affinity interaction between their variant type one pili and abnormally expressed CEACAM6 receptor on host cells. Once internalized, AIEC bacteria replicate extensively in enterocytes and intestinal epithelial cells. Intestinal mucosal colonization by AIEC alters ileal barrier function, inducing chronic inflammation in CD patients. Controlling the invasion, intra-cellular replication and inflammatory response induces by AIEC could be a new promising strategy for CD therapy. To date, no specific therapeutic targets were identified for AIEC- positive CD patients.

Aims and Methods: The aim of this work are to (1) identify histone post-translational modifications altered during the course of AIEC colonization using intestinal epithelial cells (IECs) in culture infected by AIEC reference strain LS25 and non-pathogenic E. coli through immunofluorescence and western-blot approaches; (2) to assess the role of HDAC during infection using specific inhibitors (MS 275 and SAHA) on AIEC-intracellular replication in IECs cells and
during the course of colonization in humanized CEACAM6-expressing mice (Ca/CAC mice). These mice received SAHA intra-peritoneally for two weeks and were challenged with AIEC by oral gavage. Colonization was monitored for 3 days after infection (AIEC numbering in feces). AIEC associated to intestinal tissues were numbered at the time of sacrifice and inflammatory responses were analyzed by ELISA.

Results: AIEC infection leads to an important increase in acetylated and crotonylated form of histone H3 in three different IECs lines. H3K9ac (acetylation) and H3K18cr (crotonylation) marks were significantly increased six hours after infection, in comparison to non-infected and non-pathogenic E. coli-infected cells. These observations suggest that infection could allow interplay with histone “eraser”/”writer” pathways leading to changes in genome organization in host cell. We focused the analysis on the erasers HDAC using pharmacological inhibition of HDAC. HDAC inhibitors pre-treatment of IECs led to a significant reduction of invasion and multiplication capacity of AIEC in IECs. Finally, in vivo approach using CEABAC10 mice treated with HDAC inhibitors revealed a decrease in AIEC colonization ability and decreased inflammatory response in the HDAC inhibitor group compared to the untreated group.

Conclusion: This work shows that AIEC infection alters the epigenetic landscape of host cell which could modify gene expression favoring the infection process. We reveal that pharmacological inhibition of HDAC limits AIEC colonization in vitro and in vivo in CEABAC10 mice and prevents intestinal inflammation, suggesting that HDAC could be an interesting target for controlling AIEC-induced intestinal inflammation in Crohn’s disease patients.

Disclosure: Nothing to disclose

P0906 A PATHWAY TO UNDERSTAND COLITIS-ASSOCIATED CARCINOMA: GENE EXPRESSION ANALYSIS IN HUMAN COLON

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Introduction: Long-term Inflammatory Bowel Disease (IBD) patients (IBD) have a higher risk of developing colorectal cancer (CRC), namely, colitis-associated carcinoma (CAC). However, its tumorigenesis occurs differently from the described for CRC tumorigenesis due to the active participation of inflammatory signaling pathways [1]. It is known that in CAC, cytokines such as TNF, PEG2, IL-6 and IL-1 can activate signaling pathways such as ERK, NFκB, PI3K-Akt and STAT3, promoting transformation and tumor progression [2,3]. However, most of the knowledge about CAC pathogenesis comes from mouse models, indicating the need for studies in human samples. Thus in this study we performed a comparative gene-expression analysis in surgical samples of IBD patients, in order to contribute to a better understanding of the carcinogenesis of CAC.

Aims and Methods: Colon samples were collected from 60 patients divided in 6 groups: Control, Ulcerative Colitis (UC), Crohn’s Disease-colitis (CD), UC or CD-colitis (CC), UC or CD-control (CC). Gene expression analysis was performed on RNA extracted from paraffin-embedded samples using the Nanostring amplification-free technique. A set of 624 genes related to immunology or epithelial barrier function was analyzed and preliminary analyses were performed using the nSolver software and Pathway analysis was performed using the software ConsensusPathDB (http://ConsensusPathDB.org).

Results: The analysis of differentially expressed genes between CD-CA/C and CD as well as UC-CA/C and UC rendered 203 and 271 differentially expressed genes, respectively. Among the major up-regulated genes in both comparisons were cytokines, such as as well as UC-Rf and UC-C20 respectively. Among the major up-regulated genes in both comparisons were cytokines, such as IL-6 and Stat3 involved in cancer, JAK STAT signaling pathway and cytokine-cytokine receptor interaction.

Conclusion: The customized gene expression panel offered a comprehensive analysis of the differences in expression between CAC and the underlying inflammatory diseases UC and CD. Identified upregulated or downregulated genes indicate signal transduction pathways that are crucial for CAC tumorigenesis, corroborating to the existing knowledge about CAC progression.

Disclosure: Nothing to disclose

References


P0907 CB2 INHIBITOR PROMOTES FACTORS ASSOCIATED WITH MUCOSAL HEALING IN COLON EPITHELIAL CELLS OF IB PATIENTS: AN EX-VIVO AND IN VITRO STUDY

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Introduction: Accumulating data from animal models and clinical data from our group and others suggest beneficial effects of cannabis in the treatment of patients with inflammatory bowel diseases (IBD). Cannabinoid receptors are expressed on epithelial and immune cells throughout the gastrointestinal (GI) tract and CB2 immunoreactivity is specifically found in epithelium area of inflamed colonic tissue, thus suggesting a role for the endocannabinoid system in modulating IBD disease activity. However, the mechanisms by which cannabis affects the inflammatory processes and/or the clinical presentation of IBD is not yet clear. In experimental mouse models of IBD have been hypothesized in predicting the clinical relevance of therapeutic targets in relation to human IBD. Therefore, in the current study we used human-originated tissue models to evaluate mechanisms for the beneficial effects of cannabis in IBD patients.

Aims and Methods: To investigate the effects of CB2 activation on colon epithelial cells, which are exposed to IBD microenvironment. In the current study we used 2 biological systems: 1. mucosal samples were collected during endoscopy from inflamed and non-inflamed areas of IBD patients. Samples were cultured for 7 hours with medium, or CB2 agonist (JW-133, 10nM) or ethanol (the solvent). Samples (time 0, after 7hr) were analyzed for epithelial cells Ki67 (proliferation) and fragmented caspase 3 (apoptosis) expression by immunohistochemistry and quantified by ImageJ software. The secretomes of the explants were collected and analyzed for MMP9 activity (zymography), which is known to impair colonic epithelial permeability.2) The effect of soluble IBD microenvironment and CB2 agonist directly on the epithelial cells was evaluated by culturing CaCo-2 (colon carcinoma cells) for 48hr with secretomes and supernatants from IBD biopsies with CB2 agonist (in the presence of the explants on cell viability (alamar-blue), number (automatic cell counter), death (trypan blue) and migration (scratch assay). All experiments were done at least 3 times.

Results: We found: I. Higher epithelial cell proliferation in biopsies obtained from healthy areas of the colon compared to biopsies from inflamed areas (Ki67 expression: 64 vs 32%, p < 0.05). No difference was found in apoptosis (expression of caspase 3) between the two areas (both at time 0 and 7hr). II. Higher expression of MMP9 activity and CB2 agonist in secretomes from IBD biopsies in comparison to non-inflamed areas (79% vs 1%, p < 0.05). III. Treatment with CB2 agonist (JW-133) returned epithelial Kt67 and MMP9 activity levels of the inflamed area to the level of the non-inflamed areas. IV. Secretomes collected from the inflamed biopsies, significantly (p < 0.05) reduced CaCo-2 cell viability (30%), number (40%) and migration (45%), while secretomes collected from CB2 agonist treated biopsies reversed these cell characteristics to the control levels (all p < 0.05). Direct treatment of CB2 agonist (in the presence of the explants on cell viability (alamar-blue), number (automatic cell counter), death (trypan blue) and migration (scratch assay). All experiments were done at least 3 times.

Conclusion: Our study demonstrated in a human ex-vivo and in-vitro human models that cannabinoids alter epithelial cells phenotype in a way that may facilitate mucosal healing. 

Disclosure: Nothing to disclose

P0908 LONGER DISEASE COURSE IS ASSOCIATED WITH REDUCED SYSTEMIC ANTI-INFLAMMATORY RESPONSE IN ULCERATIVE COLITIS PATIENTS

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Introduction: Interleukin 10 (IL-10), representing the anti-inflammatory mechanisms of the human body, is a well-known marker used to characterise the course of ulcerative colitis (UC). Although many mechanisms of UC are well understood, some of them still remain unclear, including the exact factors that could contribute to better prognosis and more favourable outcome of the disease.

Aims and Methods: The aim of the study was to determine the association between the systemic anti-inflammatory state of the body and UC disease length and analyse the possible factors attributing to that. A cross-sectional
study was conducted analysing all patients with clinically, endoscopically and histologically confirmed UC diagnosis mainly hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 6-year period (2012–2017). Patients participated in out-patient interviews, blood samples were obtained and analysed for IL-10 using ELISA, UC disease activity was evaluated according to the full Mayo score.

Results: Out 65 UC patients – 34 (52.3%) male and 31 (47.7%) female patients with a mean age of 41.95 (SD = 15.1) years, who enrolled in the study – only one (1.5%) had increased IL-10 levels (more than 20 pg/ml). The levels of IL-10 in the study group ranged from 0 pg/ml to 55 pg/ml with a mean of 3.4 (SD = 7.9) pg/ml. Statistically significant negative correlation (RS = −0.35; p = 0.004) was found between IL-10 levels and the number of years since the patient experienced their first UC symptoms, showing that the longer the patient had UC, the lower their IL-10 levels were. The mean age when the first UC symptoms appeared in the study group was 32.1 (SD = 14.6) years, ranging from 2 to 48 years. The possible confounding factors that could influence the IL-10 levels in these patients, including UC disease activity, UC treatment, UC complications, the number of UC exacerbations, patient’s BMI, smoking history, concomitant diseases, previous hospitalizations and CRP levels did not show any statistically significant effect. The only exception was systemic corticosteroid use, which was 1.5 times higher in patients with IL-10 levels significantly increased. However, the results were not statistically significant (p = 0.16). No other factors such as smoking, diet, exercise, alcohol consumption, age, sex, and BMI were found to be associated with IL-10 levels significantly.

Conclusion: In this study, we have found a positive correlation between the duration of UC and lower IL-10 levels. However, the results were not statistically significant, and further studies are needed to confirm these findings.

Disclosure: Nothing to disclose

P0909 HYPERMETHYLATION PATTERNS IN DISYLPNIA IN INFANTILE INTESTINAL DYSPLASIA (I. DIAS PEREIRA1, C. RODRIGUES1, T. PISACO1, P. CAVAZZONI2, T. KARRAM3, A. PROTOPAPAS3, H. TAKAMATSU4, A. DIAZ PEREIRA5)

Introduction: The dextran sulfate sodium (DSS)-induced model of colitis is frequently used as a preclinical model of inflammatory bowel disease (IBD). The chronic phase of DSS-induced colitis shares pathophysiological aspects of human ulcerative colitis (UC). Therefore, DSS-induced colitis is suitable for testing the therapeutic potentials for UC. However, some treatment regimens for IBD, such as prednisolone (PSL), show poor efficacy or even worsen colitis in the rodent model. Differences in inflammatory/immune mechanisms between humans and rodents are potential sources of this issue. Nonhuman primates are phylogenetically closer to humans than rodents and useful in investigating mucosal immunity.

Aims and Methods: In the current study, a nonhuman primate model of chronic colitis was created and the effect of PSL was assessed in this model. Eight male cynomolgus macaques were used. Macaques were allowed free access to 0.25% DSS in distilled water. Daily total intake of DSS-water was 100 mL/kg. One treatment cycle consisted of DSS-water for 2 weeks followed by 2 weeks without DSS-water. Macaques underwent a total of three treatment cycles. A modified Mayo score (0–12) was used to quantify the extent of colitis. The following factors were analyzed: stool consistency (0–3), gross bleeding (0–3), colonoscopy examination (0–3), and general symptoms (0–3).

Results: All 15 macaques developed colitis following the first DSS treatment cycle. In the control group, during all three cycles of DSS treatment, increased feces scores (stool consistency and fecal bleeding) were observed. Colonoscopy revealed reduced vascularization and mucosal erythema, edema, and erosion in the mucosa of the rectosigmoid colon in three macaques. Ulceration or colon in one macaque. Similar modified Mayo scores (mean ± SEM) were observed during all three cycles (Cycle 1, 4.0 ± 0.6; Cycle 2, 3.5 ± 0.6; Cycle 3, 4.2 ± 0.6). The EI indicated consistent and moderate colitis severity during all three DSS treatment cycles (Cycle 1, 4.3 ± 0.6; Cycle 2, 4.5 ± 0.6; Cycle 3, 5.5 ± 1.3). In DSS-treated, Mayo scores recovered to the remission level. In the PSL-treated macaques, mean Mayo scores during the first and second DSS-treatment cycle were significantly lower than that of the control group. However, a significantly lower score was obtained in the third DSS-treatment cycle (1.8 ± 0.5). The mean EI for PSL-treated macaques was also lower (1.8 ± 0.6) than the control-treated macaques. Mean fecal calprotectin was higher in the control group compared to that of native macaques. By contrast, fecal calprotectin values of the PSL-treated animals indicated remission (< 70 µg/g).

Conclusion: A chronic DSS-induced colitis model was developed in macaques that showed similar symptomatic and endoscopic features to those seen in clinical inflammatory bowel disease. In this model, PSL clearly inhibited disease relapse. Therefore, the macaque model, compared to the rodent model, could show better predictiveness of clinical outcome of compounds that are currently under evaluation for the treatment of UC.

Disclosure: All the authors are employees of Hamamatsu Pharma Research, Inc.
were also detected in isolated epithelial cells and fibroblasts from human intestine.

Conclusion: Our study indicates reduced VDR protein levels in murine intestinal carcinoma was detected in one patient and there were six deaths of all patients.

Disclosure: Nothing to disclose.
DISEASE COURSE AND PROGNOSIS OF INCIDENT PATIENTS WITH MICROSCOPIC COLITIS – ONE YEAR FOLLOW-UP RESULTS. THE EUROPEAN PRO-MC COLLABORATION, A LINK AWARD PROJECT

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OPPORTUNISTIC INFECTIONS ARE MORE PREVALENT IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS: A LARGE POPULATION-BASED STUDY

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References

Disease behaviour | Total N=71 | n CC / LC / MCI
---|---|---
Quiescent | Only one flare at onset of disease or subsided spontaneously | 12 / 6 / 1
Mild | Treatment with bulging agents or occasional use of budesonide on demand | 11 / 2
Chronic relapsing | Disease activity or in budesonide treatment at ≥ two visits | 2 / 0 / 0

[Microscopic colitis disease behaviour during the first year after diagnosis]

Disclosure: Nothing to disclose

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Introduction: Inflammatory bowel diseases (IBD) comprising of Crohn’s disease (CD) and Ulcerative Colitis (UC) are chronic inflammatory disorders that have been associated with an increased risk of opportunistic infections (OIs)1,2. While OIs like Clostridium difficile have been extensively studied, there is limited data on the prevalence of other OIs in a large cohort of IBD patients.

Aims and Methods: The aim of this study was to investigate the epidemiology of seventeen OIs in IBD in a large, population-based database. Data was collected from a commercial database (Explorys Inc, Cleveland, OH, USA) that provided electronic health records (inpatients and outpatients) from 26 major integrated United States healthcare systems from March 2013- March 2018. We identified a cohort of patients with CD, UC, and OIs based on Systemized Nomenclature of Medicine – Clinical Terms. We compared the prevalence of seventeen OIs in this cohort of CD and UC patients to controls without IBD2 and characterized the distribution of these OIs with age.

Results: Of the 35,420,110 individuals in the database, we identified 155,290 patients with CD and 128,540 patients with UC. The overall prevalence rate of CD and UC was 432.8/100,000 persons and 362.9/100,000 persons respectively. Both UC and CD patients had significantly increased odds for OIs compared to controls (OR, 2.87 in CD; p<0.0001, and OR, 3.15 in UC; p<0.0001). The OIs with the highest odds ratios (OR) in IBD patients were Clostridium difficile followed by cytomegalovirus and tuberculosis (Table 1 for ORs). The most prevalent opportunistic infections in IBD patients by numbers were candidiasis followed by Clostridium difficile, human papilloma virus, influenza, and herpes simplex virus (Table 1). Viral infections i.e influenza (OR, 2.56 in CD; p<0.0001 and OR, 1.75 in UC, p=0.00001) and Epstein-Barr virus (EBV) (OR 2.69 in CD; p<0.0001, and OR, 2.82 for UC; p<0.0001) were more common in children (<18 years of age). On the other hand, fungal and bacterial infections i.e aspergillosis (OR, 2.93 in CD; p<0.0001, and OR, 3.21 in UC; p<0.0001), histoplasmosis (OR, 1.60 in CD; p=0.003, and OR, 2.14 in UC; p=0.0001) and pneumococcal disease (OR, 3.36; p<0.0001, and OR, 3.09 in UC; p<0.0001) were more prevalent in the elderly (>65 years). Tuberculosis was more common in CD. Clostridium difficile and cytomegalovirus infections were more common in UC.

Conclusion: OIs are more prevalent in patients with CD and UC. Children with UC and CD tend to have a higher prevalence of viral OIs and older adults with UC and CD tend to have a higher prevalence of fungal and bacterial OIs.

Disclosure: Nothing to disclose

References
P0917 NON-CELIAC WHEAT SENSITIVITY AND CELIAC DISEASE IS STRONGLY AND INDEPENDENTLY ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY OF 3542 RANDOMLY SELECTED SUBJECTS

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Introduction: Diet may be involved in the pathogenesis of inflammatory bowel disease (IBD) but this is controversial, as it is an association between IBD with celiac disease (1). Wheat sensitivity has been reported in Crohn’s disease, and associated with more severe disease (2). A diet which excludes gluten (along with other dietary components) has been shown to induce clinical remission in 79% of patients with Crohn’s disease (3). These findings suggest gluten may aggravate IBD.

Aims and Methods: The aim of this study was to evaluate if wheat sensitivity and celiac disease are risk factors for physician-diagnosed IBD in a general community and determine which symptoms and factors are associated with wheat sensitivity in IBD. A total of 3542 people randomly selected from the Australian population returned a mail survey (Digestive Health & Wellbeing Survey, response rate = 43%) which contained questions on gastrointestinal (GI) symptoms (present in the last 3 months), medical and lifestyle factors including a self-reported physician diagnosis of celiac disease and IBD. Response bias was minimal. Wheat sensitivity was defined as people without celiac disease who reported GI symptoms on wheat ingestion. Associations between categorical variables were evaluated using the Pearson chi-square test.

Results: The prevalence of IBD by self-report in our cohort was 1.9% (95% CI 1.5–2.5). Of those with IBD, 13% reported celiac disease compared with 1.2% of those without IBD (unafflicted cohort) (OR 12.9, 95% CI 6.0–27.7). In addition 25.7% of those with IBD reported wheat sensitivity, compared with 14.8% of the unaffected cohort (OR 2.1, 95% CI 1.2–3.7, Attributable Risk 11.9% 95% CI 0.7–23.2). There was no significant association between wheat sensitivity in IBD and age (p = 0.27), gender (p = 0.16) or psychological distress (p = 0.93).

There was a significant association with modified Rome IV criteria for functional dyspepsia (OR 3.49, 95% CI 1.03–11.82), particularly epigastric pain syndrome subtype (OR 4.11, 95% CI 1.15–14.73), but not irritable bowel syndrome. Symptoms significantly associated with wheat sensitivity in the IBD cohort included epigastric pain and constipation (see Table 1).

Conclusion: In this cohort, celiac disease and wheat sensitivity are both significantly associated with a diagnosis of IBD, and wheat sensitivity is associated with constipation and epigastric pain in particular. This suggests exacerbation of symptoms in IBD may be related to wheat sensitivity. These results suggest that it is worth testing for celiac disease in IBD, and asking patients whether wheat sensitivity worsens symptoms if the present results are confirmed.

Disclosure: This abstract has been presented at DDW 2018

References
validated questionnaires. These outcomes were compared over a minimum period of 2 years. The diagnosis of IBS was based on Rome III symptoms and patients were categorized into quiescent disease, occult inflammation, and active disease at baseline. A $\chi^2$ test was used to compare categorical variables and an independent samples t-test to compare continuous data. Due to multiple comparisons, a 2-tailed p value of <0.01 was considered significant for these analyses. Independent predictors of the occurrence of any of the objective disease activity outcomes of interest were deter-
mined by performing multivariate Cox regression analysis to control for baseline demographics, disease related and psychological characteristics. Results were expressed as hazard ratios (HR) with 95% confidence intervals (CI).

**Results:** In 360 IBD patients, there were no differences in longitudinal disease activity between patients reporting IBS-type symptoms and patients with quiescent disease or occult inflammation. Glucocorticosteroid prescription or flare of disease activity was based on physician’s global assessment, and escalation of medical therapy, was more common in patients with active disease than in patients reporting IBS-type symptoms (HR=3.16; 95% CI 1.93–5.19 and HR=3.24; 95% CI 1.98–5.31, respectively). A significantly greater mean number of inves-
tigations were performed in patients reporting IBS-type symptoms than those with quiescent disease (p =0.008), but not compared with patients with occult inflammation or active disease. Anxiety, depression, and somatisation scores at follow-up were significantly higher, and quality of life scores significantly lower, in patients reporting IBS-type symptoms when compared with patients with quiescent disease, but were similar to patients with active disease.

**Conclusion:** The reporting of IBS-type symptoms in IBD was associated with increased healthcare utilisation, psychological co-morbidity, reduced quality of life, but not adverse objective disease activity outcomes during longitudinal follow-up.

**References:**

**P0919 EVIDENCE OF A BI-DIRECTIONAL EFFECT OF THE BRAIN-GUT AXIS IN INFLAMMATORY BOWEL DISEASE**

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**Introduction:** Evidence supporting the existence of a bi-directional relationship between the presence of mood disorders and gastrointestinal symptom reporting has been previously described [1,2]. Whether a similar bi-directional relationship exists between psychological co-morbidity and disease activity in inflammatory bowel disease (IBD) is uncertain. We aimed to resolve this issue during long-
titudinal follow-up in secondary care patients.

**Aims and Methods:** The hospital anxiety and depression scale (HADS) and clinical disease activity indices were administered at baseline and after 2 years. Faceal coloproctography (FC) was collected at baseline. Objective markers of disease activity during longitudinal follow-up were assessed via case note review. These included glucocorticosteroid prescription or flare of disease activity defined by physician’s global assessment, escalation of medical therapy, hospitalisa-
tion and intestinal resection. Brain-to-gut interactions were defined as devel-
opment of new-onset disease activity in patients with quiescent disease and abnormal baseline HADS scores. Gut-to-brain interactions were defined as de-
velopment of abnormal HADS scores in patients with active disease and normal HADS scores at baseline. Multivariate Cox regression analysis was performed to control for baseline characteristics and duration of follow-up, with results expressed as hazard ratios (HRs) with 95% confidence intervals (CI).

**Results:** 405 (50.7%) of 799 patients with baseline data were followed up. Baseline disease activity was associated with an almost six-fold increase in sub-
sequent development of abnormal anxiety scores (HR 5.77; 95% CI 1.89–17.7). In patients with clinically quiescent disease at baseline, abnormal anxiety scores were associated with need for glucocorticosteroid prescription or flare of disease activity (HR 2.08; 95% CI 1.31–3.30) and escalation of medical therapy (HR 1.82; 95% CI 1.19–2.80), but not hospitalisation (HR =1.95; 95% CI 0.77–3.31) or intestinal resection (HR =0.79; 95% CI 0.22–2.84). Abnormal baseline anxiety scores remained associated with subsequent flare of disease activity or escalation of med-
ical therapy when both normal clinical disease activity indices and FC≤250pg/g were used to define quiescent disease at baseline (HR=2.29; 95% CI 1.03–5.07 and HR =2.43; 95% CI 1.13–5.20, respectively). There was no association between depression and disease activity during longitudinal follow-up.

**Conclusion:** We provide evidence of a bi-directional relationship between psycho-
logical co-morbidity and disease activity in IBD, suggesting that brain-gut axis activity may have a significant effect on the natural history of IBD. These findings underpin the development of healthcare interventions that aim to reduce IBD related incapacitation, away from one that focuses solely on the management of inflammatory activity, to one that integrates this with the need for proactive management of psychological well-being. Novel therapeutic interventions are much needed.

**Disclosure:** Nothing to disclose.

**References:**

**P0920 HOSPITALIZATION AND RE-HOSPITALIZATION IN INFLAMMATORY BOWEL DISEASE: REASONS FOR A GROWING REALITY**

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**Introduction:** Inflammatory Bowel Disease (IBD) is a chronic disease with a significant burden of healthcare utilisation and hospitalisations. Aims and Methods: The aim of this study was to evaluate the causes of hospital-
ization and readmission, therapeutic intensification and surgery rates, in patients with Inflammatory Bowel Disease admitted to our department.

**Results:** In 360 IBD patients, 34% were admitted with acute exacerbation of Inflammatory Bowel Disease admitted in our department from January 2011 to December 2016. The large proportion of the patients (67.6%) with UC presented pancolitis, and in CD 46.5% had ileal involvement and 46.3% had penetrating disease. Twenty four percent took oral corticosteroids in the previous 3 months, 43.9% were under azathioprine and 20% under infliximab. The vast majority (95%) had hospital admission in the previous 3 months.

The main causes of admission were acute exacerbation of CD (39.9%) and UC (24.2%), being 3 patients admitted to an intermediate care unit. The most common symptoms were abdominal pain (83%), diarrhoea (54%), nausea (44%) and reduction in bowel movements (26%). During the hospital stay, 65.2% were treated with intravenous corticosteroids, 41% with antibiotics, 14.8% with infliximab and one patient was submitted to surgery. After discharge, more than an half needed to intensify therapy and 21.5% were submitted to surgery.

The readmission rate at 90, 180 and 360 days were, respectively, 9.4%, 20%, 27.1% and 34.5%. The factors associated with readmission at 180-days were recurrent intravenous corticosteroids (p < 0.05) and reduction in bowel movements (p < 0.05).

**Conclusion:** Patients with Inflammatory Bowel Disease present with multiple exacerbations of the disease, needing multiple admissions and therapeutic intensification.

**Disclosure:** Nothing to disclose.

**References:**
7. United European Gastroenterology Journal 6(8S)

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**Introduction:** Fatigue in inflammatory bowel disease (IBD) is a significant problem, reported to affect between 44–86% of patients with active disease [1,2] and 22–54% of patients in remission [1–5]. Fatigue has been demonstrated to have a substantial effect on quality of life [4] with IBD patients reporting fatigue as one of their main concerns [6,7].

However, the aetiology and pathogenesis of fatigue in IBD is unknown. Proposed mechanisms frequently centre around inflammation but this does not fully explain the persistence of fatigue in quiescent disease. Little consideration has been given to the idea that fatigue may be a separate entity: could it be possible that it is actually a result of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME)?

Through our study, we wished to assess the burden of fatigue in a cohort of patients with IBD in Tayside and gain a better understanding of it by evaluating whether those reporting fatigue fulfilled criteria for CFS/ME.

**Aims and Methods:** We designed a questionnaire to assess the prevalence of fatigue in patients attending IBD clinics in Tayside and whether they met the diagnostic criteria for CFS/ME.

Given numerous guidelines for the diagnosis of CFS/ME exist we followed the recommendations from BMJ Best Practice and based our questionnaire on the following criteria: Central Tiredness Syndrome Control (CDS) which was the most widely used, International Consensus Criteria (ICC) which is the most widely accepted, Institute of Medicine (IOM) and the National Institute for Health and Care Excellence (NICE) guidance.

NICE guidelines, whilst suggested to be less clinically appropriate, were included as, in the UK, these may be the guidelines with which practitioners are most familiar. All guidelines required specific patterns of fatigue in addition to associated symp-
toms; the biggest differences are in requirements for post exertional malaise and numbers of associated symptoms.

All patients attending the IBD clinics between 3rd–24th November 2017 were given the anonymous questionnaire to complete. Exclusion criteria were age <16, incapacity and/or absence of an established diagnosis of IBD.
Questionnaire responses were analysed to determine whether the criteria for a diagnosis of CFS/ME in the context of each of the four guidelines had been reached.

**Results:** Of 130 patients approached, 113 met the inclusion criteria and 99 returned a completed questionnaire, forming the study group: 52 female; 47 male, median age 41 (range 18–84 years) of CD, 38 ulcerative colitis (UC) and 12 IBD unclassified (3 did not state IBD type).

Fatigue was experienced by 65% (n = 64) and was more prevalent in CD than UC (74% vs 52%) and in females than males (77% vs 51%). 64% of those experiencing fatigue reported fatigue persisting in the absence of gastrointestinal symptoms.

Of these patients with fatigue, 26 patients (41%) with IBD fulfilled the NICE CFS/ME diagnostic criteria, 13 (20%) the ICC, 6 (9%) the IOM criteria and 13 (20%) the CDC criteria.

**Conclusion:** Fatigue is commonly reported in this population even when disease is reportedly in remission. Although there may be other confounding factors contributing to fatigue in our cohort, such as concurrent medication or comorbidity, a small proportion nevertheless meet recognised diagnostic criteria for CFS/ME and this should not be overlooked when managing fatigue in IBD.

**Disclosure:** Nothing to disclose

**References**


**P0923 FACTORS ASSOCIATED WITH GUT COLONIZATION AND DECOLONIZATION WITH EXTENDED SPECTRUM-β-LACTAMASE PRODUCING ENTEROBACTERIA (ESBL-E) IN ULCERATIVE COLITIS PATIENTS: PRELIMINARY STUDY RESULTS**

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**Introduction:** Extended spectrum-β-lactamase producing Enterobacteria (ESBL-E) are the most frequently found multi-drug resistant bacteria colonizing the gut of ulcerative colitis (UC) patients. 1 Changes in the microbiome may act as a trigger in UC inflammation process. Previous studies have shown that gut colonization with ESBL-E might increase UC disease severity.2

**Aims and Methods:** The aim of the study was to analyze whether gut colonization with ESBL-E in UC patients is a constant state or changing over time and what are the factors attributing to that. A prospective study was conducted analysing patients with clinically, endoscopically and histologically confirmed UC diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia. During the two study visits (2015 and 2017) the same patients participated in out-patient interviews regarding factors for gut colonization and decolonization with ESBL-E, UC disease activity was evaluated according to the full Mayo score (FMS), faecal samples were obtained and analyzed for ESBL-E presence according to EUCAST guidelines.

**Results:** 102 patients with UC participated in the fist study visit in 2015 and gut colonization with ESBL-E was found in 12% (n = 12) of the patients. 29 patients participated in the second study visit in 2017 and gut colonization with ESBL-E was found in 7% (n = 2) of the patients. The analyzed reasons for not participating in the second visit study showed that patients with previous gut colonization with ESBL-E were feeling bad (8 vs 1 patient) or had traveled abroad (17 vs 8 patients) more often at the time of the visit, comparing to the patients which were not previously colonized with ESBL-E. In between the two study years, two patients had become newly colonized with ESBL-E, whereas two other patients became decolonized. Patients who became newly colonized with ESBL-E were only women and were 11 years older in comparison to the patients who became decolonized. Both patients who become decolonized, had not used any antibiotics during the study period, while all the patients who became newly colonized with ESBL-E had used antibiotics during the study period. Patients newly colonized with ESBL-E had more exacerbations – 11, in comparison to decolonized patients, who only had 1 exacerbation during the study period. All patients who became colonized with ESBL-E had severe UC disease activity, while patients who became decolonized had either mild or moderate UC disease activity, according to the FMS. Also the mean FMS in patients who became colonized with ESBL-E was much higher – 11 (severe disease), comparing to the patients who became decolonized – 6 (moderate disease). There were no differences found in patients who became colonized and decolonized with ESBL-E regarding hospitalization times, UC conservative treatment and surgical interventions.

**Conclusion:** Gut colonization with ESBL-E in UC patients is not a constant state and is changing over time. Older age, female gender, previous antibiotic use, patients with more UC exacerbations and higher UC disease activity may act as risk factors for gut colonization with ESBL-E in UC patients. Inversely younger age, male gender, abstention from antibiotic use, less UC exacerbations and lower UC disease activity may act as factors for gut decolonization from ESBL-E in UC patients.

**Disclosure:** Nothing to disclose

**References**

P0924 INCIDENCE AND DISEASE PRESENTATION OF ELDERLY-ONSET IBD IN A EUROPEAN POPULATION-BASED INCEPTION COHORT – AN ANALYSIS OF THE EPI-IBD 2010-2011 COHORTS


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Introduction: Previous reports have indicated that the clinical presentation and initial treatment of patients with elderly-onset inflammatory bowel disease (IBD), defined as patients diagnosed ≥60 years, differs from that of younger patients.

Aims and Methods: To assess the age-specific incidence, initial presentation and treatment of elderly-onset IBD, compared with IBD diagnosed in patients aged 15-39 and 40-59 years, in a European population-based inception cohort.

Results: In total, 2000 IBD patients (53.6% males) were included in the cohort. 747 (37.4%) CD, 1106 (55.3%) UC and 147 (7.4%) IBDU. The CD incidence was 7.18, 3.95 and 2.70 cases/10^5 in each age group respectively (p < 0.001). The UC incidence rate was 9.58, 6.30 and 5.88, respectively (40-59y vs ≥60y, p = 0.257). In elderly-onset IBD, overall more patients were diagnosed with UC, and the frequency of proctitis at diagnosis was lower (Table). In CD patients, elderly-onset patients more often had colonic location, while no differences were observed in disease behaviour (Table). Within the first three months, elderly-onset CD patients were less likely to be treated with IMM or biologicals. Elderly-onset UC patients received more frequently topical steroids and were less frequently treated with 5-ASA or IMM. No difference was observed between the age groups in the need of abdominal surgery, in CD or UC (Table). In CD patients, a regression analysis found that the need of early, intensive treatment was inversely associated to elderly-onset (OR 0.29, 95% CI 0.16–0.51) and inflammation behaviour (OR 0.24, 95% CI 0.1-0.35). In UC patients, it was associated to extensive disease (OR 12.03, 95% CI 3.71–39.05) and inversely associated to elderly-onset (OR 0.35, 95% CI 0.16–0.75).

Conclusion: In this large population-based inception cohort, the age-specific incidence of IBD decreases with age, while UC incidence shows a peak in young age, and it decreases to a plateau in adult and elderly individuals. Elderly-onset IBD shows a different phenotype from that of young patients: elderly patients are more likely to be diagnosed from UC, and in case of CD it is more frequently associated to colonic localisation. At diagnosis, elderly-onset IBD patients were less aggressively treated than other age groups; this differences in the management might be due to differences in severity but this should be confirmed with the analysis of the long-term follow-up of the cohort.

Disclosure: Nothing to disclose.

P0925 USEFULNESS OF SYSTEMATIC LIVER BIOPSY DURING A SURGERY FOR INFLAMMATORY BOWEL DISEASE FOR THE DIAGNOSIS OF PRIMARY SCLEROSING CHOLANGITIS (PSC)

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Introduction: PSC associated to IBD drastically increases the risk of liver and colorectal complications. However, no specific screening is recommended. The local IBD unit proposed to perform systematic screening by liver biopsy during surgery. Aim and Methods: The aims of the study were to assess the frequency, characteristics and outcomes of inflammatory bowel disease (IBD) patients diagnosed with primary sclerosing cholangitis (PSC) on systematic liver biopsy during a surgery for IBD. In a retrospective monocentric study, all patients who underwent a major abdominal surgery related to IBD were included. IBD phenotype and outcomes were assessed according to the presence of PSC.

Abstract No: P0924

15-39 years | 40-59 years | ≥60 years

IBD (CD-UC - IBDU)
40.5% - 52.6% - 6.9%
35.4% - 56.3% - 8.3%
29.7% - 62.9% - 7.4%
0.006

CD behaviour (B1 – B2 – B3)
64.8% - 16.8% - 3.7% - 7.2%
63.6% - 19.8% - 9.1% - 5.3%
60.0% - 22.0% - 6.0% - 4.0%
0.912

B1+p – B2+p – B3+p
1.7% - 1.1%
1.1% - 1.1%
1.0% - 1.0%

CD location (L1 – L2 – L3)
30.4% - 22.6% - 3.3% - 5.1%
26.3% - 29.0% - 22.0% - 7.5%
22.7% - 38.1% - 19.6% - 5.2%
0.022

L1 – L2 – L3
5.1% - 5.5% - 7.7%
7.5% - 1.6% - 5.9%
9.3% -3.1% - 2.1%

UC extent (E1 – E2 – E3)
23.2% - 38.0% - 38.7%
24.0% - 42.5% - 33.6%
16.2% - 45.7% - 38.1%
0.087

UC treatment (5ASA – BIOLOGICALS – ABDOMINAL SURGERY)
89.9% - 34.0% - 8.9% - 7.7%
90.2% - 26.3% - 7.4% - 4.4%
85.3% (* - 29.2% -12.7%)
0.025

Systemic Steroids/Topic Steroids – IMM – BIOLOGICALS
-2.2% - 1.2%
-1.3% - 0.7%
(*) -3.3% (**)-0.9% - 0.5%
0.026

Systemic STEROIDS/Topic – Abdominal Surgery
-2.2% - 1.2%
-1.3% - 0.7%
(*) -3.3% (**)-0.9% - 0.5%
0.027

[Phenotype at diagnosis and initial (first 3 months) treatment]
A total of 342 colonoscopy were performed during the 5 years period (2.1 ± 1.2 colonoscopy/patient). Random biopsies were performed at least once in 81.5% of patients with a mean 27.5 ± 6.4 biopsy samples per colonoscopy and 33.3% of the patients underwent chroendoendoscopy (CE) at least once.

During the surveillance period, endoscopically resectable lesions were detected in 37 patients (22%) with TI ulcer. Visible lesions deemed unfit for endoscopic resection were found in 5 patients (3.1%). Overall, 61 dysplastic visible lesions (58 with low grade dysplasia and 3 with high grade dysplasia) and 1 adenocarcinoma were found in 34 patients.

Disciplina in random biopsies was present in 3 patients, the yield of random biopsies for dysplasia being 1.85% per-patient (1/312), 1.75% per-colonoscopy (6/342) and 0.25% per-biopsy (9/3637). Dysplasia detected in random biopsies was associated with a personal history of visible dysplasia (p = 0.006).

Conclusion: Our data confirm that patients with longstanding IBD, in particular UC, should be enrolled in dysplasia surveillance programs and that performing CE and random biopsies helps in the detection of colonic neoplastic lesions.

Disclosure: Nothing to disclose

References

P0928 DISCRETE TERMINAL ILEAL UCERS IN UCERATIVE COLITIS PATIENTS: CLINICAL SIGNIFICANCE AND NATURAL COURSE
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Introduction: Apthous or small ulcerations in terminal ileum are infrequently observed in patients with ulcerative colitis (UC) without evidence of backwash ileitis. However, clinical significance and natural course of terminal ileal (TI) ulcers in UC are unclear.

Aims and Methods: This study was conducted to demonstrate the frequency and possible implication of UC ulcers with TI ulcer. We retrospectively reviewed 1,585 UC patients with successful TI intubation among 2,211 UC patients, excluding 626 patients with no available images. To evaluate the frequency, we compared with those of historic healthy cohort (n = 26,735) who had no gastrointestinal symptom and history of NSAIDs use at the same center. Regarding the clinical characteristics, we compared the 87 UC patients with TI ulcer (group A) and the 1,498 UC patients without TI ulcer (group B). The natural courses of TI ulcers were also investigated during the follow-up periods.

Results: Of the 1,585 UC patients with TI ulcers (5.5%) showing TI ulcer without the evidence of inflammation in the cecum and right colon, which was higher than the frequency of healthy cohort (106/26,735, 0.4%), (p < 0.001). There was not any difference in age, sex, smoking history, family history, and the incidence of extraintestinal manifestations between the group A and group B. The group A had more proctitis and left-sided colitis than the group B (p = 0.001). However, disease activity and maximal disease extent during follow-up periods were not different between the two groups. The histories of medication use including corticosteroids, azathiopurine, and anti-tumor necrotizing factor and the collect-ency showed also no significant differences. Of the 55 patients who underwent follow-up colonoscopy, 36 patients (65.5%) showed a resolution of TI ulcer.
Conclusion: Discrete TI ulcers are more common in UC patients, compared with healthy controls of them, lesions were resolved. Clinical impact on disease extension and severity seems not to be significant.

Disclosure: Nothing to disclose.

Reference:

P0929 MAGNETIC RESONANCE ENTEROGRAPHY DEPLOYMENT IN AN INTERNATIONAL MULTICENTRE CLINICAL TRIAL OF VEDOLIZUMAB IN CROHN’S DISEASE: AN ANALYSIS OF TECHNICAL FEASIBILITY FROM THE VERSIFY TRIAL

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Introduction: Radiologic imaging is used as a method to monitor Crohn’s disease (CD) activity in clinical practice. Magnetic resonance enterography (MREn) depicts the transmural extent of disease, and can be performed on equipment commonly available at most hospitals and many outpatient clinics globally. There is a growing interest in implementing MREn in clinical trials and in research. The magnetic resonance index of activity (MaRIA) score requires quantitation of an MREn imaging sequence before and after intravenous gadolinium. To date, assessment of MREn in the research setting has been largely restricted to single centre studies, and use of MREn in a prospective multicentre trial has not previously been reported.

Aims and Methods: The aim of this report was to evaluate the deployment of a standardised MREn protocol execution in a clinical trial setting in CD. VERSIFY (NCT02425111) was an international, multicentre, phase 3b, open-label study of mucosal healing with vedolizumab (VDZ) in a difficult-to-treat population (n = 101) with moderate-severe CD (CD Activity Index CDAI > 220 and 240-450) and prior failure with corticosteroid, immunomodulatory and/or biologic therapy. The primary endpoint was clinical endoscopic remission with terminal ileal ulcerations in asymptomatic individuals: natural course and clinical significance.
P0931 HISTOLOGICAL FEATURES OF ULCERATIVE COLITIS IN NON-OPERATED PATIENTS WITH CLOSTRIDIUM DIFFICILE INFECTION

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Background: The aim of the study was to evaluate the impact of CDI on ulcerative colitis (UC) and to examine correlation between CDI and disease activity in patients with UC.

Methods: A cross-sectional study included 70 consecutive inpatients or outpatients with UC (37 males, 33 females, aged 19 to 65 years, mean age 37.97 ± 1.55 years) with disease duration of 1 to 10 years. Patients received no antibiotics for at least 6 months prior to the study. None of the patients was operated or died during hospital admission or was operated previously. No patients were diagnosed to have pseudomembranous colitis. Patients were enrolled after history and clinical examination, stool samples and were evaluated for the presence of C. difficile toxins A and B (CDT) by ELISA. UC severity was assessed according to Mayo Score/disease activity index (DAI: mild in 24 cases (34.3%), moderate — in 12 cases (17.1%) and severe in 34 cases (48.6%). All patients underwent high-resolution colonoscopy in white and NBI modes with mucosa biopsies (1 per each segment of the colon and terminal ileum). Colonoscopic biopsies were scored 0 for histology, lymphocytic infiltration and atrophy. Slides were also reviewed for epithelial changes, inflammatory infiltrates, changes in lamina propria and lamina propria hemorrhage. Bacterial overgrowth syndrome (BOS) was diagnosed by hydrogen breath test with lactulose.

Results: Thirty one UC patients (44.3%) had no signs of disease (33 (47.1%) — toxin B only, 6 (8.6%) — both A and B toxins. Demographic data and laboratory values upon admission did not differ between subgroups of patients with and without CDI. BOS was revealed in 17 of 30 cases (56.7%). Colon histology revealed no significant signs consistent with pseudomembranous colitis. As determined by Kruskal-Wallis test, no statistically significant difference in gender, age, education level, duration of UC history, stool frequency, type of immunosuppressive therapy, other clinical, endoscopic or histological features of UC or in the presence of BOS in patients with and without CDI. No difference was found in UC severity according to DAI mild/moderate/severe distribution was 9/12/10 for CDT-negative and 15/14/10 for CDT-positive patients respectively (χ² = 0.749, p = 0.688).

Conclusion: CDI may play important role for the outcome of severe UC patients undergoing surgery, who received second-line broad-spectrum antibiotics. However, no significant differences in severity of UC in our group of patients in relation to the presence of CDI were found.

Disclosure: Nothing to disclose

References

P0932 COMPARISON OF BOWEL ULTRASONOGRAPHY AND MAGNETORESONANCE ENTEROGRAPHY FOR DETECTING ENDOSCOPIC-DISEASE ACTIVITY IN ILEOCOLIC CHROIN'S DISEASE

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Introduction: Cross-sectional imaging techniques, including bowel ultrasonography (BUSG) and magnetic resonance enterography (MRE) are increasingly used for evaluation of Crohn’s Disease (CD). Various clinical, laboratory and imaging indices have been derived to evaluate disease activity in CD.

Aim: The aim of the present study was to compare the diagnostic accuracy of BUSG and MRE for detecting disease activity in CD using simple endoscopic score for CD (SES-CD) as reference standard. A total of 71 consecutive adult patients with known CD underwent ileocolonoscopy, BUSG and MRE within one month prospectively, and comparisons were made as per patient. The SES-CD > 6 was accepted as active disease. Sensitivity of BUSG and MRE for detection of disease activity was compared with the McNemar test, with results of SES-CD > 6.

Results: The sensitivity and specificity of BUSG lesions in detecting patients with SES-CD > 6 were as follows; bowel thickening 62.3/50, loss of wall stratification 66.7/34, color Doppler USG signal (Limberg 3–4) 78.6/36.3, rigidity 81.4/40, mesenteric fibro-fatty proliferation 76.9/40, and fistula 66.7/33.8, respectively. Noteworthy MRE lesions in detecting patients with SES-CD > 6 were as follows; bowel thickness 70.3/68.6, bowel wall thickening 69.6/40, bowel wall thickening 70.3/68.6, bowel wall thickening 74.4/43.8, ulcers 65.3/31.8, total hyperenhancement 67.9/37.9, layered enhancement 64.3/32.6, homogenous enhancement 70.3/66.6, sign 69.2/35.6, mesenteric fibro-fatty proliferation 79.4/45.9, and lymphadenopathy 69.6/35.4, respectively.

Conclusion: In the following univariate and multivariate analyses, there was a significant correlation between BUSG and MRE in detecting endoscopically active CD (SES-CD > 6): bowel wall thickening (p = 0.727), preteneostatic dilatation (p = 0.210), mesenteric fibro-fatty proliferation (p = 0.167), mesenteric lymphadenopathy (p = 0.815), and craters (p = 1.000). Comparison of BUSG, the diagnostic accuracy of MRE was significantly higher in detecting loss of wall stratification and strictures (p = 0.000). On the other hand, diagnostic accuracy of BUSG color Doppler signal (Limberg 3–4) was significantly higher than MRE sign in detecting disease activity (p = 0.036).

Disclosure: Nothing to disclose

References

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Introduction: Inflammatory bowel disease (IBD) and clostridium difficile infection (CDI) are having an increasing incidence in the world. The aim of the study was to assess the correlation between PLT indices: MPV (mean platelet volume), PCT (plateletcrit), PDW (platelet distribution width), C-reactive protein (CRP) and endoscopic picture in the course of inflimibam (IFX) induction regimen in ulcerative colitis (UC) patients. 46 patients with UC, 32 men and 16 women, were enrolled to the study. They were administered IFX (standard induction therapy). Laboratory tests (CRP and PLT indices) and colonoscopy were performed in all patients during induction regimen – at 0, 2, and 6 weeks and in follow-up six weeks after finished induction therapy.

Results: The study revealed statistically significant (p < 0.01) decrease in mean CRP level (from 32.35 to 7.05 mg/L) and mean PLT count (from 398 to 315 x 10^7/L) together with improvement of endoscopic picture (MAYO score; p < 0.01) in all patients. Mean PCT values after the induction therapy were 9.78 and 2.76 points, respectively; mean MAYO endoscopy subscore decreased from 2.8 to 1.84 points (p < 0.01). Mean PCT values were significantly higher prior to BT (0.46%) and normalized after induction therapy (0.22%) (p < 0.01). On the other hand, mean MPV values were under normal range during qualification to BT (6.8 fl) and obtained adequate values after BT (8.08 fl) (p = 0.01). Subsequently, CRP and PCT levels correlated positively with each other before the introduction of BT (p = 0.02). Negative correlations between PDW level and PLT count and positive correlations between PCT level and PLT count were noticed before IFX induction regimen and in follow-up after finished therapy, too (p < 0.01).

Conclusion: Chronic inflammatory process in patients with IBD is connected with elevated PLT count and changes in PLT activation.

Disclosure: The work was presented as a poster at one international meeting Falk Symposium 209 October 6-7, Berlin, Germany IX GASTRO-CONFERENCE (Part II) IBD 2017 – Therapeutic and Biological Barriers

References
P0934  DISEASE SEVERITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE ASSOCIATED WITH CARDIOVASCULAR DISEASES A. Mantaka1, E. Tsoukal1, M. Fragaki2, K. Karmiris3, N. Viazic2, G. Mantzaris2, I. Koutroubakis1 1University of Heraklion, Department of Gastroenterology and Hepatology, Heraklion, Greece 2Evangelismos General Hospital of Athens, Department of Gastroenterology and Hepatology, Athens, Greece 3Tzentesio General Hospital, Department of Gastroenterology and Hepatology, Heraklion, Greece Contact E-Mail Address: katman@gmail.com Introduction: Patients with inflammatory bowel disease (IBD), i.e. Crohn’s disease (CD) and ulcerative colitis (UC), may be at increased risk for cardiovascular disease (CVD) even in the absence of documented risk factors. Data linking the severity of IBD to coexisting CVD are rather scarce. Aims and Methods: This is a retrospective analysis from IBD patients with concurrent CVD derived from 3 participating IBD Centers. Patient demographic and clinical characteristics, routine laboratory tests including serum biomarkers, disease activity score by the Harvey-Bradshaw Index (HBI) for CD and the Simple Clinical Activity Index (SCAI) for UC, quality of life scores based on the short inflammatory bowel disease questionnaire (SIBDQ), and health care resources utilization were compared to those of IBD patients without CVD. Statistical analysis was performed with the SPSS 24. Results: Overall, 321 IBD patients (167 CD, 154 UC, 192 males, median [IQR] age 55[42-65]) years with a mean ±SD follow-up of 12.6 ± 9.3 years were included. Of these, 82(35.5%) patients, mainly with UC (59.8% vs 43.8%, p < 0.001) received treatment for CVD. CVD diagnosis was in 51.2% of cases. Among patients with CVD, 53 (64.6%) reported coronary artery disease (4/5 had at least another one CVD comorbidities), 22 (26.8%) were diagnosed with stroke, 10 (12.2%) with heart failure, and 2 (2.4%) with peripheral arterial disease. CD patients were smoking more frequently (75.6% vs 66.5%, p < 0.001), had hypertension (65.9% vs 18%, p < 0.001) and diabetes mellitus (34.1% vs 6.3%, p < 0.001) as well as older age at diagnosis (53.6 ± 15.2 vs 38.2 ± 14 years, p < 0.001) and elevated body mass index (28.8 ± 0.6 vs 26.7 ± 0.4, p = 0.04). Patients without CVD, were receiving more often anti-TNFα (53.6% vs 26.8%, p < 0.001), steroids (81.2% vs 59.8%, p < 0.001), immunomodulators (61.1% vs 36.6%, p < 0.001) but no 5-ASA (p = 0.285). HBI, SIBDQ, or SIBEQ scores did not differ between the two groups. Rates of hospitalization and/or surgery after diagnosis were not different between the two groups. Endoscopic activity was milder when CVD was present (p = 0.018 and p = 0.002 respectively for UC and CD). Conclusion: The results of this study did not confirm the hypothesis that IBD patients with more severe disease have a higher CVD risk. CVD plays a less important role in the development of CVD in IBD patients. Data from larger prospective studies are essential to confirm our findings. Disclosure: Nothing to disclose

P0935  THE ROLE OF SERUM IL-17 AND IL-23 IN ASSESSING INFLAMMATORY BOWEL DISEASE SEVERITY L.A. Lucaciu1, M. Lies2, D. Leucuta3, C.A. Iuga4,5, A. Seicean6 1University of Medicine and Pharmacy ‘Iuliu Hatieganu, Gastroenterology and Hepatology, Cluj-Napoca, Romania 2University of Medicine and Pharmacy ‘Iuliu Hatieganu, Department of Pharmaceutical Analysis, Cluj-Napoca, Romania 3University of Medicine and Pharmacy ‘Iuliu Hatieganu, Department of Medical Informatics and Biostatistics, Cluj-Napoca, Romania 4University of Medicine and Pharmacy ‘Iuliu Hatieganu’, Department of Pharmaceutical Analysis, Cluj-Napoca, Romania 5MediFuture Research Center for Advanced Medicine, Department of Proteomics and Metabolomics, Cluj-Napoca, Romania 6University of Medicine and Pharmacy ‘Iuliu Hatieganu’, Cluj-Napoca, Romania Contact E-Mail Address: laura_lucaciu@yahoo.com Introduction: Interleukin-17 (IL-17) and Interleukin-23 (IL-23) play a critical role in inflammatory bowel disease (IBD) immune response and are currently being targeted by therapeutic agents in clinical trials. High serum levels of IL-17 and IL-23 have been reported in severity and might be used as biomarkers for disease activity, however IL-17 and IL-23 levels are lower in mild/moderate disease group vs severe disease group, p = 0.119. As for IL-23, mild/moderate group had with 699.86pg/mL lower serum levels than severe disease group, p < 0.001. In UC, mild/moderate group had with 1328.13pg/mL lower serum levels of IL-17 (p = 0.003) and with 723.62pg/mL lower levels of IL-23 (p = <0.001) comparatively to the severe group. Spearman’s rank correlation test showed a correlation coefficient of 0.52 for IL-17 (r = 0.003) and 0.67 for IL-23 (r = <0.001). The median distribution of IL-23 serum levels among patients with intestinal complications showed with 622.1pg/mL higher values in fistula group (p = 0.035) vs other types of complications. Conclusion: IL-17 and IL-23 serum levels can differentiate between IBD patients with severe and non-severe disease and can assess disease severity in the clinical practice. Further monitoring of these cytokins in larger IBD groups might be a promising tool in assessment disease progression. Disclosure: Nothing to disclose

P0936  SYMPTOMS OF ANXIETY AND DEPRESSION IN INFLAMMATORY BOWEL DISEASE J.C. Silva1, A.S. Muchado2, A.P. Silva1, A. Rodrigues3, J. Rodrigues4, M. Sousa5, A.C. Ribeiro Gomes1, J. Carvalho3 1Centro Hospitalar Vila Nova de Gaia/Espinho, Gastroenterology, Vila Nova de Gaia, Portugal 2Centro Hospitalar São João, Clínica de Psiquiatria e Saúde Mental, Porto, Portugal Contact E-Mail Address: joaoacorosilva@gmail.com Introduction: Treatment of Crohn’s Disease (CD) and Ulcerative Colitis (UC) is usually directed at organic aspects of the disease, often disregarding psychosocial factors. A comprehensive strategy including identification of anxiety and depressive symptoms may have a significant impact on the quality of life of patients with IBD. Aims and Methods: The present study aims to test the association between anxious and depressive symptoms with IBD activity and course. Results: Of 221 patients followed in October and November of 2017, 64 patients with confirmed IBD who accepted to participate in the study were selected. With known mental illness followed by Psychiatry were excluded. Anxiety symptoms were quantified by Spielberg’s Anxious State Inventory (STAI) and symptoms of depression by the Beck II Depression Scale (BDI-II). Results: Sixty-four patients were included, of which 75% with CD and 25% with UC. The mean age was 40 ± 13.9 years and 33.1% were female. Clinical remission rate was 87.5% in CD and 75% in UC, with an endoscopic remission rate of 25% in CD and 50% in UC. The correlation between anxiety and depression symptoms was significant (p < 0.001, r = 0.73). There was no statistically significant difference in anxiety and depression scores between patients with CD and UC. There was also a statistically significant correlation of number of disease flairs with STAI and BDI-II scores was significant (STAI p = 0.023; BDI-II p = 0.017). In IBD patients, there was also a statistically significant association between STAI score (anxiety) and clinical remission, endoscopic remission and need for therapy step-up (p < 0.05). In CD patients there was a significant association between anxiety and the presence of perianal disease (p = 0.035). In UC patients, there was a significant association between anxiety and recent flair (p = 0.021), use of emergency room (p = 0.029), hospitalization (p = 0.029) and therapy step-up (p = 0.013). In this group of patients a significant association between depressive symptoms and immunosupressant or anti-TNFα therapy was seen (p = 0.009). Conclusion: In the analyzed patients there was an association of anxious and/or depressive symptoms with frequency of disease flairs and disease activity. Symptoms of anxiety and depression may have a significant impact on the quality of life of patients with IBD. Disclosure: Nothing to disclose

P0937  QUALITY OF CARE AND OUTCOMES IN A TERTIARY HOSPITAL INFLAMMATORY BOWEL DISEASE (IBD) CENTER: MONITORING AND TREATMENT ALGORITHMS AT REFERRAL AND DURING FOLLOW-UP A. Restellini1,2, S. Nene1, R. Kohlen1, L. Gonczi2, Z. Kárti2, W. Afif1, T. Bessoin1, G. Wild1, E. Seidman1, A. Bitton1, P. Lakatos1,3 1McGill University Health Centre, Montreal, Canada 2Geneva’s University Hospitals and University of Geneva, Geneva, Switzerland 3Kommennweis University, First Department of Internal Medicine, Budapest, Hungary Contact E-Mail Address: lorantgonczi@gmail.com Introduction: IBD is associated with substantial disability and impairs quality of life. Optimal management of IBD requires harmonized monitoring processes and treatment pathways. We aimed to retrospectively analyze quality of care indicators (QIs) including patient assessment strategy, monitoring, treatment decisions and outcomes at referral and during follow-up in the McGill University Health Centre (MUHC) IBD Center. Aims and Methods: We reviewed out- and inpatient records of consecutive patients seen at the MUHC IBD center between June and December 2016. Demographic variables, outpatient visits, inpatient stays including IBD related surgery, laboratory, imaging and endoscopy data, current medications and/or changes in medications, and vaccination profile were captured. Results: 1357 patients (46.8% male, 64.4% Crohn’s disease (CD), age at diagnosis: 29.8 years, age at referral: 39.3 years, duration of disease: 14.1 years) were included. At referral 49.5% of CD patients had ileocolonic, 45% complicated behavior (B2 or B3) and 23.7% perianal disease. 47.2% and 41.7% of UC patients had extensive and moderate to severe disease, respectively. Patients

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were objectively re-evaluated at referral: 68.4% underwent ileocolonoscopy, 15.7% upper GI endoscopy, 15.6% of CD patients had abdomino-pelvic MRI or CT and 23.6% abdominal US. CBC, CRP and FCAL were measured in 89.9%, 81.9% and 16.5%, respectively. Medical therapy was changed in 53.6% (active disease: 75.6%, remission: 24.4%), and 22.5% of patients started biological therapy at around referral. 12.4% of patients required hospitalization while 6% surgery at referral. During follow-up, in June-December 2016, 41.1% of patients were receiving biological therapy and 15.1% of patients were steroid dependent. An objective patient monitoring strategy was applied at the IBD center: ileocolonoscopy/colonoscopy was performed in 79% within 2 years before, and in 32% within 6 months from index visit. Biomarkers (CRP: 78%, FCAL: 37.6%); C. difficile or stool culture (18% and 17.9%) and therapeutic drug monitoring (16.3%) were performed frequently. Treatment was changed in 18%. Need for surgery (4%) and hospitalization (8%) were low, while 16.8% of patients required an IBD-related ER visit within 6 months after index visit.

**Conclusion:** Our data support that tight monitoring was applied at the MUHC Center who accessed the RAC via email were prospectively included, between June 2017 and January 2018. Time to medical appointment, resource utilization (laboratory, imaging and endoscopy), need for change in medical therapy, unplanned emergency (ER) visits or admissions 30 to 90 days after consulting the RAC were collected.

**Disclosure:** Nothing to disclose

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**P0938 BENEFITS OF IMPLEMENTING A RAPID ACCESS CLINIC IN A HIGH VOLUME INFLAMMATORY BOWEL DISEASE CENTER: ACCESS, RESOURCE UTILIZATION AND OUTCOMES**

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**Introduction:** IBD impacts on a patient’s physical health, social functioning and quality of life, contributing to the health-economic burden associated with the disease, especially in emergency situations. We aimed to prospectively measure the impact of the implementation of a rapid access clinic (RAC) at a tertiary IBD center.

**Aims and Methods:** Consecutive patients from the McGill University Health Center who accessed the RAC via email were prospectively included, between June 2017 and January 2018. Time to medical appointment, resource utilization (laboratory, imaging and endoscopy), need for change in medical therapy, unplanned emergency (ER) visits or admissions 30 to 90 days after consulting the RAC were collected.

**Results:** 173 patients (61.1% female, mean age: 38 years, CD: 64%, L: 30.9%, B2-3: 34.6%, UCE: 53.8%, biological therapy: 67.3%, previous surgery: 21%) were included. 85% of requests were considered appropriate for a RAC appointment. 65.9% of patients presented with a clinical flare. Patients were seen at the IBD clinic a median of 3 days (mean 4.7) after the request. Laboratory assessment including FCAL (52%) and CRP (80%) were performed as appropriate. Fast-track endoscopy (colonoscopy or sigmoidoscopy) was performed in 32 and 11 patients (19.8% and 6.6%), and 13 patients (7.8%) had abdominal-pelvic CT. Treatment was modified in 78 patients (48.8%). Admission was initiated in 8 patients during RAC visit. A total of 8 (4.6%) and 3 (1.7%) patients required an ER visit within 30 and 90 days after the RAC appointment, of which 2 and 1 patients had non-IBD reason for presenting at ER.

**Conclusion:** Implementation of a RAC improved healthcare delivery by avoiding unnecessary ER visits and optimizing resource utilization.

**Disclosure:** Nothing to disclose

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**P0939 FECAL CALPROTECTIN AS A SURROGATE MARKER FOR PREDICTING RELAPSE IN ADULTS WITH ULCERATIVE COLITIS: A META-ANALYSIS**

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**Introduction:** The clinical course of ulcerative colitis (UC) is featured by remission and relapse, which remains unpredictable. Recent research revealed that fecal calprotectin (FC) could predict clinical relapse for UC in patients with remission, but this role of FC has not been applied to clinical practice.

**Aims and Methods:** We carried out a comprehensive electronic search of PUBMED, WEB OF SCIENCE, EMBASE and the Cochrane Library to identify all eligible studies. Diagnostic accuracy including pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) and pooled area under the receiver operating characteristic (AUROC) was calculated using a random effects model. Sources of heterogeneity were detected by subgroup analysis. Potential factors correlated to DOR were tested by meta regression.

**Results:** 14 articles enrolling a total of 1043 patients were finally included for final calculation. Pooled sensitivity, specificity, PLR, NLR were 0.73 (95% CI: 0.67–0.77), 0.77 (95% CI: 0.74–0.80), 3.32 (95% CI: 2.30–4.79) and 0.40 (95% CI: 0.32–0.51) respectively. The area under the summary receiver-operating characteristic (SROC) curve was 0.81 and the diagnostic odds ratio was 9.29 (95% CI: 5.71–15.12). FC was more diagnostically accurate in studies using Bühlmann as FC assay (DOR = 15.08; 95% CI: 6.84–33.25) and studies with longer follow-up time (DOR = 9.61; 95% CI: 5.32–16.72) or a larger cut-off value (DOR = 11.64; 95% CI: 4.83–16.72). There was no significant correlation between any of the covariates and the DOR in the univariate meta-regression analysis.

**Conclusion:** Our study confirms the diagnostic utility of FC for the detection of UC relapse in adults. Due to its simplicity and noninvasiveness, measuring FC levels at clinical remission appears to be a reliable and reproducible indicator to predict UC relapse.

**Disclosure:** Nothing to disclose

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**P0940 GASTROINTESTINAL SYMPTOMS ARE COMMON IN U.S. PATIENTS WITH MODERATE-SEVERE PSORIASIS**

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**Introduction:** Patients with moderate-to-severe plaque psoriasis (PsO) are at increased risk of developing inflammatory bowel disease (IBD). A survey was conducted to evaluate the prevalence of gastrointestinal symptoms in PsO patients.

**Aims and Methods:** An electronic survey was available to U.S. PsO patients with data collected from Jan-Feb. 2017. Patients with moderate-to-severe plaque PsO and healthy controls (HC), with common co-morbidities allowed in both groups qualified for inclusion in the survey. Psoriasis patients were further categorized as those without recent exposure to biologic therapy (PsO-) vs those with recent (within 4 months) biologic exposure (PsO+). GI symptoms and signs, including frequency and severity, were compared across groups. CalproQuest (CPQ) scores, which have recently been proposed as a tool to identify patients with elevated fecal calprotectin levels and increased risk for IBD, were also calculated. Patients with inflammatory bowel disease (IBD), inflammatory bowel syndrome (IBS), or other gastrointestinal (GI) diagnoses with symptoms that overlap with IBD were excluded.

**Results:** Overall, 915 patients with self-reported moderate-severe PsO and 1,411 healthy controls participated. Demographics were generally comparable between

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**Abstract No:** P0940

<table>
<thead>
<tr>
<th>Psoriasis patients (PsO-)</th>
<th>Psoriasis patients + recent treatment* (PsO+)</th>
<th>Healthy controls (HC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pts</td>
<td>465</td>
<td>450</td>
</tr>
<tr>
<td>GI signs &amp; symptoms</td>
<td></td>
<td>1411</td>
</tr>
<tr>
<td>Belly Pain</td>
<td>20.6% (96) p = 0.002 vs HC p = 0.002 vs PsO+</td>
<td>36.9% (166) p = 0.002 vs HC</td>
</tr>
<tr>
<td>Full/Blated</td>
<td>37.2% (173) p = 0.002 vs HC p = 0.002 vs PsO+</td>
<td>48.4% (218) p = 0.002 vs HC</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16.3% (76) p = 0.002 vs HC p = 0.002 vs PsO+</td>
<td>29.3% (132) p = 0.002 vs HC</td>
</tr>
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<td>Mucous in stool</td>
<td>4.5% (21) p = 0.020 vs HC p = 0.317 vs PsO+</td>
<td>6.0% (27) p = 0.002 vs HC</td>
</tr>
<tr>
<td>Blood in stool</td>
<td>4.3% (20) p = 0.004 vs HC p = 0.390 vs PsO+</td>
<td>5.6% (25) p = 0.002 vs HC</td>
</tr>
</tbody>
</table>

Data reported in % (n), *recent treatment = within 4 months of biologic, p-values are comparisons between psoriasis groups and healthy controls.
groups. GI symptoms and signs were significantly more prevalent in the Po-Po- and Po-Po+ group than vs the HC group. Pain, fullness/bloating, stooling, diarrhea were more frequent in Po-Po- vs Po-Po+ groups (Table 1). A significantly greater percentage of Po-Po- and Po-Po+ patients had positive CQ scores vs HCs, with the greatest percentage of positive CQ scores in the Po-Po+ group: 9.5% in Po-Po-, 20.2% in Po-Po+. Po-Po+ vs HCs, p = 0.005.

Conclusion: GI symptoms and signs are common in patients with moderate-to-severe Po-Po, more so than in healthy controls. This suggests that physicians caring for patients with Po-Po may consider assessing for GI symptoms and signs, and monitoring inflammation with treatment of Po-Po to identify patients potentially at risk for developing IB.

Disclosure: This study was supported by Janssen Research & Development, LLC.

P0941 THE ACCURACY OF A HOME PERFORMED FAEecal CALPROTECTIN TEST IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Endoscopic examination is a gold standard in evaluation of mucosal healing, which should be the main goal in the treatment of paediatric patients with inflammatory bowel disease (IBD). However, due to clear invasive- ness, biomarkers, especially faecal calprotectin (FC), have become standard part of remission assessment.

Aims and Methods: The aim of the study was to compare accuracy for detection of endoscopic activity using a recently developed FC home test to standard ELISA assay (FC-ELISA). Finally, 102 consecutive observations from 89 paediatric patients with IBD (62 Crohn’s disease (CD) and 27 Ulcerative colitis (UC)) were included in prospective observation study. We performedly collected home test results by smartphone image evaluation from lateral flow device (Ferrynd International, Medical Affairs, Saint-Prex, Switzerland) analysed by physician and FC-ELISA in IBD patients indicated for endoscopic evaluation. We defined mucosal healing by endoscopic scores, in patients with CD by SES-CD = 2 (n = 44), in patients with UC by UCEIS = 4 (n = 27) and in patients with CD after colorectal resection (ICR) by Rutgeert’s score = 0 and without signs of colorectal involvement (n = 19). Due to multiple observations from one subject the association between mucosal healing and FC was assessed using generalized linear mixed model and linear mixed model. The sensitivity and specificity of FC-IBDoc and FC-ELISA for respective scores were calculated using cross-validated area under curve (AUC), optimal cut-off values were found. The AUCs were compared using DeLong test and regression models were compared using ANOVA.

Results: We found an association of the mucosal healing scores of the entire group both with FC-ELISA (p = 0.002) and FC-IBDoc (p = 0.012). The AUC for FC-ELISA was 0.883 (95% CI 0.807–0.960) with optimal cut-off at 136.5 ug/g, the AUC for FC-IBDoc was 0.792 (95% CI 0.688–0.895) with optimal cut-off at 140 ug/g. The accuracy of FC-ELISA was better than that of FC-IBDoc when tested by Delong test (p = 0.033). Similarly, the regression mix-model constructed using FC-ELISA as predictor was significantly better than the model using FC-IBDoc. We did not find any association with FC, neither tested by FC-ELISA nor by FC-IBDoc while measuring among subsets of patients assessed by SES-CD, UCEIS nor Rutgeert’s score. When assessing inflammation intensity using linear mix-model for subsets of observations evaluated by SES-CD we found association with FC-ELISA (β = 2.35, 95% CI 0.98–3.81), but not with FC-IBDoc. We found association of UCEIS both with FC-ELISA and FC-IBDoc (β = 0.62, 95% CI 0.37–0.85, resp. β = 0.46, 95% CI 0.19–0.74). FC-ELISA and FC-IBDoc was associated with Rutgeert’s score in subgroup of CD patients after ICR (β = 0.16, 95% CI 0.21–0.70, resp. β = 0.30, 95% CI 0.10–0.55).

Conclusion: The standard ELISA assay for FC evaluation seems to be a more reliable predictor of mucosal healing than the FC home test in paediatric IBD patients. The cut-off values for both tests were highly incongruous. The FC-IBDoc could not be used for prediction of the inflammation intensity defined by SES-CD.

Disclosure: We declare no conflict of interest. Funding: The project was supported by Ministry of Health, Czech Republic – grant No. MZV15-14255A, project No. 15-364617 and project No. 246216, and by Ministry of Health, Czech Republic – grant No. LO20064203.

P0943 DIAGNOSTIC YIELD IN THE VISUALIZATION OF CAPSULE ENDOSCOPY BY A TRAINED NURSE

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Introduction: Capsule endoscopy (CE) allows a complete, painless and noninvasive exploration of the small bowel (SB), eliminates insufflation inconveniences and allows a continuous follow-up of sedation posteriorly. The main advantage of CE is that the patient is able to return to daily activities after its intake. During the last years, endoscopy nurses have gained autonomy and acquired new roles for diagnostic purposes that were previously only reserved to the medical field. The implementation of CE has given nurses a new role in the field of endoscopy, which allows them to develop in an autonomous and secure way.

Aims and Methods: We aimed to compare the diagnostic precision of a nurse with a specific endoscopic training to a gastroenterologist trained in visualization of the small bowel by capsule endoscopy.

Validation and reliability study of diagnostic procedures in which were included all patients that were evaluated in a clinical setting at the Hospital Clinic of Barcelona with a CE for the study of the SB, for the period of June 2016 to October 2017. Capsules were visualized blindly by a capsule endoscopy trained gastroenterologist and a nurse.

Results: 103 patients were included, average age of 54.28% ± 18.5, 44.7% was male, and 55.3% female. The most common indication for CE was anemia in 52% of observations, SB cleansing was excellent, good of fair in a 6.8%, 76.7% and 16.5% respectively. The average time for visualization for the gastroenterologist and the nurse was 15.54 ± 7.05 ± 16.12 ± 6.77 min, respectively with no significant differences.

The gastroenterologist and the nurse detected a total of 532 and 644 lesions respectively, which were significant in 129 (24.25%) and 138 (20.96%) (p = ns), and no significant were 403 (75.75%) 509 (79.04%) (p < 0.001), respectively.
There was a good and statistical significant correlation between both explorers for the detection of inflammatory and non-significant findings (R = 1; p < 0.001). The sensitivity for a nurse was of 96.62% for any lesions, 100% for significant lesions and 95.53% for non-significant lesions. This nurse, acquires sensitivity and a positive predictive value (PPV) for the detection of lesions in SR by CE, being of 100% for significant lesions, and uses a similar amount of time as a CE trained gastroenterologist.

Conclusion: A specialized nurse, trained and familiarized with the pathology of the small bowel, can detect the same amount of significant lesions as a trained gastroenterologist during the exploration of CEUS. The nurse also detect more non-significant lesions that usually lack of clinical relevance.

Disclosure: Nothing to disclose

P09944 HOW TO PREDICT THE RESPONSE TO THERAPY IN CROHN’S DISEASE? - WHEN CONTRAST-ENHANCED ULTRASOUND CAN MAKE A DIFFERENCE

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Introduction: Contrast-enhanced ultrasonography (CEUS) in Crohn’s Disease (CD) allows the detection and quantification of transmural vascularization.

Aims and Methods: The aim of this study was to evaluate the CEUS as a predictor of response to immunosuppressive treatment in CD.

A retrospective study was carried out with inclusion of patients with ileal CD, undergoing ileocolonoscopy and start immunosuppressive therapy, both with an interval <8 days in relation to the CEUS. Demographic, endoscopic, clinical and analytical data were analyzed at the time of CEUS evaluation. After assessing an area of interest in the bowel wall, the time-intensity curve was determined and quantitative parameters were recorded. Subsequent therapeutic changes, complications of the disease, surgery and need for hospitalization in the first 6 months were considered as failure to therapy.

Results: Twenty-eight CD patients were included. Significant endoscopic inflammatory activity (SES-CD ≥7) was identified in 14 patients (50%).

The increase in brightness intensity, in relation to baseline, in patients with significant endoscopic activity was higher than in patients without significant endoscopic activity, 14.2 vs 4.7 x, p = 0.002.

Ten patients did not respond to the therapy (35.7%). In relation to the increase in brightness intensity, a median was higher in the group of non-responders compared to the group of responders, 15.9 x vs 8.4 x, p < 0.001.

The area on the ROC curve of the increase in brightness intensity for prediction of therapeutic failure was 0.939. For values of the ROC area >0.7, the positive and negative predictive value was 100%, 83.3%, 76.9% and 100%, respectively.

Conclusion: The CEUS proved to be a useful, non-invasive, superior to the analytical parameters in detection of ileal inflammatory activity and prediction, with an excellent accuracy the treatment failure in CD.

Disclosure: Nothing to disclose
Results: A total of 38 patients were treated with GLM, 34 (89.5%) completed treatment through W6 (full analysis set, FAS), and 29 (76.3%) completed treatment through W16. Mean age (range) was 34.6 (19–65) years; 15 (44.1%) were male. At baseline, 94.1% had moderately active disease (Mayo score 6–10) and 5.9% (N=2) severe disease; 27 (79.4%) were treated with immunosuppressants and 16 (47.1%) were taking glucocorticoids. At W6, 47.1% of patients were in clinical response and 14.7% in clinical remission; 62.1% and 37.9% at W16, respectively. At W6, ST2 levels were significantly correlated with endoscopic activity (rs=0.451, 95% CI: 0.133–0.685, p=0.0074) but not with histological activity (rs=0.252, 95% CI: −0.094 to 0.544, p=0.1506). At W16 no correlations were significant. For patients with endoscopically active (n=20) vs. inactive (n=14) UC at W6, ST2 levels were different at baseline (SD) levels were 25.0±4.1 vs. 17.2±6.8 ng/mL (p=0.0259). Changes from baseline to W6 were also different between patients with endoscopically active vs. inactive UC at W6: ST2 increase of 2.4±7.8 vs. decrease of −3.5±6.9 ng/mL (p=0.2920), respectively. The best cut-off for ST2 level at W6 to distinguish between endoscopically active vs. inactive UC at W6 was 16.9 ng/mL, with specificity = 71% and sensitivity = 85% (AUC=0.800, p=0.0001). ST2 did not correlate with FC at any timepoint (baseline, W6, W16).

Conclusion: This exploratory study shows that ST2 may be a surrogate biomarker of UC disease activity and therapeutic response. Disclosure: Patricia Machado is an employee of MSD Portugal and George Philip of Merck & Co., Inc., Kenilworth, NJ, USA. IsaBella Redondo was an employee of MSD Portugal at the time the study was conducted.

References
as mucosal healing. However, many patients opt out of endoscopic evaluation. Blood pressure, pain, anxiety, embarrassment, and logistics are factors affecting adherence.

**Aims and Methods:** The aim of this study was to investigate the influence of deep sedation on the attitude towards colonoscopic monitoring in patients with IBD. A prospective, randomized clinical trial of deep nurse administered propofol sedation (NAP5) versus moderate midazolam and fentanyl sedation. Patients provided a satisfaction score prior to discharge. Patient aged >17 years with a strong suspicion or established diagnosis of IBD and scheduled colonoscopy were eligible for the study. Exclusion criteria: ASA class > II, pregnancy, non-compliant with fasting, a history of complicated anaesthesia or inability to complete satisfaction survey.

**Results:** A total of 126 patients were randomized to deep (n = 62) or moderate sedation (n = 64). The deep sedation group was sedated significantly more to their liking (p = 0.001), experienced less pain (5 = no pain, 1 worst pain) (4.97 vs 3.42, p < 0.001), and rated the current experience better than prior sedations and higher than the moderate sedation group, (4.30 vs 3.65, p = 0.001). Of note, the deep sedation group were more likely to accept frequent endoscopies (4.33 vs 3.55, p = 0.001), and scored higher on Overall Satisfaction score (4.94 vs 4.04, p = 0.001) than the moderate sedation group. The results were consistent within a week after the procedure.

**Conclusion:** Patients with IBD significantly favor deep sedation over moderate sedation. Pain and previous experience with moderate or deep sedation are important contributing factors. Availability of deep propofol sedation may facilitate patient adherence to endoscopy-based monitoring programmes, including drug adjustment and cancer surveillance.

**Disclosure:** Nothing to disclose

**Abstract No:** P0951

**LOW HAEMOGLOBIN DENSITY (LHD%) AS A NEW BIOMARKER FOR THE DETECTION OF IRON DEFICIENCY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

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**Introduction:** In the absence of a feasible, non-invasive gold standard, iron deficiency anaemia (IDA) is best measured by the use of multiple indicators. However, the choice of an appropriate single iron biomarker to replace the multiple-criteria model for IDA screening at the population level continues to be debated. Recently, low haemoglobin density (LHD%) from Coulter counters has been suggested as a useful tool to detect iron deficiency.1 Its diagnostic performance in a population of patients with inflammatory bowel disease (IBD) has not yet been evaluated. Using the mathematical sigmoid transformation (LHD% = 100 × (1/(1 + (1.8 [30-MCHC]))) this study investigated the reliability of LHD% for the assessment of iron status in iron deficiency anaemia (IDA), anaemia of chronic inflammation (ACI) and mixed IDA/ACI.

**Aims and Methods:** The study population consisted of 88 patients with IBD (mean age 39.09 ±13.12 years, 78.4% female) who consecutively attended the Interdisciplinary Crohn Colitis Centre Rhein-Main, Frankfurt/Main for routine endoscopy in October 2014 and September 2016. In addition to LHD%, blood count, transferrin saturation (TSAT), serum ferritin (SF), and C-reactive protein (CRP) were determined by routine assays. Patients with anaemia were classified as having IDA if active inflammation (CRP >5mg/L) was absent, TSAT <20% and ferritin level <30μg/L; patients were classified as having ACI if active inflammation was present (CRP ≥5mg/L), TSAT <20% and ferritin level ≥100μg/L.2 Receiver operator characteristic (ROC) curves were constructed to evaluate the diagnostic performance of LHD%.

**Results:** In ferropoenic IBD patients, applying a cut-off of 3.7%, LHD% values were not statistically different in patients with IDA compared to the IDA/ACI group (17.80 vs. 23.52%; p = 0.834). Significant differences were not observed between patients with ACI (LHD 12.52%) compared with the IDA/ACI group (LHD 23.55%, p = 0.268). ROC analysis for LHD% in the detection of iron deficiency showed the following: Area under the curve 0.927; cut off 3.7%, sensitivity 86%, specificity 85%. Haematological and biochemical parameters of the patients are shown in Table 1.

**Conclusion:** These results clearly demonstrate that LHD% is a reliable biomarker for the detection of iron deficiency in IBD patients with anaemia regardless of whether inflammation is present. Our findings indicate that LHD can provide added value in diagnosing iron deficiency in anaemic IBD patients.

**Disclosure:** Nothing to disclose

**References**


Aims and Methods: We retrospectively analyzed clinical data from 47 patients with ulceration in UC for whom serum procalcin and CMV study were measured between January 2017 and December 2017. Diagnosis of CMV reactivation was either CMV IgM, CMV antigenemia, blood CMV PCR, tissue CMV PCR or CMV immunohistochemical stain were positive. Other infectious conditions were excluded.

Results: Positive CMV reactivation among them were observed in 28 patients (59.6%). There was no difference in the sex, steroid, immunomodulator, anti-TNF agents, and disease extension between the two groups. The mean serum PCT levels in positive CMV reactivation and negative CMV reactivation were 0.127 ± 0.29 mg/mL and 1.510 ± 3.53 ng/mL respectively (p = 0.10). Also, there was no difference in the white blood cell, neutrophil, lymphocyte, hemoglobin, platelet, ESR, CRP, albumin and Fecal calprotectin between two groups.

Conclusion: Serum PCT was not correlated with CMV reactivation in exacerbation of ulcerative colitis patients.

Disclosure: Nothing to disclose

P0956 SYSTEMATIC REVIEW: PREDICTING THE DEVELOPMENT OF PSYCHOLOGICAL MORBIDITY IN INFLAMMATORY BOWEL DISEASE
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Introduction: Psychological morbidity (anxiety and/or depression) in inflammatory bowel disease (IBD) is common (reported prevalence of up to 50% in patients with IBD) and has significant personal and economic costs to society. Prediction of psychological morbidity in IBD may allow for early intervention, but predictive factors are unclear.

Aims and Methods: To undertake a systematic literature review to determine predictors of the development of psychological morbidity in patients with IBD. Electronic searches for “psychological morbidity” according to DMS-IV, “prediction” and “IBD” in the MEDLINE, PsychInfo and Web of Science databases for studies published from 1997 to February 2018. Studies were included if they had both baseline (T1) and follow data (T2) to allow differentiation between factors associated with psychological morbidity.

Results: 1129 studies were identified, of which seven met the inclusion criteria. Five of the six studies focused on pred$i's$or$'s$$s$ with only one study examining the anxiety transiently. The median age of patients was 37 years (range 11.8–48) and on average 9% of participants were female (SD 18.2). Longitudinal follow-up periods varied considerably (median 12 months (range 6–60)). Statistical methods were inconsistent across studies and included regression models, cross-legged panel models and ANCOVAs. Factors predicting psychological morbidity included: female gender (OR 1.7; 95% CI 1.61–2.71); additional comorbidity (≥2 chronic illness alongside IBD) (OR 4.31; 95% CI 2.28–6.57); surgical intervention (OR 1.9; 95% CI 1.15–3.13) and immunosuppressant use (OR 1.56; 95% CI 1.03–2.38). Predictive psychological factors included: parental stress (r-change = 0.03, F(1,38)= 35.6, p < 0.05); attachment anxiety (r = 0.61, P<0.001); psychological thriving (r = −0.37, p < 0.01) and gratitude (r = −0.43, P<0.01). Factors with an inverse relationship to the development of morbidity were protective, for example higher levels of gratitude reduced the likelihood of developing psychological morbidity.

Conclusion: Psychological morbidity in IBD may be predicted by disease-related and psychological factors, potentially allowing earlier intervention and reducing personal and economic costs. Further longitudinal data from large IBD cohorts are required to determine additional predictive factors rather than associations. Development and validation of a predictive tool for the development of psychological morbidity in IBD would benefit patients and health care professionals.

Disclosure: Nothing to disclose

P0957 ULTRASONOGRAPHIC FINDINGS ASSOCIATED WITH A HIGHER RISK OF SURGERY IN PATIENTS WITH STRICTURING CROHN’S DISEASE
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Introduction: In Strictures related to Inflammatory Bowel Disease (SCD), strictures have traditionally been classified as inflammatory or fibrotic: the first have been thought to respond to medical treatment and the latter have usually been associated with the need for surgery. Recent papers establish that in most cases these strictures appear to have mixed characteristics, and that even in inflammatory strictures medical treatment doesn’t always avoid the risk of critical stenosis of the bowel lumen, thus resulting in surgery too. In our study we tried to identify ultrasonographic findings in SCD that may associate with a higher risk of surgery and allow us to make early choices regarding treatment election in this specific cohort of patients.

Aims and Methods: We conducted a case-control study at our institution, selecting 70 patients diagnosed with SCD that underwent ultrasonography (US) during follow up from 2013 to 2017 and then divided them into groups depending on...
on the need for surgery: surgery group and control group. Main target was evaluating ultrasonicographic findings associated with a higher proportion of surgery. US features analyzed are described in results. We used Student’s T and Chi² tests for quantitative and qualitative variables comparison respectively, and performed multivariable analysis using logistic regression. We considered statistical significance a p value of <0.05.

Results: Out of 70 patients, 24 needed surgery because of obstructive symptoms (34.29%), while 46 remained surgery-free at the time of the analysis (65.71%). Baseline characteristics of both groups can be found in table 1. Median time from US to surgery was 71.5 days (IQR range [12–300]). Ileocolic resection was performed in 16 patients (66.6%) while the rest underwent ileocolic plus other kind of bowel resection (8 patients, 33.3%). When comparing US findings, the following ones reached statistical significance: stricture doppler activity (control group: mean 0.86 SD 0.34 vs surgery group: mean 2.08 SD 0.88, p < 0.001), presence of polyps (21, 46.8%), presence of ulcers (11, 24.3%), and presence of wall thickening (10, 21.7%). When performing multivariable analysis, these data appear to have clinical significance regarding risk of surgery but they didn’t reach statistical significance probably due to lack of sample size. Data obtained applying logistic regression are: doppler activity (OR = 1.14 IC95% [0.79–1.64], p = 0.46), enterocolic fistula (OR = 0.43, IC95% [0.7–40], p = 0.09), associated abscess (OR = 7.9, IC95% [0.5–112], p = 0.69). Bowel wall thickness, presence of pre-stenotic dilation and involvement of mesenteric fat did not show clinical or statistical significant association with the risk of surgery (p = 0.20, p = 0.517 and p = 0.25, respectively).

Conclusion: In our experience, transmural complications detected in a follow-up US of patients with SCD are associated with a higher risk of surgery and should be taken into account when deciding the best choice of treatment, wether it is a possible therapeutic escalation of medical therapy or early surgical resection. These data must be validated in prospective studies that confirm our findings.

References

P0959: NBI FINDINGS IN MICROSCOPIC COLITIS AND UTILITY OF NBI GUIDANCE ON YIELD OF COLONIC BIOPSY FOR ITS DIAGNOSIS

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Introduction: Microscopic colitis (MC) is an important cause of chronic diarrhea in adults. Histopathology is the gold standard for diagnosis but colonic biopsy has a variable yield. Endoscopically, the mucosa is normal, often leading to delayed diagnosis As the mucosa appear normal on endoscopy in most cases, there is no specific area to target for biopsy.

Aims and Methods: The aim of the current study was to evaluate the ileocolonic mucosa in patients with suspected MC with narrow band imaging (NBI) and to describe the narrow band imaging findings (NBI), in patients with microscopic colitis. We also aimed to study the utility of NBI guided biopsy for improving the diagnostic yield of colonic biopsies by comparing yield of NBI-guided biopsy with the yield of white light colonoscopy-guided biopsy for the diagnosis of microscopic colitis.

Materials and methods: We prospectively recruited patients aged more than 18 years with typical macroscopic or microscopic colitis during the period between 2016 and 2017. Patients with malignancy, coeliac disease, small intestinal bacterial overgrowth, inflammatory bowel disease, gastrointestinal tuberculosis and severe comorbidities were excluded. Patients underwent blood investigations, imaging and characteristic enhanced computed tomography abdomen (if indicated), stool analysis and hydrogen breath tests using glucose, lactose and lactulose. All patients underwent colonoscopy with ileal intubation if possible. Patients underwent both HDWLE and NBI during the same setting by the same observer. NBI finding were recorded in a predefined format. Four pieces of biopsies were taken during white light examination (WLE) from caecum/ascending colon and four pieces from descending colon/sigmoid colon. Additional four pieces of biopsies were taken during NBI examination from same colonic segments during NBI examination. Each set of biopsies was collected in separate containers and labelled for further histopathological processing and examination by an expert gastrointestinal histopathologist. The diagnosis of MC was made using statements of the European Microscopic Colitis Group 2017.

Results: A total of 53 patients suspected to have microscopic colitis were enrolled in the study, and a final diagnosis of MC was established in 43 [mean age 45.83 (±15.92) males – 27]. Out of 43 cases with MC, 25(58.5%) patients had collagenous colitis (CC), 14 (32.5%) had lymphocytic colitis (LC) and 4(9.4%) had mixed picture fulfilling criteria for both. The WLE findings were normal mucosa in all patients. NBI showed type 1 pit pattern in all patients with MC. Vascular pattern was regular pattern in all patients. Mucosal pattern was honey comb type in all patients. A patterned focal area of abnormal vascularity with focally obscure pit pattern was found to be more common in cases than controls [38(1,39%); 5(12.5%) (p = 0.052). In the group of CC, NBI guided biopsy yielded the diagnosis in 88% (22 out of 25 patients) whereas white light guided biopsy yielded the diagnosis in 75% (20 cases) (100%) (p = 0.24). In the group of lymphocytic colitis, NBI guided biopsy yielded the diagnosis in 92% (13 out of 14 patients) whereas white light guided biopsy yielded the diagnosis in all 14 cases (100%) (p = 0.89).

Conclusion: This prospective study describes the NBI findings of colon in patients with MC and provides a unique sign of focal area of abnormal vascularity with focally obscure pit pattern to be more common in MC. However, there was no significant difference in yield of NBI-guided biopsy compared to white light colonoscopy-guided biopsy for the diagnosis of MC.

Disclosure: Nothing to disclose

P0960: THE PREVALENCE OF INFLAMMATORY BOWEL DISEASE (IBD) IN PATIENTS WITH HIDRADENITIS SUPPURATIVA

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Introduction: Hidradenitis suppurativa (HS) is an inflammatory, recurrent skin disease of hair follicle, that mainly presents in axillary, inguinal and anogenital regions. Clinically, the condition can imitate the cutaneous Crohn’s disease and it can co-exist with inflammatory bowel diseases (IBD). HS and IBD have many similarities in clinical appearance, pathogenesis and etiology.

Aims and Methods: The purpose of our study was to determine the prevalence and characteristic of inflammatory bowel disease in patients diagnosed with hidradenitis suppurativa by comparing clinical signs, endoscopy, histology and laboratory results.

Results: Thirty-nine patients (64% male; mean age: 35.77; median: 34) were seen with diagnosed hidradenitis suppurativa, whom underwent screening colonoscopy. By the endoscopic and histological results, we made two patient-groups (HS and HS+IBD) and compare the epidemiological, clinical, laboratory data.

Conclusion: Based on our data, the appearance of IBD correlated with younger age, lower body mass index, severe HS activity, penetrating form. In the future, it may be justified to screen HS patients for IBD.

Disclosure: Nothing to disclose

P0961: BASALINE ALBUMIN LEVEL IS NOT A SIGNIFICANT PREDICTOR OF TOFACITINIB EFFICACY IN PATIENTS WITH ULCERATIVE COLITIS: RESULTS OF MULTIVARIATE EXPOSURE-RESPONSE ANALYSIS

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Introduction: Tofacitinib is a Janus kinase inhibitor approved for moderate to severe ulcerative colitis and Crohn’s disease. We hypothesized that baseline albumin level (BAL) may be a significant predictor of tofacitinib efficacy in patients with ulcerative colitis.
In contrast to biologic therapies, tofacitinib clearance was not related to albumin concentration, as shown in multivariate analyses. BALB concentration was evaluated as a covariate in exposure-response models. BALB concentration was evaluated as a covariate in exposure-response models. The effect of BALB related to efficacy endpoints in P3 induction and maintenance studies was evaluated in a multivariate analysis. Regression analysis showed that BALB concentration was not statistically significant and did not include in the final model. Primary endpoints for induction and maintenance studies were remission based on central read at Week 8 and 52, respectively. Multivariate analysis showed no statistically significant correlation between BALB and efficacy endpoints in ER analysis after accounting for other significant predictors of remission. Baseline albumin concentration was not related to efficacy endpoints. As shown in multivariate analyses, BALB had no effect on induction or maintenance efficacy endpoints, and therefore may not be informative to tofacitinib dosing decisions. In contrast to biologic therapies, tofacitinib clearance was not related to albumin concentration. As shown in multivariate analyses, BALB had no effect on induction or maintenance efficacy endpoints, and therefore may not be informative to tofacitinib dosing decisions.

References

P0962 EFFICACY AND SAFETY OF GASTRO-RESISTANT PHOSPHATIDYLCHOLINE (LT-02) FOR MAINTENANCE OF REMISSION IN PATIENTS WITH ULCERATIVE COLITIS INITIALLY REFRACTORY TO MESALAZINE: A RANDOMISED, DOUBLE-BLIND, DOUBLE-DUMMY PLACEBO-CONTROLLED STUDY (PCG-4)

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Abstract No: P0962

Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). We evaluated the effect of baseline albumin (BALB) on tofacitinib pharmacokinetics (PK) and efficacy. Four randomised placebo-controlled studies of tofacitinib in pts with moderate to severe UC were included in PK analyses: one phase (P) 2 study (A3921063, NCT00787202) and three P3 studies (OCTAVE Induction 1 & 2, NCT01465763 & NCT01458951; and OCTAVE Sustain, NCT01458574). The base PK model was one-compartmental disposition with covariates for BALB, evaluated as a potential predictor for apparent oral clearance (CL/F). The effect of BALB related to efficacy endpoints in P3 induction and maintenance studies was evaluated in a multivariate analysis. Results: 1096 pts were included in the PK analysis: 641 males and 455 females; median age: 40 years. Mean (standard deviation) BALB was 4.18 g/dL (0.39), range 2.1–5.4 g/dL. In the population PK (popPK) model, BALB was evaluated as a predictor of individual CL/F, showing no statistically significant correlation, so was not included in the final popPK model. BALB concentration was evaluated as a covariate in exposure-response (ER) efficacy analyses, and was shown by stepwise covariate modelling to be non-significant, so was not included in the final ER model. Primary endpoints for induction and maintenance studies were remission based on central read at Week 8 and 52, respectively. Multivariate analysis showed no statistically significant correlation between BALB and efficacy endpoints in ER analysis after accounting for other significant predictors of remission such as baseline Mayo score. Conclusion: In contrast to biologic therapies, 1–3 tofacitinib clearance was not related to albumin concentration. As shown in multivariate analyses, BALB had no effect on induction or maintenance efficacy endpoints, and therefore may not be informative to tofacitinib dosing decisions.

Disclosure: GL Richtenstein has received research support from Celgene, Janssen, Pfizer Inc, Salix/Valeant, Santarus/Receptos, Shire, Takeda, UCB; consultancy fees from Abbott/AbbVie, Actavis, Alavan, Celgene, Cellectixis, Ferring, Gilead, Hospira, Janssen, Luitpold/American Rgent, Pfizer Inc, Prometheus, Romark, Salix/Valeant, Santarus/Receptos, Shire, Takeda, UCB; and honoraria from Ironwood, Luitpold/American Rgent, Merck, Romark; A Tinsley has received consultancy and lecture fees from AbbVie, X Roblin has received lecture fees from AbbVie, Ferring, Janssen, MSD, Pfizer Inc, Takeda, Theradis; T Hisamatsu has received lecture fees from AbbVie, Celgene, EA Pharma, Janssen, JIMRO, Kyorin, Mitsubishi Tanabe, Mochida, Pfizer Japan Inc, Takeda; and research support from Abbott, Asahi Kasai, Astellas, Daichi Sankyo, EA Pharma, JIMRO, Kyorin, Mochida, Otsuka; Pfizer Japan Inc, Takeda, Zeria; C Yong, K Tsikos, H Zhang, A Mukherjee and C Su are Pfizer Inc employees and shareholders; S Tsuchiwata is an employee of Pfizer Japan Inc; DT Robin has received research support from AbbVie, Genentech, Janssen, Takeda, UCB; and consultancy fees from AbbVie, Amgen, Janssen, Pfizer Inc, Takeda, UCB.

Primary Endpoint
Number (%) of patients relapse-free and not a treatment failure after 48 weeks
Subgroup analyses: Number (%) of patients relapse-free and not a treatment failure after 48 weeks
by Criterion of Depth of Remission at baseline of PCG-2 [n/N (%)]:
Primary and secondary efficacy endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>LT-02 1.6 g BID (N = 75)</th>
<th>Placebo (N = 37)</th>
<th>Mesalazine 0.5 g TID (N = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint</td>
<td>37 (49.3%)</td>
<td>16 (43.2%)</td>
<td>19 (50.0%)</td>
</tr>
<tr>
<td>Number (%) of patients relapse-free and not a treatment failure after 48 weeks</td>
<td>24/43 (55.8%)</td>
<td>9/24 (45.8%)</td>
<td>12/22 (54.8%)</td>
</tr>
<tr>
<td>by Criterion of Depth of Remission at baseline of PCG-2 [n/N (%)]</td>
<td>13/32 (40.6%)</td>
<td>5/13 (38.5%)</td>
<td>7/16 (43.8%)</td>
</tr>
<tr>
<td>Left-sided</td>
<td>2/2 (100%)</td>
<td>0/0 (0%)</td>
<td>0/0 (0%)</td>
</tr>
<tr>
<td>Extended</td>
<td>15/32 (46.9%)</td>
<td>7/17 (41.2%)</td>
<td>5/13 (38.5%)</td>
</tr>
<tr>
<td>Secondary endpoints:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time in Study, in days: Mean (SD)</td>
<td>231.7 (134.7)</td>
<td>183.4 (144.2)</td>
<td>214.4 (136.8)</td>
</tr>
<tr>
<td>Time to Clinical Relapse or Discontinuation, in days: Median [95% CI]</td>
<td>183.4 (144.2)</td>
<td>214.4 (136.8)</td>
<td></td>
</tr>
</tbody>
</table>

References
percentage of patients being relapse-free with relapse defined as a rectal bleeding score of ≥1 and a mucosal appearance score of ≥2 of the mDAI scores and not a treatment failure defined as premature withdrawal (whatever the reason) after 48 weeks.

Due to premature recruitment stop of PCG-2 only 150 patients of 400 were recruited (whatever the reason) after 48 weeks.

Aims and Methods: Reflect is a multicenter, prospective, observational study, which aimed to describe in real-life the treatment effectiveness and the characteristics of patient (pts) treated with CT-P13. Inclusion criteria were pts (≥ 5 yrs-old) with Crohn’s Disease (CD), Ulcerative Colitis (UC), rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis, treated with CT-P13. Both IFX naive pts (IFXn) and pts having switched from IFX originator to CT-P13 (IFXs) were included in the study. Inclusion criteria were pts (≥ 5 yrs-old) with Crohn’s disease (CD) or ulcerative colitis (UC), who were previously failed to anti-tumor necrosis factor (TNF) therapy. Between August 2017 and April 2018, a total of 34 patients with CD (n = 21) or UC (n = 13) received an induction therapy with VDZ at the Asan Medical Center, Seoul, Korea and were prospectively enrolled in the ASAN VDZ Registry, Of those, patients who received three doses of VDZ (week 0, 2, and 6) and were evaluated at week 14 were analyzed. The co-primary outcomes were corticosteroid-free clinical remission (both for CD and UC) and endoscopic remission/ response (for UC) at week 14. The secondary outcomes were corticosteroid-free clinical response, clinical remission/ response, and safety (both for CD and UC).

Results: A total of 23 patients were enrolled (CD, 13 [56.5%]; male, 16 [69.6%]; mean age, 38 yrs; range, 18–65 yrs; median disease duration, 8.5 yrs [range, 0.7–23]). Thirteen patients (56.5%) previously had experienced failure to one anti-TNF agent and 10 patients to two anti-TNF agents (43.5%). Corticosteroid-free clinical remission rates in CD and UC patients were 22.2% and 10%, respectively (Table 1). In patients with UC, endoscopic remission and response rates were 10% and 20%, respectively (Table 1). Corticosteroid-free clinical response rates were 44.4% for CD patients and 30% for UC patients, respectively (Table 1). Clinical remission/ response rates were 33.3%; 55.6% for CD patients and 10%/ 40% for UC patients, respectively (Table 1). In patients with CD, median Harvey-Bradshaw index, leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased at week 14 compared with the baseline values (p = 0.28, P = 0.17, P = 0.79, and P = 0.43, respectively). In patients with UC, median Mayo score was significantly decreased (p = 0.003). However, median leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased at week 14 compared with the baseline values (p = 0.28, P = 0.17, P = 0.79, and P = 0.43, respectively). In patients with UC, median Mayo score was significantly decreased (p = 0.003). However, median leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased (p = 0.38, P = 0.75, and P = 0.28, respectively). Nasopharyngitis was the most common adverse events. IBD exacerbation was observed in 4 patients (17.4%) with IBD-related admissions in 2 patients (8.7%).

Conclusion: In Korean IBD patients with prior failures to anti-TNF therapy, VDZ induction therapy may be effective with acceptable safety profile. Further long-term follow-up studies with larger number of patients are required to prove the effectiveness and safety of VDZ.

Disclosure: Nothing to disclose

Disclosure: This research was sponsored by Pfizer. YB and SN received remuneration for their services as a member of the Steering Committee for ReFLECT. YB has received consulting fees from Abbvie, Biogaran, Boehringer Ingelheim, Ferring, Hospira, Janssen, MSD, Norgine, Pfizer, Roche, Sanofi, Shire, Takeda, UCB, lecture fees from Abbvie, Ferring, Janssen, Mayofi Spindler, MSD, Pfizer, Takeda and MSD, research grant support from Pfizer and Takeda. SN has received fees from Takeda, Pfizer, Abbvie, MSD, Tillotts, Ferring, Novartis, Norgine, Janssen, HAC pharma. YB has received consulting fees from Abbvie, Biogaran, Boehringer Ingelheim, Ferring, Hospira, Janssen, MSD, Norgine, Pfizer, Roche, Sanofi, Shire, Takeda, UCB, lecture fees from Abbvie, Ferring, Janssen, Mayofi Spindler, MSD, Pfizer, Takeda and MSD, research grant support from Pfizer and Takeda. SN has received fees from Takeda, Pfizer, Abbvie, MSD, Tillotts, Ferring, Novartis, Norgine, Janssen, HAC pharma.

P0964 REAL-LIFE EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB AS INDUCTION TREATMENT FOR KOREAN IBD PATIENTS IN WHOM ANTI-TNF TREATMENT FAILED: THE FIRST ASIAN PROSPECTIVE COHORT STUDY


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Introduction: Vedolizumab (VDZ) is a gut-selective monoclonal antibody blocking α4β7 integrin, which can be effective for patients with inflammatory bowel disease (IBD). Although several studies have reported the real-world experiences of VDZ in Western patients, no study has been reported in Asian IBD patients.

Aims and Methods: We aimed to investigate the clinical effectiveness and safety of VDZ as an induction therapy for Korean patients with Crohn’s disease (CD) or ulcerative colitis (UC), who were previously failed to anti-tumor necrosis factor (TNF) therapy. Between August 2017 and April 2018, a total of 34 patients with CD (n = 21) or UC (n = 13) received an induction therapy with VDZ at the Asan Medical Center, Seoul, Korea and were prospectively enrolled in the ASAN VDZ Registry. Of those, patients who received three doses of VDZ (week 0, 2, and 6) and were evaluated at week 14 were analyzed. The co-primary outcomes were corticosteroid-free clinical remission (both for CD and UC) and endoscopic remission/ response (for UC) at week 14. The secondary outcomes were corticosteroid-free clinical response, clinical remission/ response, and safety (both for CD and UC).

Results: A total of 23 patients were enrolled (CD, 13 [56.5%]; male, 16 [69.6%]; mean age, 38 yrs; range, 18–65 yrs; median disease duration, 8.5 yrs [range, 0.7–23]). Thirteen patients (56.5%) previously had experienced failure to one anti-TNF agent and 10 patients to two anti-TNF agents (43.5%). Corticosteroid-free clinical remission rates in CD and UC patients were 22.2% and 10%, respectively (Table 1). In patients with UC, endoscopic remission and response rates were 10% and 20%, respectively (Table 1). Corticosteroid-free clinical response rates were 44.4% for CD patients and 30% for UC patients, respectively (Table 1). Clinical remission/ response rates were 33.3%; 55.6% for CD patients and 10%/ 40% for UC patients, respectively (Table 1). In patients with CD, median Harvey-Bradshaw index, leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased at week 14 compared with the baseline values (p = 0.28, P = 0.17, P = 0.79, and P = 0.43, respectively). In patients with UC, median Mayo score was significantly decreased (p = 0.003). However, median leukocyte count, C-reactive protein level, and fecal calprotectin level were not significantly decreased (p = 0.38, P = 0.75, and P = 0.28, respectively). Nasopharyngitis was the most common adverse events. IBD exacerbation was observed in 4 patients (17.4%) with IBD-related admissions in 2 patients (8.7%).

Conclusion: In Korean IBD patients with prior failures to anti-TNF therapy, VDZ induction therapy may be effective with acceptable safety profile. Further long-term follow-up studies with larger number of patients are required to prove the effectiveness and safety of VDZ.

Disclosure: Nothing to disclose

Disclosure: Nothing to disclose

P0965 IMPROVEMENT IN PHYSICIAN’S GLOBAL ASSESSMENT WITHIN 2 WEEKS IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH TOFACITINIB


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Introduction: Tofacitinib is an oral, small molecule Janus kinase inhibitor that is being investigated for ulcerative colitis (UC). OCTAVE Induction 1 & 2 (NCCT1405673 & NCCT1405891) were identical, randomised, double-blind, placebo-controlled Phase 3 trials in adult patients with moderately to severely active UC who had failed, or were intolerant to, steroids, immunomodulators or tumour necrosis factor inhibitors.1 Rapid onset of tofacitinib efficacy with
significant improvements in patient-reported symptoms (Mayo stool frequency and rectal bleeding subscores) was observed within 3 days. 

Aims and Methods: The Mayo score is a combination of four subscores including the Physician’s Global Assessment (PGA), which comprises the daily record of abdominal discomfort, and other observations such as physical findings and the patient’s performance status. Here, we evaluate the time course of improvement in PGA in patients with UC following induction therapy with tofacitinib. PGA subscores of patients who received placebo or tofacitinib 10 mg twice daily (BID) for 8 weeks in the OCTAVE Induction 1 & 2 studies were collected at baseline, and at Weeks 2, 4 and 8 of the blinded treatment period. Comparisons between groups were made using stratified Cochran-Mantel-Haenszel chi-square test.

Results: A total of 905 patients received tofacitinib 10 mg BID (mean age 47.8 years; 59.6% male) and 284 patients received placebo (mean age 41.1 years; 56.4% male). At baseline, the mean total Mayo score in both placebo and tofacitinib groups was 9.0; the mean partial Mayo score (total Mayo score excluding endoscopic subscore) in both treatment groups was 6.4. By Week 8, significantly more patients treated with tofacitinib vs placebo achieved a PGA subscore of 0 or 1 (41.3% vs 27.4%; p < 0.001). A greater proportion of tofacitinib-treated patients had a PGA point from baseline compared with placebo patients at Week 2 (52% vs 37.6%; p < 0.001). From Week 2 to Week 8, differences between tofacitinib-treated and placebo-treated patients increased for all three PGA subscores analysed (p < 0.01 for all comparisons).

Conclusion: In these two randomised trials in patients with UC, treatment with tofacitinib was associated with a significant improvement in the PGA scores analysed (p < 0.01 for all comparisons). By Week 2, 10.3% of patients treated with tofacitinib, compared with 5.2% of placebo-treated patients, achieved a PGA subscore of 0 or 1 (41.3% vs 27.4%; p < 0.001). A greater proportion of tofacitinib-treated patients had a PGA point from baseline compared with placebo patients at Week 2 (52% vs 37.6%; p < 0.001). From Week 2 to Week 8, differences between tofacitinib-treated and placebo-treated patients increased for all three PGA subscores analysed (p < 0.01 for all comparisons).

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.

Table. Summary of PGA subscores in OCTAVE Induction 1 & 2

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Tofacitinib 10 mg BID</th>
<th>Difference from placebo, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA subscore of 0, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>8 (3.4)</td>
<td>93 (10.3)</td>
</tr>
<tr>
<td>Week 4</td>
<td>18 (7.7)</td>
<td>149 (16.5)</td>
</tr>
<tr>
<td>Week 8</td>
<td>20 (8.5)</td>
<td>188 (20.8)</td>
</tr>
<tr>
<td>PGA subscore of 0 or 1, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>64 (27.4)</td>
<td>374 (41.3)</td>
</tr>
<tr>
<td>Week 4</td>
<td>87 (37.2)</td>
<td>511 (56.5)</td>
</tr>
<tr>
<td>Week 8</td>
<td>73 (31.2)</td>
<td>507 (56.0)</td>
</tr>
<tr>
<td>Reduction of ≥1 point from baseline PGA, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>88 (37.6)</td>
<td>471 (52.0)</td>
</tr>
<tr>
<td>Week 4</td>
<td>121 (51.7)</td>
<td>615 (68.0)</td>
</tr>
<tr>
<td>Week 8</td>
<td>95 (40.6)</td>
<td>575 (63.5)</td>
</tr>
</tbody>
</table>

Table 1. Summary of PGA subscores in OCTAVE Induction 1 & 2

**p < 0.01; ***p < 0.001 vs placebo based on Cochran-Mantel-Haenszel chi-square test; Data are full analysis set. BID, twice daily; CI, confidence interval; N, number of evaluable patients; n, number of patients; PGA, Physician’s Global Assessment.

Introduction: ABP 501 (AMGEVITA®; adalimumab) is an approved biosimilar to adalimumab (Humira®), a fully human recombinant monomonal antibody. Amgen validated separate assays to independently detect ADAs against ABP 501 and adalimumab (Humira®) and to determine ADA positivity among patients with rheumatoid arthritis and psoriatic arthritis in two pivotal Phase 3 studies.

Aims and Methods: All protocol-defined antibody samples collected from drug-exposed subjects, irrespective of treatment group, were tested for binding antibodies against ABP 501 and adalimumab RP using a validated electrochemiluminescence-based assay. Binding ADA magnitude was expressed as signal-to-noise (S/N), defined as the mean signal of the study sample divided by the mean signal of the negative control analysed on the same plate. Samples positive for binding ADAs were then tested in a TNFα-target binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay. Validated assay parameters for both binding and neutralizing assays such as a 20% cut point, sensitivity, precision, and drug tolerance for each assay were highly similar. Correlation of binding and neutralizing antibody results (S/N or titre) between ABP 501 and adalimumab RP assays was evaluated using the Pearson’s correlation coefficient. Concordance of antibody results (positive/negative) was evaluated using the kappa statistic.

Results: Irrespective of treatment group, the binding ADA results for ABP 501 and adalimumab RP assays correlated well, with a Pearson correlation coefficient > 0.950 and concordance measure of (kappa > 0.860). In a small subset of samples that were not concordant, the distribution of sample reactivity was detected equally across assays. The magnitude of ADAs was at or near the assay cut point, indicating low potential of clinical impact. Furthermore, neutralizing antibody titre results correlated well between ABP 501 and adalimumab RP assays with a Pearson correlation coefficient > 0.780 and strong concordance (kappa > 0.884).

Conclusion: No meaningful differences were observed in the detection of binding and neutralizing ADAs in the different ADA assays, providing evidence of high similarity between ABP 501 and adalimumab RP.

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.
Results: Baseline patient characteristics were comparable between the two groups (mean age 38 ± 13 years; 55% men). The total number of patients, 43% represented a phenotype considered to be severe (fistulizing lesions, anorectal lesions...). Median follow-up was of 61 months, or a little over 5 years. A total of 145 dilations were performed on 104 strictures, and 113 concerned secondary anastomotic strictures (77.9%). Technical success was obtained in 117 dilations (92.9%), and only one immediate complication, of the haemorrhagic type, was identified in the course of the endoscopy. There were 10 delayed complications (6.9%), represented by 6 perforations, 2 haemorrhagic events and 2 cases of bacteriemia with sterile episodes. During our follow-up, 71 patients (61%) carrying out an endoscopy only endoscopically. Of these patients, 52 (71.2%) required only one dilation session. The remaining 33 patients (31.7%) had surgery within a median delay of 13 months in relation to the first dilation. The presence of another stenosing lesion or a long stricture were factors predicting the need for surgery in a multivariate analysis. Early clinical success was a protective factor (p = 0.0005).

Conclusion: Endoscopic dilation appears to be an effective long term alternative to the management of Crohn’s strictures, whether they are primary or secondary in nature and this, for all phenotypes taken together. This procedure allowed two thirds of the patients with stenosing lesions to avoid the need for surgery. Disclosure: Nothing to disclose

Disclosure: ClinicalTrials.gov ID NCT02010762, funding by IOIBD and BROAD

[Table 1. Endoscopic and clinical recurrence rates at week 26]

Table: ClinicalTrials.gov ID NCT02010762, funding by IOIBD and BROAD

Vitamin D Placebo p-value
Rutgeerts ≥ 2b 58% 66% 0.37
Rutgeerts ≥ 2a 87% 82% 0.22
CDAI ≥ 220 18% 18% 0.93

Disclosure: ClinicalTrials.gov ID NCT02010762, funding by IOIBD and BROAD

**P0960**

**EVALUATING THE LONG TERM SAFETY AND EFFICACY OF ENDOSCOPIC TREATMENT FOR PRIMARY AND SECONDARY DIGESTIVE STRICTURES IN CROHN’S DISEASE**

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Introduction: Stenosing lesions in Crohn’s disease respond poorly to medical treatments alone. In the face of this problem, bowel-sparing techniques have been developed, including endoscopic dilation, as an alternative to definitive surgery. There is still insufficient evidence regarding the long term success rate, for all phenotypes taken together, and insufficient knowledge of the predictive factors for the success of endoscopic dilation. The aim of our study was to assess efficacy and safety in strictures in Crohn’s disease. The secondary objective was to highlight factors predicting the success of this procedure.

Aims and Methods: We conducted a single-centre retrospective cohort study including all patients managed endoscopically, between January 2000 and November 2016, with dilation of digestive strictures in the context of Crohn’s disease (all phenotypes taken together). The technical and clinical success was assessed, as was the complication rate. Surgical management after endoscopic management was considered as a failure.

Results: 104 patients were included in the course of this study, of whom 56 (53.8%) were women. Of the total number of patients, 43% presented a phenotype considered to be severe (fistulizing lesions, anorectal lesions...). Median follow-up was of 61 months, or a little over 5 years. A total of 145 dilations were performed on 104 strictures, and 113 concerned secondary anastomotic strictures (77.9%). Technical success was obtained in 117 dilations (92.9%), and only one immediate complication, of the haemorrhagic type, was identified in the course of the endoscopy. There were 10 delayed complications (6.9%), represented by 6 perforations, 2 haemorrhagic events and 2 cases of bacteriemia with sterile episodes. During our follow-up, 71 patients (61%) carrying out an endoscopy only endoscopically. Of these patients, 52 (71.2%) required only one dilation session. The remaining 33 patients (31.7%) had surgery within a median delay of 13 months in relation to the first dilation. The presence of another stenosing lesion or a long stricture were factors predicting the need for surgery in a multivariate analysis. Early clinical success was a protective factor (p = 0.0005).

Conclusion: Endoscopic dilation appears to be an effective long term alternative to the management of Crohn’s strictures, whether they are primary or secondary in nature and this, for all phenotypes taken together. This procedure allowed two thirds of the patients with stenosing lesions to avoid the need for surgery. Disclosure: Nothing to disclose

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CDAI ≥ 220 18% 18% 0.93

Disclosure: ClinicalTrials.gov ID NCT02010762, funding by IOIBD and BROAD

**P0970**

**ESTABLISHING PK EQUIVALENCE BETWEEN ADALIMUMAB AND ABP 501 IN THE PRESENCE OF ANTI-DRUG ANTIBODIES USING POPULATION PK MODELING**

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Introduction: Adalimumab (HUMIRA®) and its approved biosimilar ABP 501 (AMGEVITA® ; adalimumab) exhibit nonlinear pharmacokinetics (PK) following a single subcutaneous (SC) dose in healthy volunteers possibly due to target mediated disposition or development of anti-drug antibodies (ADAs). The presence of nonlinear PK leads to low and variable drug levels posing a challenge in assessing PK equivalence of these two agents. To address this we used a population PK modeling approach to assess PK equivalence.

Aims and Methods: A one-compartment PK model with first-order absorption was selected to characterize the ABP 501 and adalimumab PK in healthy subjects. The model was parameterized in terms of apparent systemic clearance and apparent central volume of distribution for subjects with or without ADAs. Body weight, albumin and ADA status were evaluated for their potential impact on adalimumab or ABP 501 PK. For subjects who developed ADAs, the model evaluated the inclusion of additional antibody mitigated clearance mechanisms using Michaelis-Menten (MM) type of saturable clearance or time-dependent clearance in all linear clearance. The PK parameters were evaluated by comparisons of the empirical Bayes’ estimates of the individual PK model parameters.

Results: In healthy subjects without ADAs, the ABP 501 and adalimumab PK after SC administration was linear and adequately described by a one-compartment model with first order absorption and linear clearance from the central compartment. Inclusion of an additive time dependent linear clearance for subjects who developed ADAs was superfluous as a model incorporating an additive MM saturable clearance for subjects with ADAs. Graphical and statistical comparisons of empirical Bayes’ estimates by treatment demonstrated no difference in any PK model parameters by treatment. The population and inter-individual variability estimates of clearance and volume were 0.399 (33.6%) L/d and 8.94 (23.5%) L, for a 72.7 kg subject (median body weight). The time to onset and magnitude of the additive ADA-related linear clearance was 33.7 (54.4%) days and 1.15 (52.6%) L/d. Diagnostic plots demonstrated good concordance between observed and population or individual predicted concentrations without any bias. Visual predictive checks demonstrated the model described well the variable PK of each individual well and was used to estimate accurately each individual’s PK. Body weight, albumin and ADA status were evaluated for their potential impact on adalimumab or ABP 501 PK. For subjects who developed ADAs, the model evaluated the inclusion of additional antibody mitigated clearance mechanisms using Michaelis-Menten (MM) type of saturable clearance or time-dependent clearance in all linear clearance. The PK parameters were evaluated by comparisons of the empirical Bayes’ estimates of the individual PK model parameters.

Disclosure: Authors have been or continue to be employees and stockholders of AMGEN.
randomized patients tested positive for neutralizing antibodies at weeks 4, 12, or adalimumab, n = 26, with similar percentages in each treatment group (ABP 501, n = 38.2%) of all patients tested positive for binding antibodies at weeks 4, 12, or adalimumab. Here we report results from a Phase 3 study in patients with rheumatoid arthritis (RA) comparing the incidence of ADA and the relative magnitude of the ADA response between ABP 501 and adalimumab reference product (RP) on background methotrexate (MTX).

**Aims and Methods:** We analysed data from a randomized, double-blind, 26 week, 1:1 active-controlled study designed to show clinical equivalence between ABP 501 40 mg and adalimumab 40 mg subcutaneously every two weeks among patients with moderate to severe RA who had an inadequate response to MTX. Patients were required to receive a stable dose of MTX (range 7.5 to 25 mg/week) for the duration of the study. Patients were also allowed to remain on oral corticosteroids at a dose of ≤10 mg/day of prednisone, or equivalent. Validated electrochemiluminescent assays were developed and used to detect binding ADAs. ADA negativity was defined as signal-to-noise (S/N), defined as the mean signal of the study sample divided by the mean signal of the control analysed on the same plate. Samples positive for binding ADAs were then tested in a TNFα-target binding assay for neutralizing antibodies. Formulation excipients of a biosimilar can differ provided there is no impact to product quality. ABP 501 is therefore formulated with different set of excipients compared to adalimumab. The seroconversion rates per ADA positive subgroup in both studies.

**Results:** The proportion of subjects with binding ADA positive results increased from 29.0% to 57.0% from week 4 to week 24 (time of primary analysis in the plaque psoriasis study) and 18.1% to 33.5% from week 4 to week 24 (time of primary analysis) in the RA study. Mean serum trough concentrations of ADAs were similar among those who tested positive for binding ADAs and those who did not. The rates of seroconversion over time for both treatment groups was similar, progressively increasing throughout the study. For subjects testing ADA positive, the magnitude of both the binding and neutralizing ADAs across the treatment groups were evenly distributed, with similar median S/N or titre values at each time point.

**Conclusion:** Similar immunogenicity rates were observed and relative magnitude of the ADAs was similar between the ABP 501 and adalimumab RP treated patients.

**Disclosure:** Authors have been or continue to be employees and stockholders of AMGEN.

**Table:**

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Week 4</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 16</th>
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<tr>
<td>ADAA negative subgroup</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ABP 501</td>
<td>4.13 (1.48)</td>
<td>7.28 (2.75)</td>
<td>8.18 (3.41)</td>
<td>6.67 (2.23)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>4.07 (1.45)</td>
<td>7.05 (2.80)</td>
<td>7.92 (3.06)</td>
<td>6.85 (2.14)</td>
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<tr>
<td>ADAA positive subgroup</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ABP 501</td>
<td>2.90 (1.77)</td>
<td>3.75 (1.38)</td>
<td>3.81 (3.79)</td>
<td>4.62 (2.16)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>2.82 (1.70)</td>
<td>3.45 (3.07)</td>
<td>3.59 (3.50)</td>
<td>3.03 (0.35)</td>
</tr>
</tbody>
</table>

`[Serum trough concentrations of ABP 501 and adalimumab in ADA negative and positive subgroups]`

**Disclosure:** The formation of binding ADAs in both studies impacted the exposure of both ABP 501 and adalimumab over time. The degree of decline in drug exposure over time was similar between ABP 501 and adalimumab arms in both studies regardless of the ADA status.

**Disclosure:** Authors have been or continue to be employees and stockholders of AMGEN.

**Table:**

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P0974 EARLY DOSE OPTIMIZATION IN NONRESPONDERS TO GOLIMUMAB INDUCTION TREATMENT FOR ULCERATIVE COLITIS IS SUPPORTED BY PHARMACOKINETIC DATA THROUGH 1 YEAR

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**Introduction:** In the PURSUIT-M study, ulcerative colitis (UC) patients who were nonresponders to golimumab (GLM) induction treatment at Wk6 (by full Mayo score) were given GLM 100mg q4wk from Wk6 through Wk60. We previously showed that, compared with Wk6-Responders, Wk6-Nonresponders have lower GLM trough levels (TLs) at Wk6, and that Wk6-Nonresponders on the 100mg maintenance dose (at Wk6 and Wk10) achieved TLs at Wk14 that were similar to the TLs at Wk14 in Wk6-Responders on the 50mg dose (1). At Wk14, 28% of the Wk6-Nonresponders became responders (by partial Mayo score) after receiving 100mg at Wk6 and Wk10 (2). Here, we report on GLM TLs in the PURSUIT-M trial, in responders and nonresponders to induction treatment, through Wk52.

**Conclusion:** GLM TLs were measured at Wk 6, 10, 14, 18, 26, 34, 42 and 50. To eliminate artefactual changes in median values due to dropouts/missing data, only patients with TLs available at all the timepoints were included in this post-hoc analysis. Also, subgroups based on body weight (BW) <80kg and

**Disclosure:**
≥80kg were examined: Week6-Responders with BW<80kg on 50mg (n=42), Week6-Responders with BW<80kg on 100mg (n=42), and Week6-Nonresponders with BW≥80kg on 100mg (n=18), and Week6-Nonresponders with BW<80kg on 100mg (n=62). The 80kg cutpoint was selected based on the maintenance does currently approved in the EU: either 50mg for BW<80kg, or 100mg for BW≥80kg.

**Results:** At Wk14 (steady-state), Week6-Responders with BW<80kg on 50mg and Week6-Responders with BW<80kg on 50mg had the same median TL (0.98 μg/mL). At Wk26, 42, and 50, the IQ ranges of GLM TL were largely overlapping in these same two subgroups (Table). At each time point, the highest median TLs were observed in Week6-Responders with BW<80kg on 100mg, a posology that is not approved in the EU label of GLM for UC.

**Conclusion:** Based on TLs observed at steady state then followed over 1 year, these data suggest that patients with initial nonresponse to GLM induction who weigh <80kg may require the GLM 100mg maintenance dose to achieve TLs similar to the TLs in induction responders receiving the maintenance doses currently approved in EU (either 50mg for BW<80kg, or 100mg for BW≥80kg).

**Serum golimumab trough concentrations (μg/mL) at selected timepoints**

<table>
<thead>
<tr>
<th>Week</th>
<th>Responders, a</th>
<th>Nonresponders, a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 6 (post-induction)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>2.40</td>
<td>2.54</td>
</tr>
<tr>
<td>IQ range</td>
<td>(1.34; 4.32)</td>
<td>(1.17; 4.25)</td>
</tr>
<tr>
<td>Week 14 (steady-state)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>0.98</td>
<td>1.75</td>
</tr>
<tr>
<td>IQ range</td>
<td>(0.50; 1.37)</td>
<td>(1.31; 2.15)</td>
</tr>
<tr>
<td>Week 26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>0.29</td>
<td>1.70</td>
</tr>
<tr>
<td>IQ range</td>
<td>(0.14; 0.67)</td>
<td>(1.08; 2.30)</td>
</tr>
<tr>
<td>Week 42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>0.80</td>
<td>1.77</td>
</tr>
<tr>
<td>IQ range</td>
<td>(0.40; 1.23)</td>
<td>(1.27; 2.92)</td>
</tr>
<tr>
<td>Week 50</td>
<td></td>
<td></td>
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<tr>
<td>Median</td>
<td>0.79</td>
<td>1.74</td>
</tr>
<tr>
<td>IQ range</td>
<td>(0.55; 1.33)</td>
<td>(1.23; 2.75)</td>
</tr>
</tbody>
</table>

*Responders status at Week 6 based on achieving a Clinical Response (defined as: Decrease [from the Week-0 full Mayo score] of ≥3 points, with either a rectal bleeding subscore of 0 or 1 or a decrease in the IQ range (0.55; 1.33) (1.23; 2.75) (0.81; 1.42) (0.67; 1.83) |

**Table**

**Disclosure:** G. Philp is an employee of Merck & Co., Inc., Kenilworth, NJ, USA and may hold stock and/or stock options in the company. C. Marano and J. Adedokun are employees of Janssen Research & Development, LLC, Spring House, PA, USA and may hold stock and/or stock options in the company. R. Melsheimer is an employee of Janssen Biologics BV, Leiden, Netherlands and may hold stock and/or stock options in the company. F. Cornillie is an employee of MSD Switzerland and may hold stock and/or stock options in the company.

**References**

1. G. Philp et al., Early dose optimization in nonresponders to golimumab induction treatment for ulcerative colitis is supported by pharmacokinetic data.
2. P. Rutgeerts et al., (2014), How long should golimumab treatment be continued in patients with ulcerative colitis who do not respond to initial induction therapy.

**P0975 REAL-WORLD DATA ON THE USE OF 5 AMINOSALICYLIC ACID (5ASA) IN NON-FISTULATING, NON-STRICITURING CROHN’S DISEASE IN AN IBD TERTIARY CENTRE**

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**Introduction:** Historical studies showed 5ASA to be effective in Crohn’s disease. However, more recently, several meta-analysis of trial data have now shown no improvement over placebo. The latest ECCO guidelines published in 2016 advises against the use of 5ASA in Crohn’s disease.

**Aims and Methods:** Our retrospective study aims to assess our current practice. Using the IBD registry, we identified every patient diagnosed with Crohn’s disease between 2009 and 2017. We included patients with L1/L2/L3 B1 Montreal classification as these patients are more likely to be treated with 5ASAs. Our patients are then subdivided into Group I: small bowel Crohn’s (L1/L3 B1) and Group II: colonic Crohn’s (L2 B1).

**Results:** Between 2009 and 2017, we had 453 patients diagnosed with Crohn’s disease, 139 were in Group I and 49 in Group II. In our Group I, 35% were prescribed 5ASA within first year of diagnosis (n = 49). 27 patients were L1 B1 and 22 patients were L3 B1, 18 patients were given 5ASAs as monotherapy. When looking at the prescriber, 16 were consultants, 14 were registrars and there was no documentation for the rest. In 24 patients, the prescriber clearly documented awareness of diagnosis of ileal/ileocolonic Crohn’s disease. 13 patients are still on 5ASAs today. Only 2 were discontinued after a discussion about the lack of evidence in CD. In Group II, 76% were prescribed 5ASAs (n=19); 10 as monotherapy. In 14 patients, the prescriber documented awareness of diagnosis of colonic Crohn’s. 6 patients remain on 5ASAs today, 3 were lost to follow-up and 10 stopped 5ASAs for various reasons including 1 for nephrotoxicity.

**Conclusion:** This retrospective study assess current practice in an IBD tertiary centre. 5ASAs are still being used in this unit. There is awareness of the lack of evidence for using it but there remain patients on it. We recommend a discussion on the potential side effects and the lack of evidence for its use with every patient who remain on 5ASAs. It should be an alternative option in patients where steroids are contraindicated or intolerant.

**Disclosure:** Nothing to disclose.

**P0976 PERSISTENCE OF BIOLOGIC THERAPY AND MAPPING OF SEQUENTIAL BIOLOGIC USE RESULTS OF A SINGLE CENTRE COHORT WITH 841 PATIENTS TREATED OVER 18 YEARS**

P. Jenkinson1, N. Plevris1, C.S. Chuah1, M. Lyons1, G. Rhyes-Jones1, L. Merchant1, I. Arnott1, C. Lees1

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**Introduction:** Biologic therapy has revolutionised the treatment of IBD in the last 20 years. There is limited data on the patient journey through multiple lines of biologies and mapping this to outcomes. We aimed to establish the prevalence of biologic use in a single tertiary IBD centre and assess outcomes defined by biologic persistence.

**Aims and Methods:** Retrospective review of electronic health records (TrakCare) was performed on all patients who have received infliximab (IFX), adalimumab (ADA), vedolizumab (VEDO) or ustekinumab (UST) in Edinburgh from January 1999 to October 2017. We collected data for demographics, phenotyping details and duration of treatment. Kaplan-Meier survival curves and log-rank analyses were used to compare time to either discontinuation or resectional surgery.

**Results:** 841 patients were identified who have had biologic therapy for IBD. Median interval from diagnosis to biologic therapy was 4.9 years (IQR 1.3–11.0). The multiple combinations of biologics used is displayed in Figure 1. 665 CD patients (79.7% of total) were treated with biologics; 486 received IFX (73.1%), 169 ADA (25.4%) and 10 VEDO (1.6%) as first line therapy. Second-line therapy was required in 238 patients and consisted of ADA 189 (79.4%), IFX 25 (10.9%), VEDO 18 (7.6%) and 6 (2.5%). Third-line therapy was required in 57 patients, 21 VEDO 18 (31.8%) and 29 ADA (46.8%). Median interval from diagnosis to biologic therapy was 80 months in ADA, 118 months in IFX and 14 months in VEDO. Median interval of treatment on the potential side effects and the lack of evidence for its use with every patient who remain on 5ASAs. It should be an alternative option in patients where steroids are contraindicated or intolerant.

**Disclosure:** Nothing to disclose.
Introduction: Faecal loss of antibodies against anti-tumor necrosis factor (TNF) is a primary reason for non-response to anti-TNF agents in patients with severe ulcerative colitis (UC) ADDIN EN.CITE ADDIN EN.CITE DATA [1]. For the intravenously administered infliximab, faecal loss has been demonstrated in the first days after start of treatment. The highest faecal infliximab concentrations were approximately 50-fold lower compared to infliximab serum concentrations. Evidence is lacking about faecal antibody loss with other anti-TNF agents.

Aims and Methods: The aim of this study was to investigate faecal loss of golimumab (GLM), a subcutaneously (sc) administered anti-TNF agent, in patients with moderate to severe UC. GLM concentrations were measured in serum and faeces using an ELISA developed by Sanquin Laboratories (lower limit of quantification (LLOQ) 0.005 μg/mL). First, this ELISA developed for GLM serum measurements, was validated for the measurement of GLM in faeces. Homogenized faecal samples (0.95-1.05 g) of moderate to severe UC patients naive to biological therapy were spiked with GLM to obtain three different concentrations (QC-1: 3 μg/mL; QC-2: 0.5 μg/mL and QC-3: 0.05 μg/mL) and stored at −20°C. Second, faecal samples of patients with moderate to severe UC (endoscopic Mayo score ≥2) starting GLM treatment, (200 mg (day 1) and 100 mg (day 14) sc) followed by maintenance treatment according to the registered label, were prospectively collected at day 1 and 4-6 days after the first GLM dose and stored at −20°C. Simultaneously, serum samples for the measurement of GLM serum concentrations were collected.

Results: For the assay validation, faecal samples of three anti-TNF naive patients with moderate-severe UC were collected. The median interquartile range (IQR) faecal GLM concentrations of samples spiked with QC-1, QC-2 and QC-3 were 3.5 μg/mL [IQR 3.4-3.6 μg/mL], 0.3 μg/mL [IQR 0.3-0.4 μg/mL] and 0.05 μg/mL [IQR 0.04-0.05 μg/mL] respectively. For the clinical validation of faecal loss of GLM, faecal samples of 12 UC patients were collected. Median serum GLM concentrations at day 1 and day 4-6 were 4.9 μg/mL [IQR 2.8-10.3 μg/mL] and 11.5 μg/mL [IQR 8.9-12.8], respectively. In all faecal samples collected at these time points, faecal GLM concentrations were below the LLOQ. A cut-off was defined at the median serum GLM concentrations of samples spiked with QC-1, QC-2 and QC-3 were 3.5 μg/mL, QC-2: 0.5 μg/mL and QC-3: 0.05 μg/mL.

Conclusion: We validated the assay for measurement of GLM in a homogenized faecal matrix. With a hypothetical serum/faeces ratio of 50 for infliximab, faecal GLM concentrations should have been above the LLOQ in a real-life clinical setting. However, no GLM could be detected in faeces of treated UC patients. This could be explained by the fact that maximum serum drug concentrations after sc administration are much lower compared to intravenous administration. Moreover, the variation in bioavailability after sc administration is significantly greater than for iv agents. Furthermore, degradation of GLM in the gut may also play a role. Additional studies are needed to explore these phenomena.

Disclosure: Nothing to disclose.

Reference:

P0978 EFFECTIVENESS AND SAFETY OF THE SWITCH FROM REMICADE® TO CT-P13 IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE


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9Hospital Universitario de Galicia-Uñan, Gastroenterology Unit, Galdakao, Spain
10Hospital de Sabadell, Institut Universitari Parc Taulí, UAB and CIBERehd, Unitat de Malalties Digestives, Barcelona, Spain
11Hospital Universitario de Domostia and CIBERehd, Gastroenterology Unit, Donostia, Spain
12Hospital Universitario Marqués de Valdecilla, Gastroenterology Unit, Santander, Spain
13Hospital Clínico Universitario Lozano Blesa, Gastroenterology Unit, Zaragoza, Spain
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15Hospital Universitario de Fuenlabrada, Gastroenterology Unit, Fuenlabrada, Spain
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Introduction: Switching from Remicade® to CT-P13 could be cost-saving strategy for inflammatory bowel disease (IBD) patients.

Aims and Methods: We aimed to evaluate the clinical outcomes in patients with IBD after switching from Remicade® to CT-P13 in comparison with patients who maintain Remicade®.

Results: 476 patients were included: 199 (42%) in the SC and 277 (58%) in the NS (table 1). The switch to CT-P13 was volunteered in only 25% of cases. Median follow-up was 18 months in the SC and 23 months in the NC (p < 0.01). 24 out of 277 patients relapsed in the NC after a median follow-up of 23 months; the incidence of relapse was 5% per patient-years. The cumulative incidence of relapse was 2% at 6 months and 10% at 24 months in this group. 38 out of 199 patients relapsed in the SC after a median of 18 months; the incidence rate of relapse was 14% per patient-years. The cumulative incidence of relapse was 5% at 6 months and 28% at 24 months. In the multivariate analysis, to have been switched to CT-P13 adjusted by duration of Remicade® treatment before entry was associated with a higher risk of relapse (HR = 3.5, 95% CI = 2-6.13%) of patients had adverse effects in the NS and 6% in the SC (p < 0.05).

Conclusion: In this large real-life population of IBD patients in remission, switching from Remicade® to CT-P13 was associated with a higher risk of relapse (in comparison with those maintaining the infliximab originator). Nocceo effect might have influenced this result. Switching from Remicade® to CT-P13 was safe.

Disclosure: M. Chaparro has served as a speaker, or has received research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma. J.P. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Bard, Sanoﬁ, Ferring, Faes Farma, Ph. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Bard, Sanoﬁ, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Vifor Pharma. J Hinojosa has served as a speaker, a consultant and advisory member for, and has received research funding from MSD, Abbvie, Ferring, Faes Farma, Shire Pharmaceuticals, Chiesi, Otsuka Pharmaceutical, Pfizer – Hospira, Kern Pharma, UCB Pharma, Vifor Pharma, Janssen, Takeda and Dr. Falk Pharma. Montserrat Rivero has served as a speaker, a consultant and advisory member for, and has received research funding from MSD, Abbvie, Hospira, Pfizer, Bard, Sanoﬁ, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Biogen, Takeda, Roche, Celgene, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Vifor Pharma. J Hinojosa has served as a speaker, a consultant and advisory member for, and has received research funding from MSD, Abbvie, Ferring, Faes Farma, Shire Pharmaceuticals, Chiesi, Otsuka Pharmaceutical, Pfizer – Hospira, Kern Pharma, UCB Pharma, Vifor Pharma, Janssen, Takeda and Dr. Falk Pharma.
served as a speaker, a consultant and advisory member for Merck Sharp and Dohme, Abbvie and Janssen. Dr. Bermejo has served as a speaker and advisory member for or has received research funding from MSD, Abbvie, Pfizer, Takeda and Janssen. Manuel Van Domselaar has received funding for attending congresses from Kern Pharma and MSD.

P0979 NEED FOR ADALIMUMAB DOSE OPTIMIZATION IN PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS

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Introduction: During treatment with adalimumab (ADA), a variable proportion of Crohn’s disease (CD) and ulcerative colitis (UC) patients lose of efficacy need dose optimization to regain response. A meta-analysis showed that the mean percentage of CD patients who needed ADA dose optimization was 24.4% per patient-year. Conversely, real-life need for ADA optimization in UC is not well known. No studies have directly compared the need for ADA dose optimization in CD and UC in the same real-life clinical setting.

Aims and Methods: The aim of the study was to compare the need for and timing of ADA dose optimization in two cohorts of patients with luminal CD or UC. In this single centre, observational, cohort study, dose optimization was determined by two senior staff specialized in IBD. CD patients with active perianal disease were excluded. We compared the rates of patients-months on ADA who needed dose optimization in the cohorts of CD or UC patients. We also compared the interval between ADA first induction dose and the first escalated ADA dose. Escalation-free survival was estimated by the Kaplan-Meier method. We also evaluated the rate of de-escalation.

Results: We included 43 patients with CD (mean age 43 years; 56% female) and 43 patients with UC (mean age 50 years; 42% female). Forty-eight% CD patients vs 51% UC patients (p = 0.92) were receiving an immunomodulator at baseline. After a median follow-up of 22.8 months (interquartile range [IQR] 9–49 months) and 13.9 months (IQR 5–31 months) for CD or UC patients, respectively (p = 0.14), 24 CD patients (56%) vs 28 UC patients (65%) required ADA optimization. In 88% of cases, ADA was escalated to 40 mg weekly. The rate of patient-month who needed ADA dose optimization was 2.5% vs 8.1% (p < 0.001) for CD and UC, respectively. In patients who underwent ADA optimization, median time between the first ADA induction dose and the first escalated dose was 11.8 [IQR 6–33] months vs 3.3 [IQR 2–10] months (p = 0.001) for CD and UC, respectively. Twelve CD patients (50%) vs 9 UC patients (32%) were able to de-escalate dose. Survival curves showed that patients with CD had an increased probability of ADA de-escalation when compared with UC patients (HR 2.32; 95% CI 1.10–5.59; p = 0.030). Median time to de-escalation was 3.8 months (IQR 3–13) vs 8.9 months (IQR 3–30) for CD and UC patients, respectively (p = 0.12). In the multivariate analysis, UC patients (HR 8.44; 95% CI 0.45–32.3; p = 0.004) and short-term non-response (HR 3.92; 95% CI 1.79–8.59; p = 0.001) were associated with a higher rate of ADA optimization.

Conclusion: In clinical practice, the rate of patient-month who needed ADA dose optimization is higher in UC compared with luminal CD. Patients with UC required optimization of ADA dosing earlier and also had lower ADA escalation-free survival. The probability of dose de-escalation was also significantly higher in CD patients with moderate to severe UC.

Disclosure: Nothing to disclose

Reference

P0980 ANALYSIS OF NON-MELANOMA SKIN CANCER IN THE ULCELERATIVE COLITIS PROGRAMME FOR TOFACITINIB

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Introduction: Tofacitinib is an oral, small-molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). We present an integrated analysis of non-melanoma skin cancer (NMSC) events in the tofacitinib Phase (P) 3 programme for patients (pts) with moderate-to-severe UC.

Aims and Methods: NMSC events were evaluated from 3 randomised placebo (PBO)-controlled studies (2 identical 8-week induction studies [OCTAVE Induction 1 & 2; NCT01465765, NCT01458951], a 52-week maintenance study [OCTAVE Sustain, NCT01458574]) and an ongoing, open-label extension study (OCTAVE Open, NCT01470612). Pts were analysed as 3 cohorts: Induction (P3 induction studies); Maintenance (P3 maintenance study); Overall (pts receiving > 1 dose of tofacitinib 5 or 10 mg twice daily [BID] in the P3 programme). An independent, blinded adjudication committee reviewed all potential NMSC. Proportions and incidence rates (IRs; unique pts with events per 100 pt-years [PY] of exposure) for NMSC were evaluated. Cox proportional hazards model was used for risk factor analysis. Data shown are as of 16 December 2016.

Results: 1124 pts were evaluated for NMSC, with 1648 PY of tofacitinib exposure and up to 4.4 years of treatment. NMSC was reported in 2 Induction pts receiving 10 mg BID, 1 PBO Maintenance pt (IR 0.97) and 3 Maintenance pts receiving 10 mg BID (IR 1.91) (Table). In the Overall Cohort, NMSC was reported in 11 pts (IR 0.67), including 7 pts with squamous cell carcinoma (SCC) and 4 pts with basal cell carcinoma (BCC); 2 pts had both SCC and BCC. No NMSC was metastatic or led to study discontinuation. Of all tofacitinib-treated pts with NMSC, 6 had prior NMSC history, 10 had prior use of thiopurines and 10 had prior tumour necrosis factor inhibitor (TNFi) failure. In the Overall Cohort, higher IRs were observed for subgroups aged ≥ 65 years vs <65 years, and for subgroups with prior TNFi failure or prior immunosuppressant treatment, vs those without. Cox regression selected prior NMSC diagnosis and TNFi failure for subgroups with prior TNFi failure or prior immunosuppressant treatment, as significant risk factors.

Conclusion: NMSC occurred infrequently with tofacitinib treatment in the UC clinical programme. NMSC IRs were similar to those reported for tofacitinib in other indications, including rheumatoid arthritis1 and for biologic UC treatments. Cox regression analysis selected prior NMSC diagnosis and TNFi failure

Abstract No: P0980

Table. Incidence rates for all NMSC events for Induction, Maintenance and Overall Cohorts, and univariate subgroup analyses for the Overall Cohort

<table>
<thead>
<tr>
<th>All NMSC</th>
<th>Induction Cohort</th>
<th>Maintenance Cohort</th>
<th>Overall Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo N = 234</td>
<td>Tofacitinib 10 mg BID N = 905</td>
<td>Placebo N = 198</td>
</tr>
<tr>
<td>Exposure (PY)</td>
<td>N/A</td>
<td>N/A</td>
<td>0.97 (0.2, 5.40)</td>
</tr>
<tr>
<td>Number (%) of patients with events</td>
<td>0 (0)</td>
<td>2 (0.2)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>IR (95% CI)</td>
<td>N/A</td>
<td>N/A</td>
<td>103.20</td>
</tr>
<tr>
<td>Overall Cohort, Tofacitinib All, N = 1124</td>
<td>Baseline characteristic</td>
<td>Univariate subgroup analysis</td>
<td>N</td>
</tr>
<tr>
<td>Age &lt;65 years</td>
<td>1048</td>
<td>7 (0.7)</td>
<td>0.46 (0.18, 0.94)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>76</td>
<td>4 (5.3)</td>
<td>3.35 (0.91, 8.59)</td>
</tr>
<tr>
<td>Prior TNFi failure</td>
<td>Yes</td>
<td>583</td>
<td>10 (1.7)</td>
</tr>
<tr>
<td>No</td>
<td>541</td>
<td>1 (0.2)</td>
<td>0.12 (0.00, 0.65)</td>
</tr>
<tr>
<td>Prior immunosuppressant treatment</td>
<td>Yes</td>
<td>838</td>
<td>11 (1.3)</td>
</tr>
<tr>
<td>No</td>
<td>286</td>
<td>0 (0.0)</td>
<td>0.00 (0.00, 0.92)</td>
</tr>
</tbody>
</table>

BID, twice daily; CI, confidence interval; IR, incidence rate for unique patients with events per 100 PY; N, number of patients randomised and treated; n, number of patients with event; N/A, not available; NMSC, non-melanoma skin cancer; PY, patient-years; TNFi, tumour necrosis factor inhibitor.

[Table]
P0981 LONG-TERM SAFETY IN THE OPEN-LABEL PERIOD OF A PHASE 2A STUDY OF BRAZIKUMAB, AN ANTIBODY AGAINST INTERLEUKIN-23

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Introduction: Brazikumab (MED2070), a human monoclonal antibody that is an anti-p19 subunit inhibitor of interleukin-23, was shown to be effective over 8 weeks of treatment for patients with moderate-to-severe active Crohn's disease.1 Here, we report the long-term safety and tolerability of brazikumab.

Aims and Methods: The Phase 2a study (NCT01714726) consisted of a 12-week double-blind induction period with randomisation to intravenous brazikumab (700 mg) or placebo, followed by the open-label (OL) period where all patients were administered subcutaneous brazikumab (210 mg) every 4 weeks. Patients were aged 18–65 years, had a clinical diagnosis of moderate-to-severe active Crohn's disease, had failed or were intolerant to anti-TNFα therapy, and were aged 18–65 years, had a clinical diagnosis of moderate-to-severe active Crohn's disease, had failed or were intolerant to anti-TNFα therapy, and entered the 100-week OL period. Adverse events (AEs) and vital signs were recorded every 4 weeks.

Results: 104 patients entered (n = 52 from placebo to brazikumab and n = 52 from brazikumab to brazikumab) and 57 (54.8%) patients completed the OL period. 87 (83.7%) patients experienced ≥1 treatment-emergent AE (TEAE); 12 (11.5%) experienced ≥1 TEAE leading to permanent discontinuation of study drug and 20 (19.2%) experienced ≥1 serious AE (SAE). The most common TEAEs were headache (22.1%), nasopharyngitis (22.1%), abdominal pain (18.3%) and Crohn's disease (16.3%) [Table]. Half of the SAEs observed were gastrointestinal disorders associated with Crohn's disease. Five SAEs of infection were reported, none of which were opportunistic, such as herpes zoster or tuberculosis; all resolved and the investigational product was permanently discontinued for only one patient. No cases of cancer were reported. The AE profile was similar between patients who completed a previous 12-week course of either placebo or brazikumab treatment.

Conclusion: In this 100-week OL period, brazikumab was well tolerated in patients with moderate-to-severe active Crohn's disease, warranting future studies in larger patient populations.

Treatment-emergent adverse events occurring in ≥5% of patients, n (%)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Total (N = 104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>23 (22.1)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>23 (22.1)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>19 (18.3)</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>17 (16.3)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>14 (13.5)</td>
</tr>
<tr>
<td>Influenza</td>
<td>13 (12.5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (10.6)</td>
</tr>
</tbody>
</table>

(continued)
of 33.5 in the pre-intervention group (p = 0.002), indicating less decisional conflict (DC) and SDM) by patients in management decisions in the post-intervention group.

Conclusion: Implementing an evidence-based DST in the outpatient setting significantly improves quality of care, as measured by an increased use of process indicators. The DST improved the quality of the delivery of the psychological and preventive health aspects of care which may be neglected during routine IBD care. DSTs therefore have the potential to minimize errors of omission via a standardized approach to care.

Disclosure: Nothing to disclose.

P0983 USTEKINUMAB IMPROVES PRODUCTIVITY AND REDUCES WORK LIMITATION OF PATIENTS WITH MODERATE TO SEVERE CROHN’S DISEASE: RESULTS FROM THREE PHASE 3 CLINICAL TRIALS

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Introduction: UNITI-1 & 2 and IM-UNITI are Phase 3 multicenter, randomized, double-blind, placebo-controlled studies to evaluate the safety and efficacy of ustekinumab (UST) in adults with moderately to severely active Crohn’s disease (CD).

Aims and Methods: To assess the effect of UST on improving work productivity with 8 weeks of induction therapy and maintaining improvement over the next 44-week period in patients with active CD. Patients with moderately to severely active CD (defined by a CD Activity Index (CAI) score of >220-450) who had an inadequate response or intolerance to TNF inhibitors (UNITI-1, N = 741) or conventional therapy (UNITI-2, N = 639) were randomized in a 1:1 ratio to receive placebo or UST (mg/kg intravenously (IV) or UST 130mg subcutaneously (SC) at week 0. Patients who had a clinical response at week 8 defined as having a reduction in CAI score ≥ 100 points, or CAI score ≤ 150 if baseline CAI score ≥ 240 were re-randomized to receive placebo or UST (SC) 90mg q12w or q8w through week 44 (IM-UNITI, N = 388). The impact of CD on productivity at work, school or home was measured using a visual analog scale (VAS) ranging from 0–100 (0 = no impact at all and 10 = very much impact). CD activity was assessed at PAWS visits (0, 4, 8) and at week 44. The impact of CD on productivity (loss on the job) was assessed using the Work Limitation Questionnaire (WLQ). The WLQ has 4 domains (time management, physical, mental-interpersonal and output demands) with each domain scoring from 0–100 and higher scores indicating greater work limitations. Productivity VAS and WLQ outcomes were collected and compared between treatment groups at baseline, week 8 (induction), and 22 and 44 weeks after induction (maintenance).

Results: At induction baseline, mean productivity VAS values ranged from 6.3–6.6 (23.2% improvement) in UNITI-1 and -2. 1 (33.3% improvement) in UNITI-1 group and -2.1 (33.3% improvement) in UNITI-2, compared to placebo (0.8 [11.9% improvement] in UNITI-2, p-values < 0.001). Overall, percent improvement from baseline was numerically greater for UST-treated vs. placebo patients in 3 out of 4 WLQ domain scores at Week 8: time management (24.1% vs. 17.6% in UNITI-1, and 35.1% vs. 27.3% in UNITI-2), physical demand (21.2% vs. 11.9% in UNITI-1, and 25.6% vs. 21.9% in UNITI-2), output demand (21.4% vs. 20.1% in UNITI-1, and 38.3% vs. 21.0% in UNITI-2) and mental-interpersonal demand (19.5% vs. 20.3% in UNITI-1, and 33.7% vs. 24.5% in UNITI-2). Improvements in productivity VAS and WLQ scores were better maintained in the UST groups vs. the placebo group in the IM-UNITI study through Week 44.

Conclusion: UST treatment improves productivity and reduces work limitations in patients with moderate to severe CD.

Disclosure: This study was supported by Janssen Research & Development, LLC.

Reference

P0985 RATIONALE AND PHASE 2 CLINICAL TRIAL DESIGN FOR PRV-6527, AN ORAL INHIBITOR OF THE CSF1RECEPTOR KINASE (CSF1R) FOR CROHN’S DISEASE

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Introduction: Bone marrow-derived myeloid antigen presenting cells, such as monocytes (Mo) and myeloid dendritic cells (mDCs) have been increasingly linked to pathogenesis of Crohn’s disease (CD). Monocytes (Mo) recruited to the intestinal lamina propria differentiate into an inflammatory Mo/mDC phenotype, which then expresses high levels of TNF alpha, IL-12 and IL-23 upon activation and induces differentiation of T helper (Th)17 cells. The CSF-1 receptor (CSF-1R) is a key receptor on Mo and mDCs and plays an essential role in Mo and mDC development and maturation. PRV-6527, also known as CSF1R antagonist (CSF1R) FOR CROHN’S DISEASE

Disclosure: None.

Contact: Fabian Schnitzler has received honoraria from Abbvie and MSD.

Reference

P0984 SWITCH OF INFLIXIMAB ORIGINATOR TO BIOSIMILAR CT-P13 IN PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS WITH MODERATE TO SEVERE ACTIVITY: RESULTS FROM THE NOR-SWITCH STUDY

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Introduction: The infliximab biosimilar CT-P13 has been approved by the FDA (Food and Drug Administration [FDA]) and Crohn’s disease (CD) based on extrapolation of data from rheumatology trials. Since then, several un-controlled and controlled studies have later-on shown that CT-P13 could be safe and effective for IBD patients who switched from originator to biosimilar or who received CT-P13 as first infliximab. If switch from infliximab to CT-P13 is associated with a worse outcome, the original treatment might be the better choice.

Aims and Methods: The NOR-SWITCH study will compare the efficacy and safety of infliximab originator and biosimilar infliximab in patients with moderate to severe CD.

Study design: The study is an open-label, prospective, randomized, non-inferiority, multicenter trial in 13 countries with about 225 centers. Patients were randomized to receive infliximab originator or biosimilar infliximab and were followed for 1 year. The primary endpoint is the clinical remission and continuation of study drug at 52 weeks. The secondary endpoints include other measures of clinical remission, relapse, and side effects.

Results: A total of 261 patients were enrolled in the trial. At week 52, 77% of patients were in remission in the originator group and 74% in the biosimilar group. The proportion of patients who discontinued therapy due to adverse events was 7% in the originator group and 8% in the biosimilar group. There were no significant differences in the proportion of patients who developed serious adverse events.

Conclusion: The NOR-SWITCH study is ongoing and will provide valuable information on the efficacy and safety of switching from infliximab originator to biosimilar CT-P13 in patients with moderate to severe CD.

Disclosure: Nothing to disclose.

Contact: Fabian Schnitzler has received honoraria from Abbvie and MSD.

Reference
Mice were treated orally with 15 mg/kg PRV-6527, a selective inhibitor of CSF-1 receptor, monophosphatically on day 42. A total of 165 CD11c-Cre / C11+ mononuclear cells were isolated from the spleen and CD mucosal biopsies (RutgersGSE16879). The PRINEO (PRInvention in Crohn's Disease) Phase 2 study (EudraCT Number: 2017-00307-25) is a randomized, double-blind, placebo-controlled, parallel-group, multicenter study in adult subjects with moderately to severely active CD. The study hypothesis is that PRV-6527, a CSF-1R inhibitor, will be superior to placebo in treating subjects with moderate to severe active CD over 12 weeks, as measured by the change from baseline in the Crohn’s Disease Activity Index (CDAI) score. Approximately 50 subjects per group were enrolled. Parenteral administration was allowed in secondary endpoints, including mucosal changes on endoscopy and histology and the presence of inflammatory myeloid cells by immunohistochemistry and gene signature in mucosal biopsies. Remission was defined as improved CDAI score in CD and remained elevated in anti-TNF-non-respondent patients. Infusion of the CSF-1 receptor inhibitor by PRV-6527 significantly reduced histological disease scores by ~60% in established murine colitis. Results of CD3+ T cells was reduced and F4/80 mononuclear cells were decreased to levels similar to control. RNAseq analysis demonstrated significant concordance of disease pathways between human CD and the mouse model. Treatment of mice with either PRV-6527 or CNT0548 impacted those pathways in a manner comparable to patients who respond to infliximab.

Conclusion: Pre-clinical and human biomarker data support the study of PRV-6527, a CSF-1R inhibitor, in CD and the promise for an oral therapy with potential to benefit in anti-TNF non-responders. Furthermore, these PD and biomarker data could be useful for patient stratification for future clinical studies or for tailored therapy in CD patients.

Disclosure: Authors 1, 4, 5 and 6 employees of Janssen R&D

References:
Aims and Methods: The effect of etrolizumab treatment on serum levels of sMAdCAM-1 (PD biomarker) and β7 RO in patients with moderate to severe Crohn’s disease were evaluated in a substudy of cohort 1 of the Phase 3 BERGAMOT trial (NCT02394026). Patients were randomly assigned to receive subcutaneously administered etrolizumab 105 mg once every 4 weeks, etrolizu- mab 210 mg at weeks 0, 2, 4, 8, and 12 or placebo during a 14-week period. Biomarker and pharmacokinetic (PK)/PD analysis was conducted using serum and whole blood samples obtained at baseline and weeks 1 (days 3, 4 or 5), 2, 4, 10 and 14 from patients who enrolled in the PK/PD substudy. Measurements of serum sMAdCAM-1 were performed using a validated assay on the Gyrolab xP immunassay platform. Whole blood samples were evaluated by flow cytometry within 24-48 hours of collection to assess β7 expression, β7 occupancy and enumeration of peripheral blood lymphocyte subsets using previously established methods.

Results: This preliminary analysis included 64 patients with Crohn’s disease (etrolizumab 105 mg, n = 29; etrolizumab 210 mg, n = 24; placebo, n = 11). Patients treated with etrolizumab showed a sustained decline in sMAdCAM-1 from baseline (week 1: group median decrease of ~40%), weeks 4 through 14: group median decline of ~80%) with minimal (<10%) changes from baseline observed in the placebo arm (Table). β7 integrin receptors on “β7++” intestinal homing CD3+ T cells were rapidly and completely occupied in etrolizumab-treated patients as indicated by a near 100% decrease in CD3+ T cells with “available” β7 receptors. Similar RO results were observed with CD4 T, CD8 T and CD19 B lymphocytes. There were no dose-related differences observed in sMAdCAM-1 reduction and RO.

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Introduction: A sizable proportion of patients with Crohn’s disease (CD) will undergo intestinal resection. Most will experience early post-operative endo- scopic and clinical disease recurrence. The superiority of anti-TNF agents over placebo and immunomodulators in the prevention of post-operative recurrence using a risk-stratified approach was previously demonstrated.

Aims and Methods: To evaluate the efficacy of an early unstratified approach comparing anti-TNF (adalimumab) with thiopurine (6-mercaptopurine, 6MP) therapy on post-operative CD recurrence, as demonstrated by endoscopy at 24 weeks.

All CD patients undergoing a first ileocecectomy for inflammatory complications were prospectively recruited to the Post Operative Adalimumab Recurrence Trial (POPART). Patients were randomized within 45 days to receive either adalimumab or 6MP. All patients underwent ileocolonoscopy at 24 weeks post operation to assess for endoscopic recurrence as defined by the Rutgeerts score. Endoscopic recurrence was defined as a Rutgeerts score of ≥24.

Results: Forty-one patients were recruited to the study. Four patients were lost to follow-up, and two who did not adhere to treatment were excluded from the final analysis. A total of 35 patients completed the study protocol—16 were treated with 6MP and 19 with adalimumab. Mean age 32.2 ± 21.6, 62.9% males, 54.3% non-smokers. Follow-up endoscopy was performed at week 24. Baseline clinical parameters and smoking status were comparable between treatment arms (43.8% vs. 38.9% respectively, p = 0.774).

Endoscopic recurrence was defined as a Rutgeerts score of ≥24.

Table 1. Absolute Change From Baseline of Serum sMAdCAM-1 and β7 “Available” Intestinal Homing CD3+ T Cells After Etrolizumab Treatment

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>6MP n = 16</th>
<th>Adalimumab n = 19</th>
<th>P &lt;</th>
<th>6MP n = 16</th>
<th>Adalimumab n = 19</th>
<th>P &lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m2)</td>
<td>18.6 ± 8.0</td>
<td>24.1 ± 3.5</td>
<td>0.01</td>
<td>19.0 ± 7.8</td>
<td>22.4 ± 7.0</td>
<td>0.11</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>6.9 ± 14.0</td>
<td>2.4 ± 3.6</td>
<td>0.20</td>
<td>4.6 ± 6.9</td>
<td>2.4 ± 2.1</td>
<td>0.21</td>
</tr>
<tr>
<td>Calprotectin (mg/kg)</td>
<td>256.1 ± 228.1</td>
<td>255.5 ± 27.3</td>
<td>0.29</td>
<td>193.8 ± 192.0</td>
<td>391.8 ± 695.1</td>
<td>0.01</td>
</tr>
<tr>
<td>CDAI score</td>
<td>94.6 ± 58.3</td>
<td>88.0 ± 45.2</td>
<td>0.78</td>
<td>105.8 ± 71.5</td>
<td>71.5 ± 73.0</td>
<td>0.15</td>
</tr>
<tr>
<td>IBDO (score)</td>
<td>180.1 ± 29.4</td>
<td>178.7 ± 32.6</td>
<td>0.83</td>
<td>180.0 ± 28.1</td>
<td>182.1 ± 32.7</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Endoscopic recurrence (≥R2) (%) 56.3

Table 1.
EVALUATING EFFICACY, SAFETY AND PHARMACOKINETICS AFTER SWITCHING FROM INFliximab ORIGINATOR TO BIOSIMILAR CT-P13: RESULTS FROM A LARGE TERTIARY REFERRAL CENTER

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21 Department of Gastroenterology and Hepatology, Leuven, Belgium
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41 Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, Leuven, Belgium

Introduction: The use of infliximab (IFX) biosimilar CT-P13 has dramatically increased in patients with Crohn’s disease (CD) and ulcerative colitis (UC), but doubts about the efficacy and safety of switching from IFX originator to biosimilar still exist with patients and health care professionals.

Aims and Methods: We investigated pharmacokinetics as well as efficacy and safety of a mandatory switch from IFX originator to CT-P13. In our tertiary referral center, CT-P13 was introduced in a 2 step procedure, with initiation of CT-P13 in IFX naïve patients from November 2015 onwards (controls). In March 2017, all patients receiving IFX originator were electively switched to CT-P13 (cases). Patient reported outcome (PRO2), C-reactive protein (CRP), IFX trough levels (TL, ELISA apDia) and anti-drug-antibodies (ADA, drug sensitive assay apDia) were measured at switch (T0), the next infusion of CT-P13 (T1) and 6 months after switch (T2).

Results: A total of 410 patients (53% male, median age 25 years, 71% CD, 61% in clinical remission) were enrolled, including 361 cases and 49 controls. Both groups were comparable except for median disease duration (7.0 vs. 1.5 years, p = 0.011), median duration of IFX treatment (6.0 vs. 9.9 years, p < 0.0001), concomitant immunosuppressive therapy (6% vs. 20%, p = 0.002), and median CRP (1.5 vs. 2.3 mg/l, p = 0.032). IFX discontinuation within 6 months of switch was observed in 4% of cases and 13% of controls (p = 0.04). The percentage of patients developing loss of clinical remission (22% vs. 99%, p = 0.011), adverse events (2% vs. 8%, p = 0.052) and ADA (0.6% vs. 2.5%, p = 0.18) were significantly different. In addition, the frequently needed treatment optimization (24.9% vs. 42.5%, p = 0.02) Table 1 shows the evolution of median PRO2, CRP and IFX TL over time. Although PRO2 increased significantly in cases between T0 and T2, this difference was not statistically different compared to the increase in PRO2 in controls (p = 0.61). In both groups, CRP and IFX TL remained stable over time.

Conclusion: Compared to continued therapy with biosimilar CT-P13, switching from IFX originator to CT-P13 was not associated with an increased risk of treatment discontinuation, loss of response or adverse events. In addition, no differences in IFX TL or immunogenicity could be identified. Inclusion: Mouricy A., Bronswijk M., Lenfant M., Compernolle G., Assche G., Gils A., Ferrante M.

Disclosure: Prof. Van Assche G.: Research grant: Abbvie, Pfizer; Consultancy: Abbvie, MSD, Ferring, Takeda, Janssen, Pfizer Inc, Genentech Roche, Speakers fee: Abbvie, MSD, Takeda, Ferring, Dr. Falk Pharma, Pfizer, Prof. Vermeire S.: Research grant: Takeda, MSD, Abbvie, Pfizer; Consultancy: Abbvie, MSD, Ferring, Takeda, Shire, Janssen, Pfizer Inc, Galapagos, Genentech Roche, Celgene, Mundipharma, Eli Lilly, Second Genome, GSK; Speakers fees: AbbVie, MSD, Takeda, Ferring, Dr. Falk Pharma, Hospira, Pfizer Inc and Tilottos. Prof. Gils A.: Lecture fees: MSD, Janssen Biologicals, Pfizer, Takeda, Abbvie: Advisory board: Takeda; Financial research support: Pfizer, Merck, Speck, Kubicka, apDka, Merek, Prof. Ferrante M.: Research grant: Janssen, Takeda; Consultancy: Abbvie, Boehringer Ingelheim, Ferring, Janssen, Mitsubishi Tanabe, MSD, Pfizer; Speakers fee: AbbVie, Boehringer Ingelheim, Chiesi, Ferring, Janssen, Lamepro, Mitsubishi Tanabe, MSD, Pfizer, Tramedico, Tilottos, Zeria

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (IQR)</th>
<th>p-value</th>
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<tr>
<td>PRO2 T0</td>
<td>3.0 (2.0–9.0)</td>
<td>0.0001</td>
</tr>
<tr>
<td>PRO2 T1</td>
<td>2.0 (2.0–9.0)</td>
<td>0.22</td>
</tr>
<tr>
<td>PRO2 T2</td>
<td>2.0 (2.0–9.0)</td>
<td>0.06</td>
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**E**valuation of **C**RP, **F**IX TL, **P**RO2 between **T**0 and **T**2 within groups (Wilcoxon ranked sum test).

**E**valuation of **C**RP, **F**IX TL, **P**RO2 between **T**0 and **T**2 between cases and controls (Mann Whitney U test). **CRP:** C-reactive protein, **IQR:** interquartile range; **F**IX TL: infliximab trough level; **P**RO2: patient-reported outcome.
**P0992 IMMUNOGENICITY AFTER TRANSITION FROM ADALIMUMAB TO ABP 501 IN PATIENTS WITH PLAQUE PSORIASIS**

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**Introduction:** Adalimumab therapy is associated with appearance of anti-drug antibodies (ADAs) and the relative magnitude of the ADA response among patients that transitioned from adalimumab RP to ABP 501. In this report we have examined the incidence of anti-drug antibodies (ADAs) and the relative magnitude of the ADA response among patients that transitioned from adalimumab RP to ABP 501.

**Aims and Methods:** Patients were randomized 1:1 (ABP 501: n = 175; adalimumab RP: n = 175) to receive ABP 501 or adalimumab every 2 weeks for 16 weeks. Eligible subjects who continued treatment beyond week 16 were re-randomized in a blinded fashion such that all patients who initially transitioned to ABP 501 continued treatment with ABP 501, and subjects initially randomized to adalimumab RP either continued treatment with adalimumab RP or underwent a single transition to ABP 501 in a 1:1 ratio. The last dose was at week 48; end of study at week 52.

After re-randomization, ADAs were assessed on weeks 20, 32 and 52. A validated electrochemiluminescent assay was used for detection of binding ADAs. Samples positive in the binding assay were then tested in a TNFα binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay.

**Results:** The proportion of subjects positive for binding and neutralizing antibodies from baseline through week 52, regardless of the transition from adalimumab RP/adalimumab RP 74.7% (59/79) binding and 20.3% (16/79) neutralizing; adalimumab RP/ABP 501 74.0% (57/77) binding and 24.7% (19/77) neutralizing. The overall incidence of binding antibodies that formed after the re-randomization at week 16 was comparable from week 16 through end of study [adalimumab RP/adalimumab RP 72.2% (57/79) vs. adalimumab RP/ABP 501 72.7% (56/77)]. To determine the true effect of transition from adalimumab RP to ABP 501, the rate of ADA development was assessed in subjects who were binding ADA negative through week 16. In this subset, the incidence of binding ADA was similar between the transition group (28.6% (8/28)) and those who remained on adalimumab RP (35.5% (11/31)). None of these subjects that tested ADA negative through week 16 developed neutralizing antibodies after transition through week 52.

**Conclusion:** Transition from adalimumab RP to ABP 501 was not associated with higher immunogenicity.

**Disclosure:** Authors have been or continue to be employees and stockholders of AMGEN.

**P0993 TIME COURSE OF THE INCIDENCE AND MAGNITUDE OF ANTI-DRUG ANTIBODIES TO ABP 501 AND ADALIMUMAB IN PATIENTS WITH PLAQUE PSORIASIS TREATED FOR 16 WEEKS**

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**Introduction:** Immunosuppressive therapy is associated with appearance of anti-drug antibodies (ADAs). ABP 501 (AMGEVITA®; adalimumab) is an approved bio-similar to adalimumab (HUMIRA®). Here we report immunogenicity results from a Phase 3 study in patients with moderate to severe plaque psoriasis without concurrent immunosuppressive therapy that undergo a single transition from adalimumab reference product (RP) to ABP 501. In this report we have evaluated the incidence of anti-drug antibodies (ADAs) and the relative magnitude of the ADA response among patients that transitioned from adalimumab RP to ABP 501.

**Aims and Methods:** Patients were randomized 1:1 (ABP 501: n = 175; adalimumab RP: n = 175) to receive ABP 501 or adalimumab every 2 weeks for 16 weeks. Eligible subjects who continued treatment beyond week 16 were re-randomized in a blinded fashion such that all patients who initially transitioned to ABP 501 continued treatment with ABP 501, and subjects initially randomized to adalimumab RP either continued treatment with adalimumab RP or underwent a single transition to ABP 501 in a 1:1 ratio. The last dose was at week 48; end of study at week 52.

After re-randomization, ADAs were assessed on weeks 20, 32 and 52. A validated electrochemiluminescent assay was used for detection of binding ADAs. Samples positive in the binding assay were then tested in a TNFα binding assay for neutralizing activity. Neutralizing antibody titre was reported as the highest dilution that tested positive in the assay.

**Results:** The proportion of subjects positive for binding and neutralizing antibody from baseline through week 52, regardless of the transition from adalimumab RP/adalimumab RP 74.7% (59/79) binding and 20.3% (16/79) neutralizing; adalimumab RP/ABP 501 74.0% (57/77) binding and 24.7% (19/77) neutralizing. The overall incidence of binding antibodies that formed after the re-randomization at week 16 was comparable from week 16 through end of study [adalimumab RP/adalimumab RP 72.2% (57/79) vs. adalimumab RP/ABP 501 72.7% (56/77)]. To determine the true effect of transition from adalimumab RP to ABP 501, the rate of ADA development was assessed in subjects who were binding ADA negative through week 16. In this subset, the incidence of binding ADA was similar between the transition group (28.6% (8/28)) and those who remained on adalimumab RP (35.5% (11/31)). None of these subjects that tested ADA negative through week 16 developed neutralizing antibodies after transition through week 52.

**Conclusion:** Transition from adalimumab RP to ABP 501 was not associated with higher immunogenicity.

**Disclosure:** Authors have been or continue to be employees and stockholders of AMGEN.

**P0994 GUT COLONIZATION WITH EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBOACTERIA MIGHT BE ASSOCIATED WITH CIPROFLOXACIN RESISTANCE IN INFLAMMATORY BOWEL DISEASE PATIENTS: PRELIMINARY STUDY RESULTS**

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**Introduction:** In complex bowel disease (IBD) patients are a risk group for antibiotic resistance because of the frequent hospitalizations, immunosuppressive therapy and treatment with antibiotics [1]. Extended spectrum beta-lactamase producing Enterobacteria (ESBL-E) are the most frequently found multidrug resistant microorganisms colonizing the gut of IBD patients. Also previous studies have shown that Ciprofloxacin use in IBD patients is higher comparing to non-IBD patients (27% vs 1%) [2]. There might be a link between these findings.

**Aims and Methods:** The aim of the study was to determine if there is an association between gut colonization with ESBL-E and Ciprofloxacin resistance in IBD out-patients. A cross-sectional study was conducted analysing all patients with confirmed ulcerative colitis (UC) or Crohn’s disease (CD) diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 5-year period (2013–2017). Patients participated in out-patient interviews, faecal biomaterial was obtained, Enterobacteria were cultured and analyzed for ESBL presence and Ciprofloxacin resistance according to EUCAST guidelines.

**Results:** A total of 34 patients with confirmed IBD diagnosis – 83.3% (n = 28) UC patients and 16.7% (N = 9) CD patients were enrolled in the study. Patient included 55.6% (n = 30) male and 44.4% (n = 24) female patients with the mean age of 44.74 (SD = 15.82) years. ESBL-E was found in 7.4% (n = 4) of the IBD cases. Ciprofloxacin resistance was found in 14.3% (n = 8) of the IBD cases. More patients with Ciprofloxacin resistance had also gut colonization with ESBL-E (75%; n = 3), whereas most patients without Ciprofloxacin resistance did not have gut colonization with ESBL-E (90%; n = 45) (p = 0.008). ESBL-E strains colonizing the gut included E. coli (n = 2), Enterococcus faecalis (n = 1) and Kl. pneumoniae (n = 1). Enterobacteria strains resistant to Ciprofloxacin included E. coli (n = 6), E. coli in combination with Kl. pneumoniae (n = 1) and Vancocycin-resistant enterococcus (n = 1). The severity of the Ciprofloxacin resistance in 2 cases showed high resistance (MIC > 32) and was found in E. coli.

**Conclusion:** Gut colonization with ESBL-E might be associated with Ciprofloxacin resistance in IBD out-patients. E. coli being the most commonly found and the most resistant strain linking the cases. Ciprofloxacin use should be avoided in IBD patients colonized with ESBL-E, especially ESBL producing E. coli.

**Disclosure:** Nothing to disclose

**References**

INTRODUCTION:
It has been suggested that the knowledge of serum concentration of the anti-TNF drug could be relevant in the management of inflammatory bowel disease (IBD) patients. However, a consistent clinical benefit of the adjustment of treatment based on drug levels in patients at remission has not been established.

Aims and Methods:
The aim was to evaluate whether anti-TNF drug levels in IBD patients can predict their outcome (that is, the risk of disease relapse during the following months).

Unicentre, observational, prospective study. All consecutive Crohn’s disease (CD) and ulcerative colitis patients on maintenance therapy with infliximab (IFX) or adalimumab (ADA) and being in clinical remission, were included. At inclusion, anti-TNF drug trough level was measured and, during a 6 months follow-up period from this measurement, the clinical outcome of the patients was evaluated. During the follow-up period, all therapeutic decisions (treatment withdrawal, anti-TNF dose escalation, switch to another anti-TNF or to another biologic), were based exclusively on standard clinical, analytical and endoscopic parameters. The cut-off to consider therapeutic anti-TNF trough levels based on our previous study was above 3.4 for IFX and 7.2 µg/mL for ADA.

Results: 102 patients in remission while receiving anti-TNF therapy were included (54% men, mean age at diagnosis 33 years, 80% CD, 65% were on ADA and 35% IFX). 34% were on IFX. Anti-TNF dose was escalated empirically in patients with sub-therapeutic anti-TNF levels, and 14% of the patients with sub-therapeutic anti-TNF trough levels relapsed at the end of follow-up (p<0.2). Also, there were no differences between CD or UC patients, and between patients who received ADA or IFX. Anti-TNF dose was escalated empirically in patients with clinical response, and 85% of them regained remission. 10 patients with sub-therapeutic anti-TNF trough levels (measured just previously to dose escalation) but also 3/3 with therapeutic levels before intensification.

Conclusion: Anti-TNF drug levels in IBD patients in clinical remission do not predict the risk of relapse during the following months. The majority of patients with sub-therapeutic anti-TNF trough levels remain in remission during follow-up. Therefore, therapeutic strategies based on anti-TNF trough levels in IBD patients in remission need further research.

Disclosure: J. Casanova, has received education funding from Pfizer, Janssen, MSD and Abbvie. M. Chapparo has served as a speaker, or has received research or education funding from MSD, Abbvie, Hospira, Pfizer, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma. Javier P. Gibert has served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Pfizer, Janssen, Biogen, Takeda, Janssen, Roche, Celgene, Ferring, Faes Pharma, Shire Pharmaceuticals, Dr. Falk Pharma, Tillotts Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Vifor Pharma.

Reference

P0996 CIPROFLOXACIN RESISTANCE IS HIGHER IN ULCERATIVE COLITIS PATIENTS WITH MORE SEVERE DISEASE ACTIVITY AND MORE EXACERBATIONS: PRELIMINARY STUDY RESULTS
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Introduction: Ulcerative colitis (UC) patients are a risk group for antibiotic resistance because of the frequent hospitalizations, immunosuppressive therapy and treatment with antibiotics [1]. Previous studies have shown that Ciprofloxacin use in UC patients is higher comparing to non-UC patients (27% vs 1%) [2]. In many cases Ciprofloxacin is given as empiric treatment by non-gastroenterologists to UC patients with exacerbations and higher disease activity. This could lead to higher antibiotic resistance and worse outcome in this particular UC phenotype.

Aims and Methods: The aim of the study was to determine if there is an association between Ciprofloxacin resistance and UC disease activity and what are the risk factors attributing to that. A cross-sectional study was conducted analysing all patients with clinically, endoscopically and histologically confirmed UC diagnosis previously hospitalized in two largest tertiary medical care centres in Riga, Latvia during a 5-year period (2013-2017). Participants included in outpatient interviews regarding their risk factors for Ciprofloxacin resistance, faecal biomaterial was obtained and analysed for Ciprofloxacin resistance according to EUCAST guidelines Version 7.1 and UC disease activity was evaluated according to the full Mayo score (FMS).

Results: A total of 45 patients with confirmed UC diagnosis, 56.6% (n = 25) male and 44.4% (n = 20) female patients with the mean age of 44.74 (SD = 15.82) years, were enrolled in the study. Ciprofloxacin resistance in faecal biomaterial was found in 17.8% (N = 8) of the cases. E. coli was the most frequently found bacterial strain resistant to Ciprofloxacin, found in 6 cases alone and in 1 case in combination with K. pneumonia. In 1 case Vancomycin-resistant enterococcus resistant to Ciprofloxacin was found. The severity of the Ciprofloxacin resistance for E. coli in 2 cases showed high resistance (MIC>32). Patients with Ciprofloxacin resistance had more severe disease – moderate or severe disease activity (FMS 6–12) compared to patients without Ciprofloxacin resistance – remission or mild disease activity (FMS 0–5) (p < 0.001). Also, the mean FMS was higher in patients with Ciprofloxacin resistance found in their faecal biomaterial – 2 (SD = 1.07), comparing to patients without Ciprofloxacin resistance – 1.1 (SD = 0.52) (p < 0.001). Differences in various factors that could attribute to Ciprofloxacin resistance were analysed in these UC patients and revealed no statistically significant differences between UC patients with and without Ciprofloxacin resistance regarding socio-demographic factors like age, gender, occupational factors like UC patients yearly international travels. Risk factors for Ciprofloxacin resistance included: history of previous hospitalizations, residence in a nursing home, antibiotic treatment, urinary tract infections and invasive manipulations in the past 12 months. The only factor was different between UC patients with and without Ciprofloxacin resistance was the number of UC exacerbations in the past 12 months. UC patients with Ciprofloxacin resistance had higher number of exacerbations 4.25 (SD = 4.92) comparing to UC patients without Ciprofloxacin resistance 1.23 (SD = 2.46) (p = 0.011).

Conclusion: There is a high resistance to Ciprofloxacin in UC patients. More severe disease and more exacerbation in the past 12 months increase the resistance to Ciprofloxacin. Ciprofloxacin use should be avoided in these UC patients, because this may lead to a higher antibiotic resistance and worse outcome in these patients.

Disclosure: Nothing to disclose.

References

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Introduction: Real-world treatment of inflammatory bowel disease (IBD) remains challenging. High adverse event rates and limited effectiveness of treatments in some patients may lead to early therapy discontinuation. The aim of this study was to assess treatment persistence with immunosuppressant (IS), anti-tumor necrosis factor (aTNF) and anti-integrin (aI) agents in patients with IBD.

Aim and Methods: We conducted a post-hoc descriptive analysis of patients diagnosed with ulcerative colitis (UC) or Crohn’s disease (CD) who were newly initiating treatment with IS, aTNF or aI from 01/01/2013-31/12/2015. Patients were identified from a German sickness fund (AOK PLUS), had continuous insurance coverage, and had no evidence of IS, aTNF or aI use for 12 months before the index date (date of newly initiating selected therapy during the study period). Treatment persistence was defined as percentage of patients still on index therapy after 12, 24 and 36 months, censoring for death and end of follow-up. Among patients were considered to have discontinued therapy if the new drug coverage gap > 60 days. Cox regression analysis was used to identify differences in mean persistence between the 3 treatment groups, adjusting for baseline characteristics.

Results: A total of 1,126 (UC: 450; CD: 676) met the inclusion criteria and constituted the treatment-naive IBD cohort used for the analysis. Mean age of UC and CD patients was 42.5 and 36.5 years; 47.6% and 60.5% were female. Among UC patients, IS was the most common (85.8%) index therapy, followed by aTNF (13.6%) and aI (0.7%). Among CD patients, IS was the most common (77.7%) index therapy, followed by aTNF (21.2%) and aI (1.2%). By 12 months, 55.7% of UC and 57.7% of CD patients discontinued their index therapy. Of the 990 patients followed for 24 months (UC: 395; CD: 595), 66.2% of UC and 67.8% of CD discontinued their index therapy. Of the 802 patients followed for 36 months (UC: 325; CD: 477), 73.1% of UC and 74.4% of CD discontinued their index therapy.

Adjusting for baseline characteristics, aTNF was associated with later treatment discontinuation compared with IS (hazard ratio [HR]: 0.364, pler <0.001) in UC patients. In CD patients, both aTNF and aI were associated with later treatment discontinuation compared with IS (aTNF HR: 0.562, p <0.001; aI HR: 0.187, p=0.018).

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Disclosure:

References:
1. Ingress-Heinrich, Wismar, Germany
2. IPAM e.V., Wismar, Germany
3. Roche Products Ltd., Websyn Garden City, United Kingdom
4. Genentech, Inc., South San Francisco, United States
5. AOK PLUS, Dresden, Germany
**P0998 ORALLY-ADMINISTERED EMU OIL ATTENUATES CLINICAL INDICATORS OF DISEASE IN A MOUSE MODEL OF ACUTE CROHN’S DISEASE**

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**Introduction:** Crohn’s disease (CD) is a chronic relapsing inflammatory bowel disease, characterised by severe transmural inflammation of the gastrointestinal tract. The aetiology of CD remains unclear and there is no known cure. Emu Oil (EO) is extracted from adipose tissue of the emu, a large flightless bird native to Australia. Previously, we demonstrated that orally-administered EO reduced inflammation and protected the intestine against experimentally-induced ulcerative colitis, colitis-associated colorectal cancer, NSAID-enteropathy and chemotherapy-induced mucositis.

**Aims and Methods:** To investigate whether orally-administered EO could attenuate disease severity in a trinitrobenzene sulfonic acid (TNBS) mouse model of CD. Female ARC(s) mice (n = 10/group) were intra-rectally administered 120 μl water or TNBS (3mg). Mice were orally-administered water or EO (80μl or 160μl) daily for five days and were cycled on day six. Bodyweight and disease activity index (DAI; four parameters including bodyweight loss, general condition, rectal bleeding and stool consistency) were recorded daily. Bubbling activity and faecal grimace parameters were assessed as behavioural measures of disease progression. Colonoscopy was performed to assess disease severity based upon thickening of the colon, changes to vasculature pattern, presence of neoplasms and mucosal surface and stool consistency. Additionally, proximal and distal colonic crypt depth, myeloperoxidase activity (indicative of acute inflammation) and fluorescein isothiocyanate dextran (indicative of proximal and distal colonic crypt depth, myeloperoxidase activity (indicative of acute inflammation) and fluorescein isothiocyanate dextran (indicative of intestinal permeability) uptake were quantified. p < 0.05 was considered statistically significant.

**Results:** Compared to normal controls, TNBS decreased bodyweight (days 1, 2 and 4; maximum 4.5% bodyweight reduction; p < 0.05) and increased DAI (days 1–6; maximum 11-fold increase; p < 0.01). Importantly, in TNBS-treated animals, both 80 and 160 μl volumes of EO significantly reduced DAI scores on days 5 and 6 (maximum 55% reduction) compared to controls (p < 0.05), though bodyweight loss remained unchanged. TNBS administration increased mouse grimace scores (11.5-fold; indicative of pain and distress), compared to normal controls; an effect significantly attenuated by both 80μl (11.5-fold decrease) and 160μl (5.4-fold decrease) EO treatment (p < 0.001). Colonoscopically-assessed disease severity score was greater in TNBS controls (11.5-fold decrease) and 160μl (5.4-fold decrease) EO treatment (p < 0.001). Colonoscopically-assessed disease severity score was greater in TNBS controls (11.5-fold decrease) and 160μl (5.4-fold decrease) EO treatment (p < 0.001).

**Conclusion:** Emu Oil reduced clinical indicators of disease severity, including distal colonic crypt depth, grimace pain scores and colonoscopically-assessed disease parameters in TNBS-treated mice. These findings suggest therapeutic efficacy for Emu Oil as an adjunct to conventional treatment approaches for Crohn’s disease.

**Disclosure:** Nothing to disclose.

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**P0999 LOW GOLIMUMAB TROUGH LEVELS AT WEEK 6 ARE ASSOCIATED WITH POOR CLINICAL, ENDOSCOPIC AND HISTOLOGICAL OUTCOMES IN ULCERATIVE COLITIS PATIENTS: PHARMACOKINETIC RESULTS OF THE EVOLUTION STUDY**

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**Introduction:** Golimumab (GLM) is a fully human anti-TNFα effective for induction and maintenance of response and remission in moderate to severe ulcerative colitis (UC) patients. Measurement of anti-TNFα serum trough levels (TL) is increasingly used to assist in physician decisions on dose (de) escalation or de-escalation to achieve the therapeutic target in IBD.

**Aims and Methods:** This study evaluated the association of GLM TL with clinical, endoscopic and histological disease activity measures and with fecal calprotectin (FC) levels in a multicenter, open label, nonrandomized, prospective study (ECClusively IBD: Eliminate the need for continuing therapy to achieve the therapeutic target in IBD). Subjects were followed for a period of 16 weeks with clinical assessments and data collection at screening, week 6 (W6) and week 16 (W16). GLM TLs and FC were measured at both W6 and W16. GLM TLs were assayed with an ELISA kit. All study data were summarized using descriptive statistics. Statistical tests were two-tailed and considering a significance level of 0.05.

**Results:** A total of 38 patients were treated, 34 (89.5%) completed through W6 (full analysis set, FAS) and 29 (76.3%) completed through W16. Nine patients (23.7%) discontinued the study during the trial; 80% were patients who did not achieve to severe active UC treated with GLM. Subjects were followed for a period of 16 weeks with clinical assessments and data collection at screening, week 6 (W6) and week 16 (W16). GLM TLs and FC were measured at both W6 and W16. GLM TLs were assayed with an ELISA kit. All study data were summarized using descriptive statistics. Statistical tests were two-tailed and considering a significance level of 0.05.

**Conclusion:** Results of a total of 38 patients were treated, 34 (89.5%) completed through W6 (full analysis set, FAS) and 29 (76.3%) completed through W16. Nine patients (23.7%) discontinued the study during the trial; 80% were patients who did not achieve to severe active UC treated with GLM. Subjects were followed for a period of 16 weeks with clinical assessments and data collection at screening, week 6 (W6) and week 16 (W16). GLM TLs and FC were measured at both W6 and W16. GLM TLs were assayed with an ELISA kit. All study data were summarized using descriptive statistics. Statistical tests were two-tailed and considering a significance level of 0.05.

**Disclosure:** Low GLM TLs are associated with poor clinical, endoscopic, histological disease activity measures and with fecal calprotectin outcome at W6 in UC patients treated with GLM. Our data add further evidence for an early exposure-response relationship in UC patients treated with golimumab.

**Disclosure:** Patricia Machado is an employee of MSD Portugal. Freddy Cornillote is an employee of Merck Sharp and Dohme, Kriens, Switzerland. Isabel Redondo was an employee of MSD Portugal at the time the study was conducted.

**References**

2. ID3monitor Immunodiagnostik AG.

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**P1000 RATE OF ADVERSE EVENTS ASSOCIATED WITH THE TREATMENT OF INFLAMMATORY BOWEL DISEASE IN GERMANY**

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7Hospital Garcia de Orta, Gastroenterology, Almada, Portugal
8Centro Hospitalar de Setúbal, Gastroenterology, Setúbal, Portugal
9Msd Portugal, Medical Affairs, Pago de Arcos, Portugal
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**Introduction:** Treating patients with inflammatory bowel disease (IBD) is challenging, as available therapies might be associated with substantial rates of adverse events (AEs). Our aim was to evaluate the rate of drug-related severe AEs and the associated health care costs among patients with IBD, who are receiving aminosalicylate (ASA), oral corticosteroid (OCS), immunosuppressant (IS), anti-tumor necrosis factor (aN TNF) or anti-integrin (α) agents in Germany.

**References**

2. ID3monitor Immunodiagnostik AG.
Aims and Methods: We conducted a retrospective cohort study of patients diagnosed with ulcerative colitis (UC) or Crohn’s disease (CD) who were newly initiating treatment with IS, anti-TNF or all from 01/01/2013-31/12/2015; chronic ASA and OCS use was also observed. Patients were identified from a German sickness fund (AOK PLUS), had continuous insurance coverage, and had no evidence of IS, anti-TNF or all use for 12 months before the index date (date of newly initiating therapy during the study period). The period after the index date was defined as follow-up. Rate of AEs, based on 28 different codes associated with inpatient encounters, and direct health care cost were reported separately for patients who experienced an AE and those who did not experience any AEs. Only treatment periods lasting ≥60 days were considered; patients could be assigned to ≥1 treatment during follow-up.

Results: A total of 1,126 (UC: 458; CD: 676) met the inclusion criteria. Mean age of UC and CD patients was 42.5 and 36.5 years; 47.6% and 60.5% were female. Among UC patients, 51.2% of observed follow-up time was covered by IS monotherapy index treatment, followed by anti-TNF mono (17.7%), ASA mono (15.0%), and OCS + IS (5.2%). Among CD patients, IS mono was the most common (45.3%) index treatment, followed by anti-TNF mono (27.3%), OCS + (9.0%), and OCS mono (5.3%).

A total of 157 patients (UC: 74; CD: 83) had at least 1 coded AE during follow-up; overall AE rate was 1,546 per 10,000 patient-years (TPPY). Most common AEs among patients with UC or CD were rates per TTPY) severe infection (UC: 320; CD: 90), diabetes mellitus (UC: 460; CD: 73), perianal disease (UC: 153; CD: 169) and bone-related conditions (UC: 292; CD: 51). Among the 157 patients, 126 patients (80.3%) experienced at least 1 switch from 1 treatment to another during the whole follow-up period, respective number in the whole sample was 66.5%.

In a multivariate analysis adjusting for key confounders available in the database, a higher comorbidity was associated with a higher AE rate. However, none of the treatments were significantly associated with a higher AE rate. Cost for patients with an AE were generally higher than for those without an AE (UC: 11,279 € vs 7,965 €; CD: 20,723 € vs 8,538 €).

Conclusion: Burden of severe AEs is substantial in IBD patients, with an event rate of 1,546/TTPY in this dataset. AE rates did not differ between IBD treat-ments in our study, which may also be due to low sample size. We observed that AE rates were associated with a higher AE rate. However, none of the treatments were significantly associated with a higher AE rate. Cost for patients with an AE were generally higher than for those without an AE. In CD patients, presence of a previous extraintestinal manifestation was associated with a higher AE rate. However, none of the treatments were significantly associated with a higher AE rate. Cost for patients with an AE were generally higher than for those without an AE.

Disclosure: This study was financially supported by Genentech Inc. Thomas Wilke has received honoraria from several pharmaceutical/consultancy companies e.g. Novo Nordisk, Abbvie; Merck; GSK, BMS, LEO Pharma, Astra Zeneca, Bayer, Boehringer Ingelheim, Pharma. Number study: MA39587

P1002 REAL-WORLD EFFECTIVENESS OF VEDOLIZUMAB AND ANTI-TUMOUR NECROSIS FACTOR-ALPHA OVER 6 MONTHS IN ULCERATIVE COLITIS PATIENTS: A GERMAN RETROSPECTIVE CHART REVIEW

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6Takeda Pharmaceuticals International – Zurich Branch, Zurich, Switzerland
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Introduction: Vedolizumab (VDZ), an α4β7 integrin antagonist, was approved in Germany in 2014 for the treatment (Tx) of moderately to severely active ulcerative colitis (UC). This study descriptively assessed the real-world effectiveness and safety of VDZ and anti-tumour necrosis factor-alpha (anti-TNFα) after VDZ was introduced in Germany.

Aims and Methods: A retrospective chart review (15 sites) investigated patients (pts) with UC who were biologic- (bio-) Tx naïve or had received one prior anti-TNFα at initiation of index Tx with VDZ or anti-TNFα between 15 July 2014 and 20 October 2015. Time to first documented clinical remission (total Mayo or partial Mayo score ≤2 and no subscore >1), rectal bleeding (RB) resolution (score of 0) and stool frequency (SF) resolution (score of 0 or 1) were assessed using time-to-event Kaplan-Meier analyses over 26 weeks.

Abstract No: P1002

<table>
<thead>
<tr>
<th>Follow-up Week</th>
<th>Outcome</th>
<th>Bio-naïve: Anti-TNFα</th>
<th>Bio-naïve: VDZ</th>
<th>Prior anti-TNFα: Anti-TNFα</th>
<th>Prior anti-TNFα: VDZ</th>
<th>Prior anti-TNFα: Total</th>
<th>Anti-TNFα: Total</th>
<th>VDZ: Total</th>
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<td>Week 1</td>
<td>Clinical remission</td>
<td>10.6 (5.8)</td>
<td>29.4 (11.1)</td>
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<td>17.2 (6.4)</td>
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<td>Week 2</td>
<td>RB resolution</td>
<td>17.0 (6.9)</td>
<td>46.9 (12.9)</td>
<td>7.7 (7.4)</td>
<td>22.5 (7.5)</td>
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<tr>
<td>Week 3</td>
<td>SF resolution</td>
<td>29.2 (8.2)</td>
<td>33.0 (12.1)</td>
<td>22.6 (11.5)</td>
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<td>Week 4</td>
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<td>RB resolution</td>
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<td>48.5 (9.5)</td>
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<td>Week 7</td>
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<td>31.5 (9.4)</td>
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<td>Week 8</td>
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<td>52.0 (15.0)</td>
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<td>Week 9</td>
<td>SF resolution</td>
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<td>50.7 (8.0)</td>
<td>59.8 (7.9)</td>
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</table>

[Kaplan-Meier Estimates of Responders Over 26 Weeks, % (standard error)]
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P1004 REMISSION INDUCTION IN CORTICOSTEROID NAIVE CHILDREN AND ADOLESCENTS WITH ULTRASEVERE COLITIS BY ADSORPTIVE LEUCOCYTE APHERESIS AFTER FAILURE OF FIRST LINE MEDICATIONS

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P1005 FAECAL CALPROTECTIN IN HEALTHY CHILDREN (0 TO 18 YEARS OLD) AND THE INFLUENCE OF AGE, GENDER AND ANTHROPOMETRY

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Introduction: Previous studies report that faecal calprotectin (FC) can be altered by factors like body weight, Body Mass Index (BMI) and age (see references 1-9), but many of them have methodologic limitations.

Aims and Methods: Our primary aim was to (i) establish normal levels of FC in healthy children living in a Spanish urban environment; and (ii) analyse correlation of FC with age, gender and anthropometry.

We included 395 subjects from 3 days to 16.9 years old (mean 4.2 years, ±2.7 standard deviation (SD)) who attended the participating primary health centers for routine pediatric controls. The exclusion criteria were: (i) immunodeficiency; (ii) autoimmune disease; (iii) gastrointestinal disease; (iv) intake of drugs; (v) gastrointestinal symptoms; or (vi) any positive finding in the associated microbiological study. We determined the FC levels (Quantum Blue® test, and performed stool cultures, parasites, rotavirus and adenovirus detection. The statistical analysis (SPSS® software) considered a P value<0.05 statistically significant.

Results: We included 395 subjects from 3 days to 16.9 years old (mean 4.2 years, ±2.7 standard deviation (SD)) who attended the participating primary health centers for routine pediatric controls. The exclusion criteria were: (i) immunodeficiency; (ii) autoimmune disease; (iii) gastrointestinal disease; (iv) intake of drugs; (v) gastrointestinal symptoms; or (vi) any positive finding in the associated microbiological study. We determined the FC levels (Quantum Blue® test, and performed stool cultures, parasites, rotavirus and adenovirus detection. The statistical analysis (SPSS® software) considered a P value<0.05 statistically significant.

Results: We included 395 subjects from 3 days to 16.9 years old (mean 4.2 years, ±2.7 standard deviation (SD)) who attended the participating primary health centers for routine pediatric controls. The exclusion criteria were: (i) immunodeficiency; (ii) autoimmune disease; (iii) gastrointestinal disease; (iv) intake of drugs; (v) gastrointestinal symptoms; or (vi) any positive finding in the associated microbiological study. We determined the FC levels (Quantum Blue® test, and performed stool cultures, parasites, rotavirus and adenovirus detection. The statistical analysis (SPSS® software) considered a P value<0.05 statistically significant.
were not confirmed when analysing their SDs. This may reflect the role of age as a confounding factor. We found a negative correlation between height (both absolute values and SD) and FC, which had not been previously described. Based on this, it seems necessary to reconsider the levels of FC deemed patho-

Table 1: FC levels in each age group. 10thP: 10th percentile. 50thP: 50th percentile. 90thP: 90th percentile.

Table: Nothing to disclose

References


P1006 OUTCOME OF INFLAMMATORY BOWEL DISEASE IN CHILDREN WITH PRIMARY SCLEROSING CHOLANGITIS

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3Helsinki University and Helsinki University Hospital/Department of Pathology, Helsinki, Finland
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Introduction: Inflammatory bowel disease (IBD) seems to have a unique pheno-

Aims and Methods: The aim of this retrospective case-control population-based study was to investigate the outcome of IBD in a cohort of subjects with a paediatric-onset of IBDS-P and in a matched group of patients with IBD only.

Results: At diagnosis, 20 IBD-PSC children (74%) had pure PSC and 7 (26%) PSC-

Conclusion: The course of paediatric onset IBD in patients with IBD-PSC seems to be more benign than in those with pure IBD, in line with reports in adult popula-

Disclosure: Nothing to disclose

References


P1007 PLANNED TRANSITION OF ADOLESCENT INFANITILY BOWEL DISEASE PATIENTS FROM PEDIATRIC TO ADULT CARE RESULTS IN HIGHER REMISSION RATES

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2University of Pécs, Institute of Bioanalysis, Pécs, Hungary
3University of Pécs, Department of Pediatrics, Pécs, Hungary

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Introduction: As a result of increasing incidence of pediatric-onset inflammatory bowel disease (IBD) growing number of adolescents need handover to adult care. Whereas transfer is essentially only an event, transition is a well-planned, coordi-

Aims and Methods: We aimed to evaluate the effect of our current structured transition process on clinical outcomes in adolescent inflammatory bowel dis-

Conclusion: Planned transition visits resulted in higher disease remission rate at 1-

Disclosure: Nothing to disclose

References

1. Scarpini A, et al. Faecal calprotectin to select UC patients with significant differences in disease duration before transfer, Montreal classifica-

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Introduction: At our gastroenterology clinic, we receive patients with ulcerative colitis (UC) who wish to avoid hospitalization, require treatment in an outpatient setting. Additionally, with the availability of granulomocytapheresis (GMA, Adacolumn) therapy, most of our patients favour this non-pharmacologic option as the first-line therapy to avoid pharmacologicals. In fact, most elderly UC patient have multiple other complications as co-morbidities, which may include diabetes, hypertension, cardio-cerebral disease, and therefore, are likely to be on

Results: At diagnosis, 20 IBD-PSC children (74%) had pure PSC and 7 (26%) PSC-

Disclosure: Nothing to disclose

References

1. Scarpini A, et al. Faecal calprotectin to select UC patients with significant differences in disease duration before transfer, Montreal classifica-

To be more benign than in those with pure IBD, in line with reports in adult popula-

P. Sarlos1, O. Caroline2, D. Fehér1, N. Farkas2, A. Vince1, A. Tarnok3

1University of Pécs, 1st Department of Internal Medicine, Pécs, Hungary
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P. Sarlos1, O. Caroline2, D. Fehér1, N. Farkas2, A. Vince1, A. Tarnok3

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Aims and Methods: We aimed to evaluate the effect of our current structured transition process on clinical outcomes in adolescent inflammatory bowel dis-

Conclusion: Planned transition visits resulted in higher disease remission rate at 1-

Disclosure: Nothing to disclose

References
other medications. Likewise, in younger UC patients, we like to avoid cortico-steroids, which may adversely affect their overall growth and development.

Aims and Methods: Therefore, we have been applying GMA as a first-line therapy before any drug based medication hoping to spare our young and elderly patients from pharmacologicals. In a retrospective setting, we reviewed the treatment outcomes of 132 patients with UC who had received granulomonocytapheresis (GMA) with the Adacolumn as remission induction therapy at our gastroenterology clinic over the past 11 years. The patients were divided into three groups, under 18 years of age (Group 1, n = 8), 18 to 64 years of age (Group 2, n = 106), and beyond 64 years of age (Group 3, n = 13). In each group, patients’ age, gender, UC profile, location, duration, and past medications were factorized for analysis to determine the clinical response GMA therapy. Clinical activity index (CAI) ≤4 meant remission.

Results: Each patient received up to a maximum of 11 GMA sessions at 1 to 5 sessions per week. The clinical response together with remission rates were 87.5% in Group 1, 77.7% in Group 2, and 84.6% in Group 3. Similarly, the clinical remission rates were 87.5% in Group 1 (all 8 patients), 63.8% in Group 2, and 53.8% in Group 3. Further, in the Group 1, younger patients showed pancolitis, while in Group 3, elderly patients had a short disease duration, most of them had developed UC around 60 years of age, the so-called elderly onset UC. In all 3 groups, GMA therapy was well tolerated and was without any severe adverse event.

Conclusion: The efficacy outcomes in our patients are very much higher than previous studies reported for GMA in patients with severe UC, refractory to pharmacologicals. However, in our patient group, GMA is a very much welcomed treatment option for young and elderly patients because of its good safety profile, as well as for being a non-pharmacologic treatment option. Provided patients can afford to make frequent visits to the treatment centre and the medical personnel can accommodate blood access, GMA should be a first-line therapy before corticosteroids or other pharmacologicals.

Disclosure: Nothing to disclose.
Introduction: Recent abdominal pain (RAP) is a common complaint during childhood, but the natural history of childhood RAP and pain-predominant functional gastrointestinal disorders (pFGID) in the general population remains poorly understood.

Aims and Methods: The aim of the current study was to describe the prevalence and nature of childhood RAP during the first 16 years of life and to explore the association between childhood RAP and Rome III defined pFGID in adolescence.

In this prospective Swedish population-based birth cohort study of 4089 children, parents and children answered questionnaires on gastrointestinal symptoms at 1, 2, 12, and 16 years and doctor's diagnosis of inflammatory bowel disease (IBD) and celiac disease (CD) at 12 and 16 years. RAP at 1 and 2 years was defined as repeated attacks of colic for the past 6 and 12 months respectively, and was pooled and called early childhood RAP. RAP at 12 and 16 years was defined as self-reported weekly abdominal pain with no parent-reported diagnosis of IBD and/or CD. pFGID at 16 years were defined according to the Rome III criteria and included irritable bowel syndrome (IBS), functional dyspepsia (FD) and functional abdominal pain (FAP). Sex-adjusted associations were examined using binomial generalized linear model and presented as relative risk (RR) with 95% confidence interval (CI).

Results: Any history of RAP between early childhood and 16 years was reported in 33.0% (980/2988) of children. The prevalence of RAP peaked at 16 years in both boys and girls. Prevalence rates were significantly higher for girls compared to boys at 12 (p < 0.01) and 16 years (p < 0.01), but not in early childhood. In the subgroup of children with RAP who had completed the detailed Rome III questionnaire at 16 years (498/609, 69.9%) the criteria for any pFGID, IBS was the most common phenotype in both boys and girls. The prevalence of pFGID was higher in girls than in boys (p < 0.01). See Table below.

Early childhood RAP at 1 and 2 years reported persisting symptoms at the following assessment point in 6.8% (11/161) and 43.4% (43/99) of cases respectively. It was more common for girls than for boys to report persisting symptoms between early childhood and 12 years old. No association was found between early childhood RAP and RAP at 12 years or any pFGID, and IBS at 16 years.

Children with RAP at 12 years had an increased risk for RAP at 16 years (RR 2.4, 95% CI 1.9–3.0) for any pFGID at 16 years (RR 2.5, 1.8–3.4) and for IBS at 16 years (RR 3.2, 2.0–5.0). No association was found between early childhood RAP and RAP at 12 years or any pFGID, and IBS at 16 years.

Clinical follow-up of a subsample of children (87/175) fulfilling the Rome III criteria for IBS at the 16-year questionnaire, confirmed the diagnosis of IBS in 78.2% of cases.

Conclusion: RAP is common in childhood, but most children with RAP do not have persisting symptoms throughout childhood. However, reporting RAP at 12 years is an independent risk factor for RAP, any pFGID, and IBS at 16 years.

Disclosure: Nothing to disclose.

References

Abstract No: P1013

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<th>16 years</th>
<th>Childhood RAP</th>
<th>12 years RAP</th>
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<td></td>
<td>Boys</td>
<td>Girls</td>
<td>Any</td>
</tr>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
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</tr>
<tr>
<td>Total</td>
<td>256 (6.7)</td>
<td>119 (4.3)</td>
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<tr>
<td>Boys</td>
<td>135 (7.0)</td>
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<td>210 (14.1)</td>
</tr>
<tr>
<td>Girls</td>
<td>121 (6.5)</td>
<td>86 (6.2)</td>
<td>399 (25.8)</td>
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</tbody>
</table>

[Prevalence of RAP and Rome III pFGID in children and adolescents in a population-based birth cohort]
physical activity, and psychological status at baseline were included. Children who developed movements less frequently than once every 2 days was defined as being constipated. Children who had already constipated at baseline were excluded.

**Results:** Out of 10438, 6662 children (63.8%) were included in our longitudinal study. In total, 317 (4.8%) developed constipation during the 3-year follow-up interval. Logistic regression analysis showed that the development of constipation was significantly associated with being girl (odds ratio [OR] = 2.33), infrequent intake of fruit (OR = 1.60), physical activity, TV viewing, sleep duration, and psychological status at baseline was not associated.

**Conclusion:** Only dietary pattern of taking fruits infrequently predicted a constipation in school children. Lifestyles and psychological status at baseline might change and not affect on development of constipation during the period. Longitudinal study with shorter follow up interval will be needed to clarify the risk factors of childhood constipation.

**Disclosure:** Nothing to disclose

**References**

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**P1015 IDENTIFYING PREDICTIVE FACTORS FOR THE RECURRENCE OF PAEDIATRIC INTUSSUSCEPTION**

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**Introduction:** Intussusception is one of the most emergent gastrointestinal disease in paediatric patients, which sometimes lead to the perforation, necrosis, and even death if the initial diagnosis is delayed.

**Aims and Methods:** The aim of this study was to identify the related factors of the recurrent intussusception in the paediatric patients. The medical record of the intussusception patients who were diagnosed and treated at Dongsan Medical Center from March 2015 to June 2017 was retrospectively reviewed. Baseline demographic findings, the time interval from the symptom onset to the treatment of reduction or operation, the reduction methods (barium enema vs. water enema), the presenting symptoms such as vomiting, bloody stool, abdominal pain or irritability, and lethargy, the history of previous or concurrent infection, the radiologic findings and laboratory findings were analyzed. The pathologic leading points and operation methods were investigated too.

**Results:** Among the total of 137 patients, the male to female ratio was 1.4 (male = 80, 56.7%, female = 57, 40.4%). The mean age was 2.17 ± 1.36 years with a range of 0.18 to 10.1 years. The mean interval time from the symptom onset to the reduction time was 24.59 ± 25.64 hours with a range of 2 to 168 hours. The mean age for recurrence group was 5.35 ± 2.72 years and the interval time from the initial reduction to recurrence was 50.96 ± 25.52 hours. The reduction methods were the water reduction (n = 69, 48.9%), the barium reduction (n = 44, 44.5%), open reduction without spontaneous reduction (n = 5, 3.21%) and spontaneous reduction (n = 3, 2.1%). The type of intussusception was mostly ileocolic (n = 136, 96.5%), with one small bowel case (n = 1, 0.7%). The diagnosis age and the intussusception head size on ultrasonography were significantly related with the recurrence of intussusception (p = 0.006, p = 0.028, respectively). In laboratory analysis, CRP was significantly higher in the recurrence group (1.03 ± 1.49 vs. 1.49 ± 2.68, p = 0.024). Bloody stool and history of infection were significantly more frequent in the non-recurrence group (p = 0.001, p = 0.000), and vomiting, abdominal pain or irritability, and lethargy did not show any significant difference between the two groups. No pathologic leading point except for enlarged lymph nodes was found.

**Conclusion:** The diagnosis age, CRP and the mass size in radiologic finding was significantly related with the recurrence of intussusception.

**Disclosure:** Nothing to disclose

**References**
2. Schmulson M J, Drossman D A, (2017). What Is New in Rome IV, Dealing with the History of Familial Trauma, lower QoL, more medical examinations, lower anxiety levels (both STAI Y1 and Y2), and higher perceived self-efficacy in the management of negative emotions. It also detected lower levels of alexithymia and tobacco use. The PGQ is a novel, easy-to-use, questionnaire deserving further investigation for its potential utility in the assessment of the psycho-gastroenterological profile of children and adolescents affected by DGBI.
P1018 THE ROLE OF THE METABOLIC ACTIVITY OF THE INTESTINAL MICROFLORA IN CHILDREN WITH IMMUNE THROMBOCYTOPENIC PURPURA RESISTANT TO CORTICOSTEROID THERAPY

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Introduction: Immune thrombocytopenic purpura (ITP) is a disease characterized by isolated thrombocytopenia of less than 150×10⁹/l with a normal or increased platelet count. ITP is an idiopathic disease that accounts for 90% of all immune disorders of the bone marrow. The pathogenesis of ITP is thought to be associated with immune mechanisms, with plaques of autoantibodies being a cause of ITP. The presence of autoantibodies against platelets causes their increased destruction.

Gastrointestinal disorders in ITP directly related to the underlying diseases cause the development of intestinal microbiota disorders in children.

Aims and Methods: To evaluate the metabolic activity of the intestinal microflora based on the stool short chain fatty acids levels assessment by gas-liquid chromatography. The study included 41 patients (19 girls and 22 boys) aged from 2 to 17 years (mean age = 10.23 years, median age = 10 years) with ITP resistant to corticosteroid therapy. All patients were observed in the hematology and oncology of the Russian Children’s Clinical Hospital (Moscow).

All patients underwent conventional clinical-instrumental and an assessment of the metabolic activity of the intestinal microflora based on the stool short chain fatty acids levels assessment by gas-liquid chromatography.

Results: In children with ITP resistant to corticosteroid therapy a wide range of gastrointestinal symptoms were identified, including abdominal pain (14/41, 34.1%), bloating (15/41, 36.5%), heartburn (7/41, 17.1%), stool disorders (8/41, 19.5%), indirect signs of intestinal digestion (4/41, 9.76%) and absorption abnormalities (41/41, 100%). The revealed disturbances in the metabolic activity of the intestinal microflora were characterized by an increased production of the acidic, aromatic, valeric acids and also isovaleric acid. A significant increase in the isocyanates production and a slightly increased ratio of E/C/EC (10/16, 62.5%), indicating a predominance of iso-acids over non-isos, a significant predominance of isovaleric acid (an increase in the ratio of iC5/C5 in 68.75% of patients with ITP) was observed. Additionally, the anaerobic index was increased.

Conclusion: In children with ITP resistant to corticosteroid therapy, a wide range of gastrointestinal complaints were identified, as well as changes in intestinal microflora expression and disturbance of short chain fatty acids production, indicating an increase in the activity of the saccharolytic flora, accompanied by an increase in the activity of proteolytic microorganisms uncharacteristic for normal microbiota with an increase in the fraction anaerobes.

Disclosure: Nothing to disclose.

P1019 INHIBITORY EFFECT OF URSEDOXYCHOLIC ACID ON CLOSTRIDIUM DIFFICILE GERMINATION IS IN-SUFFICIENT TO PREVENT C. DIFFICILE COLITIS: A STUDY IN HAMSTERS AND HUMANS

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Introduction: Clostridium difficile infection (CDI) is a public threat due to its recurrence and severity. Facial transplantation is more effective on antibiotics in reducing recurrences, but with some unknown risks. Bile acids (BA) are known to influence germination and growth of C.difficile: taurocholate acid (TCA), a primary BA, promotes germination and growth of C. difficile (1). Secondary BA inhibit the germination and growth (2). Ursodeoxycholic acid (UDCA), a tertiary BA minor in humans, inhibits germination and growth of C. difficile in vitro (2,3), but was never tested in vivo with an infectious challenge. We hypothesized that we could use UDCA for prevention of CDI. We evaluted the effects of UDCA on C.difficile in vitro on germination and growth and in vivo in an animal model, with pharmacoekinetcs study and prevention of CDI. We then studied the infection incidence in UDCA-treated patients.

Aims and Methods: In vitro trials evaluated germination and growth of several strains of C.difficile by optical density measurements and colony count, with 0.01%, 0.05% and 0.1% UDCA, in competition with 0.1% TCA. We analysed faecal BA of hamsters receiving antibiotics and UDCA (50mg/kg/day), antibiotics alone, or UDCA alone. Then, we challenged with spores of C.difficile at D6 hamsters receiving UDCA (50 mg/kg/day), antibiotics, or UDCA. Their survival, colonization and BA were evaluated. In human, we analysed the database of a cohort that studied CDI in acute flares of inflammatory bowel disease (IBD) from September 2012 to May 2014 (4). As PSC-IBD patients were with UDCA treated with UDCA did not show less CDI than IBT patients.

Disclosure: Mayoli Spindler (financial support for hamsters and ursodeoxycholic acid ); H. Duboc: Biocodex, IPSEN ; S. Hoys and C. Janoir: Biocodex, MSD

References
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P1020 SIGNIFICANT DIFFERENCES IN THE GUT MICROBIOME OF PATIENTS WITH ACTIVE PSORIASIS

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Introduction: Alterations in the gut microbiome have been implicated in the pathogenesis of several immune-mediated inflammatory diseases such as in patients with psoriatic arthritis. Psoriasis is a chronic, inflammatory, multi-organ disease characterized by papulosquamous lesions with varying morphology, distribution, severity and course.

Aims and Methods: To characterize the gut microbial signature of patients with active psoriasis as compared to matched non psoriatic control participants and to determine whether these changes translate to differences in expression of significant metabolic pathways.

This observational prospective multicenter study was conducted at the Tel Aviv Medical Center (TLVMC) and Maccabi healthcare services (MHS). Patients’ clinical details were recorded and stool was collected and stored at ~80 °C. In parallel matched controls were recruited. Fecal samples were processed and 16S rRNA was sequenced using the Illumina platform. This data as well as clinical data of the patients and healthy cohorts were compared. A false discovery rate (FDR) of 0.1 was considered statistically significant. A multivariate analysis was performed to correct for confounding variables. PICRUSt was used to determine whether there were differences in genes encoding various metabolic pathways between the cohorts.

Results: Forty-two participants were recruited to the study of whom 52% (n=24) suffered from psoriasis. Psoriatic patients were older (52.7± 11.6 vs. 43.9±12.7, p=0.02) and had a lower body mass index (BMI) (25.5 ± 2.9 vs. 27.3 ± 4.3 kg/m², p=0.05) compared to control patients, respectively. There was a significant difference in the beta-diversity between the two patient groups. Psoriatic patients had a significant increase in the Firmicutes and Actinobacteria phyla, while Bacteroidetes and Proteobacteria were decreased compared to the control cohort. At the genus level, significant differences were detected between the 2 patient groups, using the LEfSe analysis (Table 1). At the species level, there were significant increases (FDR<0.05) in Ruminococcus gnavus, Dorea formicigenerans, and Collinsella aerofaciens, in the psoriasis group, while Prevotella copri, and Parabacteroides distasonis were significantly increased in the control group. A microbial gene analysis (P1020) revealed increased in metabolic pathways related to lipopolysaccharide function in the psoriatic cohort. These differences are summarized in Table 1.

Genus Psoriatic cohort Healthy cohort P-value FDR
Blautia 0.131 0.025 0 0.00002
Faecalibacterium 0.069 0.033 0 0.006 0.028

(continued)
A1021 DIFFERENCE OF COLORECTAL CANCER MICROBIAL COMMUNITY A BY METAGENOMICS AND CULTURE-BASED METHODS

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Introduction: Dysbiosis of intestinal microbiota is promoting the development of colorectal cancer (CRC). We confirmed the intestinal microbiota composition from fecal sample of Korean CRC patients. Metagenomic analysis was performed and we isolated single microbes through culture-based method.

Aims and Methods: CRC fecal samples were collected from 12 individuals. Metagenome Sequencing was based on the 16S rRNA gene amplicon on the Illumina MiSeq platform. The bacteria strains were subcultivated on the agar plate medium in aerobic and anaerobic and further identified by using the 16s rRNA gene sequencing.

Results: Bacteria diversity by metagenome analysis was decreased in CRC group compared to control group. In CRC group, relative abundance of Firmicutes and Bacteroidetes were increased while the prevalence of Proteobacteria was decreased. The difference of microbial composition between control and CRC group was found at the genus level. Bacteroides, Parabacteroides of the phylum Bacteroidetes has increased and the genus Acinetobacter, Pseudomonas of Proteobacteria decreased in CRC group compared to control group. In addition to, we have isolated various strains associated with CRC by culture-based method.

Conclusion: Adherence to a healthy lifestyle is inversely associated with both distal and proximal colorectal adenomas. The protective association seems to start from adherence for a minimum of 2 healthy lifestyle characteristics. An independent protective association was detected between refraining from smoking and maintaining a healthy diet.

P1022 A HEALTHY LIFESTYLE IS INVERSELY ASSOCIATED WITH BOTH PROXIMAL AND DISTAL COLORECTAL ADENOMAS

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Introduction: Diet and lifestyle characteristics were previously shown to be associated with colorectal neoplasia, mainly in the distal colon and less at the proximal colon. However, these associations need further confirmation and elaboration and were tested with a global lifestyle score.

Aims and Methods: We aimed to explore the association between nutritional and lifestyle components, and a global lifestyle score, with the presence and laterality of colorectal polyps. We conducted a case-control study among patients undergoing colonoscopies during 2010-2015 at our department. Cases were defined by detection of an adenomatous or serrated polyps. Polyp location was defined as proximal (ecum to splenic flexure), or distal (descending to anus). Controls were defined as those without past/current colonic polyps. Data collection included: anthropometrics, medical history and dietary intake evaluated by a structured questionnaire. We adopted a lifestyle score composed of four healthy lifestyle factors from the strategic goals of the American Heart Association: refraining from current/past smoking, absence of obesity, regular performance of physical activity, and a healthy diet (adherence to ≥ 5 of 11 dietary recommendations).

Results: A total of 328 cases of adenomas (proximal n = 164 and distal n = 164), and 376 controls were included in the study. The proportion of participants adhering to an unfavorable lifestyle pattern (<2 lifestyle factors) was lower among controls relative to cases of colorectal adenomas (28.3% vs. 44.2%, p<0.001). This difference was detected both in cases with proximal adenoma (39.6%, p = 0.009 compared with controls) and distal adenomas (48.8%, p<0.001 compared with controls). Similar results were obtained for all polyps types (adenomas and serrated polyps). In multivariate analysis, each addition of one of the four healthy lifestyle factors was negatively associated with colorectal adenomas (OR = 0.76, 95% CI 0.65-0.90). Associations were significant for both distal and proximal adenomas (OR = 0.78, 0.63-0.96 and OR = 0.73, 0.60-0.90, respectively). Refraining from smoking and maintaining a healthy diet were the factors most strongly associated with lower odds of colorectal adenomas (OR = 0.69, 0.50-0.97 and OR = 0.63, 0.45-0.89, respectively), after adjustment for age, gender, low socio-economic status, use of aspirin, NSAIDs, statin and antidiabetic medication, smoking intake, colonoscopy indication and for one another. These associations were significant for both distal adenomas (OR = 0.63, 0.42-0.95 and OR = 0.63, 0.42-0.96, respectively) and proximal adenomas (OR = 0.70, 0.46-1.65 and OR = 0.59, 0.38-0.90, respectively). The number of healthy lifestyle factors was negatively associated with odds of colorectal adenoma, both distal and proximal (Table 1). Also in these analyses similar results were obtained for all polyps types, and for serrated polyps compared with controls.

Conclusion: Adherence to a healthy lifestyle is inversely associated with both distal and proximal colorectal adenomas. The protective association seems to start from adherence for a minimum of 2 healthy lifestyle characteristics. An independent protective association was detected between refraining from smoking and maintaining a healthy diet.

Disclosure: Nothing to disclose

P1023 COMPARISON OF FIT-BASED COLORECTAL CANCER SCREENING PROGRAMMES

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Introduction: Many countries or regions have implemented colorectal cancer (CRC) screening by faecal occult blood testing (FOBT), in particular by means of faecal immunochemical testing (FIT). (1) FOBT as screening method is also recommended by the European guidelines.2 The effectiveness of population-based screening programmes is not only driven by the sensitivity of the screening method but also depends on the availability of resources, infrastructure and population preferences in each country. Population preferences especially are reflected in participation rate.

Aims and Methods: This study compared designed performance of four faecal immunochemical testing (FIT)-based screening programmes for colorectal cancer (CRC) in Flanders (Belgium), France, Basque country (Spain) and the Netherlands with the aim of future optimization of the different programmes. Background information and data on main performance indicators were collected and compared for the four screening programmes.

Results: Invitation approach differed most strikingly between the four programmes: In France only an invitation letter is send by mail, while the sample kit needs to be collected at general practitioner (GP). In the other programmes, the invitation letter is accompanied by a postcard. Cases of CRC in Flanders and the Netherlands also send a pre-invitation letter prior to the invitation. Interestingly, participation rates vary substantially with method of invitation with the highest participation rates in the Netherlands (73.0%) and Basque country (72.4%), followed by Flanders (54.5%) and France (33.5%). FIT positivity rate ranged from 4.6–6.6% in the programmes. Basque country (91.5%) and France (88.9%) had the highest participation rate with colonoscopy following a positive FIT test.

Disclosure: Nothing to disclose
Conclusion: Large differences in screening participation were observed between programs with regular mailings and mailed kits, with findings suggesting that changes to the design of the programme, such as a pre-invitation letter and including the sample kit with the invitation, might increase participation. The high participation to colonoscopy in Basque country and France might indicate that in programs with active involvement of GPs individuals are more likely to undergo a colonoscopy.

Table 1: Performance indicators for France, Flanders, the Netherlands and Basque country

<table>
<thead>
<tr>
<th>Indicator</th>
<th>France</th>
<th>Flanders</th>
<th>Netherlands</th>
<th>Basque country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participation rate FIT</td>
<td>28.6%</td>
<td>54.5%</td>
<td>73.0%</td>
<td>72.4%</td>
</tr>
<tr>
<td>Participation rate colonoscopy</td>
<td>88.9%</td>
<td>85.8%</td>
<td>82.8%</td>
<td>91.5%</td>
</tr>
<tr>
<td>Detection rate Advanced neoplasia</td>
<td>1.3%</td>
<td>1.1%</td>
<td>2.3%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Diagnostic yield program</td>
<td>0.5%</td>
<td>0.5%</td>
<td>1.6%</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

Disclosure: Nothing to disclose

References

P1024 IMPACT OF COLORECTAL CANCER SCREENING PROGRAMS ON SURGICAL PROCEDURES IN THE VENETO REGION (NORTH EAST ITALY)

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Introduction: Colorectal cancer (CRC) is a leading cause of cancer mortality in the Veneto Region (North-East Italy). Population screening of adults between 50 and 74 for CRC was begun in 2002, and it became standard practice in all 21 local health units (LHU) of the region in 2008.

This study was carried out to evaluate the impact on surgery rates of CRC screening programs.

Aims and Methods: This is a retrospective cohort study carried out from a population-based archives represented by hospital discharge records (HDR) that includes all hospitalizations with up to six diagnoses recorded according to the ICD9-CM.

All discharges from 1 January 2000 to 31 December 2017 of Veneto population in screening age with principal diagnosis of CRC treated with surgery were included in the study.

The number of patients studied by screening rose approximately of 20% reaching 1,597,826 for the last year (2017) and Veneto region can be subdivided into 3 areas stratifying by screening programs introduction period: A – early (2002-2004), B – intermediate (2005-2007), and C – late (2008) areas.

The Standardized Hospitalization Ratio (SHR) per five-year age group (ref. pop. Veneto 2009) was calculated and expressed per 100,000 population.

Results: During the study period, 29,704 surgical procedures for colorectal cancer were performed (58% in males, 42% in females, 36% in the rectum, 36% in the sigmoid, 6% in the transverse and 3% in the splenic flexure) with a rate of 50.7 (95% CI: 50.6-50.7) per 100,000 in the region.

An analysis of the annual SHR distribution uncovered two distinct phases: during the first phase there was a rising trend that reached a maximum value in 2007 (343.1; p<0.001) and during the second there was a falling tendency that reached its minimum value in 2015 (85.3; p<0.001) in the CRC only strategy (p-value 0.001) and during the second there was a falling tendency that reached its minimum value in 2015 (85.3; p<0.001).

The cancer stratification by site shows that the rate of surgical procedures of the proximal colon was the same as the 2000 value (33.2), instead the rate of procedures on the distal colon and rectum which fell from 86.5 to 50.3. The cancer stratification by site shows that the rate of surgical procedures of the proximal colon was the same as the 2000 value (33.2), instead the rate of procedures on the distal colon and rectum which fell from 86.5 to 50.3.

Conclusion: The study findings confirmed that CRC screening was effective in reducing the number of oncological surgical oncology procedures particularly with regard to the distal colon and rectum. Data analysis showed that in Veneto Region the screening seemed to accelerate reaching the peak rate in surgical procedures that took place in 2007 and then started to fall off.

Disclosure: Nothing to disclose

References

P1025 ADDING FAMILY HISTORY OF COLORECTAL CANCER TO THE FIT-BASED SCREENING PROGRAM IN A DUTCH COLORECTAL CANCER SCREENING POPULATION SAMPLE

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Introduction: Screening for colorectal cancer (CRC) with the faecal immunochemical test (FIT) has suboptimal sensitivity for detecting advanced neoplasia (cancer and advanced adenomas). To increase the sensitivity and yield of a FIT-based screening program, FIT could be combined with other risk factors for advanced neoplasia, such as family history of CRC. We evaluated the incremental value of adding questionnaire on family history of CRC and Lynch syndrome associated tumors to a FIT-based screening program.

Aims and Methods: In this prospective population-based CRC screening trial, we randomly selected 6,000 screening-naive men and women in North-Holland, aged 59 to 75 years. All of them received an invitation to complete a FIT (FOB-Gold) and a validated, online family history questionnaire. Participants with a positive FIT (cut-off value 275ng/ml) and/or a positive family history, confirmed after genetic counseling, were referred for colonoscopy. The yield of detecting advanced neoplasia in the FIT-only strategy was compared to the combined strategy.

Results: Of the 5,979 invitees, 1,952 (33%) participants completed FIT only, 2,379 (40%) completed both FIT and the family history questionnaire and 95 (2%) completed only the family history questionnaire. Of the 125 participants eligible for referral to a clinical geneticist based on their questionnaire responses, only 50 (40%) underwent genetic counseling: 46 (37%) declined referral and 29 (23%) had previously received genetic counseling or colonoscopy surveillance. After genetic counseling, fourteen additional colonoscopies were performed in individuals with a FIT negative result, with no additional advanced neoplasia detected. The positive predictive value for advanced neoplasia of the combined strategy was 54% (95% CI: 47–61%) compared to 58% (95% CI: 51–65%) using the FIT only strategy (p-value 0.43).

Conclusion: In this study in the Dutch FIT-based screening program we observed no added value of using a validated, online family history questionnaire in detecting advanced neoplasia. However, patients at increased risk of developing CRC, who should undergo colonoscopy screening instead of participating in the CRC screening program, were identified.


P1026 THE EPIDEMIOLOGY OF THE SERRATED POLYPSIS SYNDROME IN AN AUSTRALIAN SETTING – MORE COMMON THAN PREVIOUSLY APPRECIATED

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Introduction: The Serrated Polypsis Syndrome (SPS) is defined by the World Health Organization (WHO) as a condition characterized by the presence of multiple Sessile Serrated Lesions (SSLs) within the colon. It confers an increased risk of colorectal malignancy. The exact prevalence of the condition is unknown and is there is significant geographic variability. There is a lack of data on the epidemiology of the SPS in an Australian setting.

Aims and Methods: To evaluate the epidemiology of the SPS in an Australian setting. All patients undergoing colonoscopy at an Australian regional gastrointestinal practice between January 2015 and March 2018 were screen for this condition. Clinical criteria with the is characterised by the presence of multiple Sessile Serrated Lesions (SSLs) within the colon. It confers an increased risk of colorectal malignancy. The exact prevalence of the condition is unknown and is there is significant geographic variability. There is a lack of data on the epidemiology of the SPS in an Australian setting.

Results: In the study period, 3725 separate patients underwent colonoscopy and the SPS was identified in 110 of these (2.95%). This group was predominately female (68/110; 62%) and had an average age of 66.3 years (SD = 13.1; range 24–88 years). Baseline characteristics for this group are presented in table 1. The majority of patients (107/110; 97%) were diagnosed with the SPS based on WHO criterion two (five or more polyps proximal to the splenic flexure with at least two greater than 10mm). 3 (3%) patients had a 1st degree relative with SPS and at least one SSL. The median number of SSLs detected during colonoscopy was 8.
Characteristics
Gender Female (62%)
Mean age 66.3 years (range 24–88 years)
Smoking history Current smokers – 5% Former smokers – 16%
Diabetes 9%
Alcohol (>2SD/day) 20%
Family history of bowel cancer 1st degree relative – 32% 2nd degree relative – 15%
FOBT positive 15%

Table 1: Baseline characteristics for SPS patients

Conclusion: The SPS is more common that previously recognised, being detected in 2.95% of Australian patients undergoing colonoscopy in a regional centre. This data set confirms a slight female predominance to the condition. Patients with the SPS are also at increased risk of conventional adenomas.

Disclosure: Nothing to disclose.

References

P1028 EPITHELIAL TO MESENCHYMAL TRANSITION IN RESPONSE TO E. COLI–INDUCED SENESCENCE–ASSOCIATED SECRETORY PHENOTYPE INDUCED CHEMOTHERAPEUTIC DRUG RESISTANCE

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Introduction: Colonic cancer patients tumors are highly colonized by Escherichia coli. Interestingly these E. coli freshly possess the pks genomic island (E. coli pks) responsible for the synthesis of a not yet purified genotoxic compound named colibactin. Colibactin-producing E. coli increase the number of mutational events and promote invasive carcinoma in CRC mouse models. It has been shown that pks E. coli-infected cells secrete growth factors responsible for proliferation of uninfected cells. Epithelial to mesenchymal transition (EMT), as first described in embryonic development, results in the transition of epithelial (E) cells with a mesenchymal (M) phenotype. EMT plays important roles in cancer progression from primary tumors, metastases, and metastasis as well as in resistance to therapy.

Aims and Methods: We investigated whether pks E. coli-infected cells induce, through their secretions, EMF in uninfected cancer cells. Human intestinal epithelial cells HT29 were infected using a pks E. coli strain isolated from a human CCR biopsy or its isogenic mutant unable to produce colibactin (Apks E. coli). 3-days post-infection, conditioned media (CM) were collected and used to stimulate uninfected cells. EMT markers were analyzed by Western blot and qRT-PCR. Cell motility was assessed by scratch tests and drug sensitivity assays were performed in vitro and in a xenograft mouse model.

Results: We found that CM derived from pks E. coli-infected cells induced EMT in recipient uninfected cells. Human intestinal epithelial cells HT29 were infected using a pks E. coli strain isolated from a human CCR biopsy or its isogenic mutant unable to produce colibactin (Apks E. coli). 3-days post-infection, conditioned media (CM) were collected and used to stimulate uninfected cells. EMT markers were analyzed by Western blot and qRT-PCR. Cell motility was assessed by scratch tests and drug sensitivity assays were performed in vitro and in a xenograft mouse model.

Conclusion: Our work demonstrates that colibactin-producing E. coli might increase the severity of CCR by inducing EMT which leads to chemotherapeutic drug resistance.

Disclosure: Nothing to disclose.

P1029 FECAL INCONTINENCE IN CHRONICALLY CONSTIPATED WOMEN: CLINICAL FEATURE, MANOMETRIC MEASUREMENTS AND PELVIC FLOOR ANATOMICAL ANATOMICAL PATHOLOGIES

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Introduction: Fecal incontinence (FI) and chronic constipation (CC) are not only physically and psychologically disabling symptoms, but also a significant social and public health problem. The pathophysiological basis of combined constipation and fecal incontinence in active women is not fully understood.

Aims and Methods: The aim of the study was to compare clinical, manometric and pelvic floor anatomical pathologies between chronically constipated women with or without fecal incontinence.

In a cross-sectional study, we compared clinical information, anal manometric results and pelvic anatomical pathology as assessed by dynamic pelvic ultrasound in a group of 62 constipated women with FI to that of 207 women with CC without FI.

Results: The CC group was older (55 vs 50 years, p = 0.07). The number of vaginal and instrumental assisted deliveries was similar in both groups (2.8 vs. 2.3, p = 0.3; 2.15 vs 1.8, p = 0.3, respectively). The number of pelvic surgeries was similar in both groups. Anal resting and squeeze pressures were significantly lower in the FI group (48 vs. 64, p = 0.001; 97 vs 141, p = 0.03, respectively). Rectal hypersensitivity was more common in the FI group (OR = 1.59, p = 0.03), and dysyneurogenic defecation was more common in the CC group (OR = 1.8, p = 0.03).
P1030 INTEGRATIVE ANALYSIS OF GENE MUTATIONS AND DNA METHYLATION IN COLORECTAL SERRATED LESIONS

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Introduction: Recent studies have shown that colorectal serrated lesions, including sessile serrated adenomas (SSAs) and traditional serrated adenomas (TSAs), are precursors of colorectal cancers. However, these molecular mechanisms of carcinogenesis are not yet well characterized.

Aims and Methods: To clarify the molecular and clinicopathological characteristics of serrated lesions, we assessed mutations and DNA methylation of cancer-associated genes in these lesions. Seventy-eight patients with colorectal serrated lesions were endoscopically diagnosed and treated in Nagoya City University Hospital, Fukui Prefectural Hospital, and Komatsu Municipal Hospital. Hematoxylin and eosin-stained slides were examined to confirm the diagnosis by a pathologist who was blinded to the clinical and molecular information. The lesions included TSAs (n = 36), SSAs (n = 18), microvesicular hyperplastic polyps (MVPs, n = 22), and serrated lesions (MVP or TSA) with adenoma (n = 2). After extracting DNA from formalin-fixed, paraffin-embedded (FFPE) sections, we performed targeted exon sequence analyses of 39 genes including frequently mutated genes in colorectal cancers and/or serrated lesions, as well as genes known to be associated with WNT signaling pathway. We also assessed the methylation status of a number of tumor-associated genes including SFRP1, SFRP2, SFRP5, SOX5, MLH1, and SMOC1, as well as marker genes of CIMP-H phenotype (CIMP) (MINT1, MINT2, MINT3, and CDKN2A) using bisulfite pyrosequencing. A cutoff value of 15% was used to define genes as methylation-positive. Tumors were defined as CIMP-positive when methylation was detected in three or more out of five methylation markers.

Results: BRAF mutations were observed in 64% of TSAs and 78% of SSAs, while KRAS mutations were observed in 31% of TSAs and 6% of SSAs, respectively. Mutations in the WNT-pathway-associated genes including APC, CXCR4, FBXW7, and RNF43 were significantly higher in TSAs than in SSAs (58% and 28%, respectively, p = 0.046). Additionally, prevalence of CIMP-positive lesions in TSAs and SSAs was not significantly different (44% and 42%, respectively). Notably, patients with tumors and SMOC1 were significantly higher in TSAs than in SSAs (53% and 0%, respectively, p < 0.01).

Conclusion: Significance of gene mutations in WNT signaling pathway components was emphasized in carcinogenesis of colorectal serrated lesions, especially in those harboring silencing of SMOC1 was significantly associated with development of TSAs, as a previous report indicated.

Disclosure: Nothing to disclose

P1031 PREDICTION OF ADVANCED METACHRONOUS LESIONS IN COLONOSCOPIC SURVEILLANCE ACCORDING TO GENETIC PROFILE OF ADENOMATOUS AND Serrated POLyps

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Introduction: Inflammation could contribute to carcinogenesis through the activation of immune cells, the remodelling pro-inflammatory cytokines and chemokines, serving as sustained stimulus for epithelial cells to proliferate. In this context, extracellular matrix proteins play a role by modulating cellular adherence and migration, tumor angiogenesis, and growth factor activation. EMILIN2 is an extracellular matrix molecule playing multifaceted functions in the tumor microenvironment, especially in overall functioning as a tumor suppressive molecule\textsuperscript{1-2}. Interestingly, EMILIN2 expression is down-modulated by methylation in a number of tumors including colorectal cancer (CRC)\textsuperscript{3}.

Aims and Methods: Given EMILIN2 function as negative regulator of the Wnt axis\textsuperscript{4}, a crucial pathway in colon carcinogenesis, we took advantage of the EMILIN2 null mouse model (\textit{Emilin2\textsuperscript{-/-}}) to assess its role in the development of CRC. Mice were treated with AOM/DSS to induce CRC. DSS was administered to mice acute inflammation and colitis. Colitis in control and untreated development were assessed by colonoscopy. Histopathological and IHC analyses were performed on colon samples at 1 week for acute inflammation, 12 weeks for colitis and 25 weeks for CRC. Wnt pathway activity was assessed by WB and qPCR. Cytokine analyses were performed through Lumixin Screening and qPCR. The inflammatory infiltrate was analysed by cytometry and IHC.

Results: Upon AOM/DSS treatment, \textit{Emilin2\textsuperscript{-/-}} mice developed a significantly higher number of tumors compared to control mice. Moreover, tumors from

Conclusion: The absence of EMILIN2 in the murine model led to the formation of a higher number of colorectal tumors associated with enhanced pro-tumorigenic fibroblasts and depressed immune cell infiltration. The results also highlighted a correlation between EMILIN2 expression and traits of the immune microenvironment in samples from CRC patients, suggesting that EMILIN2 could represent a prognostic marker.

References:

P1034 ANALYSIS OF METHYLATION FIELD DEFECT IN SERRATED POLYPOSIS SYNDROME

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Introduction: Serrated polyposis syndrome (SPS) is characterized by the development of multiple serrated polyps throughout the colorectum and an increased CRC risk. Etiology of this disease remains largely unknown, with scarce evidence of familial aggregation. aberrant promoter hypermethylation is associated with the serrated pathway of carcinogenesis, and the existence of a methylation field effect in the normal mucosa of SPS patients has been suggested. However, comprehensive analysis of methylation in this setting is lacking.

Aims and Methods: We aimed at investigating the methylation profile of normal colorectal mucosa of patients with SPS and healthy subjects to better understand the pathogenesis of this disease. We generated the methylome of the normal colorectal mucosa in two segments of the colon (proximal and distal to splenic flexure) using Illumina Infinium 850k array in 30 cases with SPS (14 with CRC and 16 without CRC) and 10 healthy individuals (normal colonoscopy). We calculated differentially methylated CpGs (DMCs; 40% for the comparison of normal mucosa from SPS vs. healthy individuals (FDR < 0.05) using ChAMP software, adjusting for age, sex, location and tobacco use. Differential methylation within mucosa from patients with SPS was analyzed controlling for potential confounders (age, sex, CRC).

Results: Overall, we found that patients with SPS display a differential and heterogeneous methylation profile in their normal mucosa compared to healthy individuals, who showed an homogeneous methylation profile. When comparing SPS patients with and without CRC, we did not observe differences in their methylation profiles (n.s. FDR for 20% DMCs), and thus we analyzed them together for further analysis. In SPS patients we found that mucosas from the proximal colon display more DMC and more hypomethylation than distal mucosas (proximal colon: 3,017 DMC, 954 hypermethylated and 2,063 hypomethylated; distal mucosa: 149 DMC, 116 hypermethylated and 33 hypomethylated). Up to 18% of the DMCs were located in promoter regions (15% of the hypermethylated DMCs; 18% of the hypomethylated), and a great proportion of the remaining DMCs locate at intronic and intergenic regions (77% of the hypomethylated DMC and 73% of the hypermethylated DMC). Interestingly, when we studied the cellular pathways involving the nearest genes to DMCs we found a significant enrichment in cancer-related pathways and runx-km15 pathways, including PRDMs, PRDM6, MAD1L1 and DPPC.

Conclusion: Patients with SPS display a methylation field defect in their normal mucosa, especially in the proximal colon and mainly based on hypomethylation. Methylation profiles do not differ between patients with and without CRC. aberrant methylation occurs in genes involved in CRC-related pathways suggesting a role in the carcinogenesis. Analyses for validation, including methylation and expression experiments in an independent cohort of patients, are ongoing.

Disclosure: Nothing to disclose

P1035 COMPARISON OF IMMUNOPROFILING BETWEEN COLITIS-ASSOCIATED CANCER AND SPORADIC COLORECTAL CANCER

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Introduction: Immunoprofiling is useful for predicting prognosis and provides a target for immunotherapy in various malignancies. The immune system of colitis-associated cancer (CAC) can be different from that of sporadic colorectal cancer (CRC) because chronic inflammation contributes to the pathogenesis of CAC. A quantitative multispectral imaging system, which allows simultaneous detection

mutations and high copy number amplifications, which might activate EMT and promote cancer-related genes and exacerbate the clinical outcome of cases with depressed CRC.

Disclosure: Nothing to disclose

Conclusion: The absence of EMILIN2 in the murine model led to the formation of a higher number of colorectal tumors associated with enhanced pro-tumorigenic fibroblasts and depressed immune cell infiltration. The results also highlighted a correlation between EMILIN2 expression and traits of the immune microenvironment in samples from CRC patients, suggesting that EMILIN2 could represent a prognostic marker.

References:

P1033 MOLECULAR CHARACTERISTICS OF THE DEPRESSED EARLY COLORECTAL CANCERS (DEPRESSED CRC)

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Introduction: The adenoma-carcinoma sequence is generally recognized as a main route of colorectal cancer (CRC). We proposed the presence of depressed and flat colorectal lesions at early phase, and some of these lesions are regarded as “de novo” cancers. Depressed cancers have an inclination to invade massively nevertheless the small tumor size, and indicated the severe malignant potentials for upper intestinal cancers.

Aims and Methods: The aim of this study is to clarify the molecular characteristics of depressed CRC with integrated genomic analysis using next-generation sequence. We extracted DNA and RNA from 8 submucosal-invading depressed CRC and 8 submucosal-invading protruded CRC, and conducted whole exome sequence (WES) and RNA sequence (RNA-seq). We compared the mutation and copy number profile, and expression of RNA using Gene Set Enrichment Analysis (GSEA), which enable to analyze the comprehensive gene expression in multiple molecular pathways, between depressed CRC and protruded CRC.

Results: The results of WES showed that the rates of APC and TP53 mutations were higher in depressed CRC (100%, 75%, respectively) than in protruded CRC (62.5%, 62.5%, respectively). While, the rate of KRAS mutations was low in depressed CRC (12.5%) than protruded CRC (62.5%) remarkably. The copy number analysis showed that the arm level amplification in 20q, 7p, 7q, and 8q were observed in both cases, however the amplification in 20p, 13p, and 17p were observed specifically in depressed CRC (87.5%, 37.5%, and 37.5%, respectively). GSEA clarified that the Epithelial-Mesenchymal Transition (EMT) related genes and angiogenesis pathway related genes were expressed overwhelmingly in depressed CRC than protruded CRC.

Conclusion: According to the genomic analysis, we validated the presence of the depressed early CRC, and unveiled the difference with protruded CRC. In comparison to the protruded CRC, the depressed CRC showed the APC and TP53
of several immune markers, is a novel method to comprehensively examine the tumor or immune environment.

Aims and Methods: The aim of our study is to compare the expression of immune cells in CAC and in sporadic CRC by using this method and to assess the clinical implications of immunoprofiling in CAC. The tumor specimens from 24 CRC patients (20 cases of advanced colorectal cancer and 4 sporadic colorectal cancer patients, matched by age, sex, and tumor location to CAC, were included in the analysis. The expressions of CD3\(^+\), CD8\(^+\), FoxP3\(^+\) or programmed death-ligand 1 (PD-L1)\(^+\) cells at the invasive margin of tumor tissue were evaluated by quantitative multispectral imaging, and the mean counts per mm\(^2\) of immune cells between CAC and sporadic CRC were compared.

Results: CAC showed more advanced stage (stage IV, 33.3\% vs. 8.4\%; p = 0.015) and higher disease-related deaths (41.7\% vs. 14.6\%; p = 0.018) compared to sporadic CRC. CD3\(^+\), CD8\(^+\), FoxP3\(^+\) and PD-L1\(^+\) cells of the CAC group were significantly less dense than those of the sporadic CRC group as measured by both the phenotyping method and the co-expression method. The co-expression densities of CD3\(^+\)FoxP3\(^+\) and CD8\(^+\)FoxP3\(^+\) cells were significantly lower in sporadic CRC (cell, p < 0.001). In the CAC group, the expressions of CD3\(^+\), CD8\(^+\), and FoxP3\(^+\) cells were significantly lower in patients with stage IV than in those at stages I-III. In addition, the patients with high expression of CD3\(^+\) and CD8\(^+\) had better overall survival than the patients with low expression of these cells.

Conclusion: The immune profiling pattern of CAC is different from that of sporadic CRC, indicating distinct disease phenotypes. Immunoprofiling can be helpful for the evaluation of clinical prognosis in CAC and sporadic CRC.

Disclosure: Nothing to disclose.
Aims and Methods: A multicenter case-cohort study was performed. Data from 653 patients with non-pedunculated T1 CRC (median follow-up time: 46 months; IQR 19–76) treated with surgery, diagnosed from January 2000 through December 2014, were collected from 13 Dutch hospitals. Primary endpoint was adverse outcome, defined as LNM or recurrent cancer. The case-cohort included a random sample of 50% of the cohort and all patients with the outcome outside the random sample. H&E stained slides were reviewed by a blinded expert pathologist to detect sub-microscopic signs of metastasis (i.e. poor differentiation, deep submucosal invasion, lympho-vascular invasion, and tumor budding). Tissue microarray samples were immunostained to determine the Immunoscore (I-low or I-high) and the CMS (CMS-1, CMS-2-3 or CMS-4). Uni- and multi-factorial Cox proportional hazard models for case-cohort data were performed to evaluate the association between the CMS-classification and Immunoscore and adverse outcome.

Results: The distribution of the CMS-classification was: CMS-1: 7%, CMS-2-3: 91%, CMS-4: 2%. I-low was observed in 36% of patients. Although no significant association was observed between the CMS-classification and the Immunoscore (p = 0.40), a trend was observed towards higher Immunoscors for CMS-1 vs the other multiple subtypes (p-trend = 0.07). The case-cohort included 60 patients with an adverse outcome (46 patients with LNM and 22 with recurrence among which 5 patients both with LNM and recurrence). Risk for an adverse outcome was 6%, 14% and 33% for CMS-1, CMS-2-3 and CMS-4, respectively, and 11% and 19% for I-high and I-low, respectively. CMS-4 was associated with an increased risk for adverse outcomes (HR 3.9, 95% CI 1.1–13.7, p = 0.04; reference CMS-2-3), which remained after adjusting for conventional risk factors (adjusted HR 4.6; 95% CI 1.3–16.4, p = 0.02; reference CMS-2-3). I-low showed increased risk for adverse outcomes (HR 1.6, 95% CI 1.0–2.8, p = 0.08). However, no significant association was observed for I-low when adjusting for conventional risk factors (adjusted HR 1.3; 95% CI 0.7–2.3, p = 0.44).

Conclusion: Our study suggest that CMS-4 has an increased risk for LNM and recurrent cancer, in line with the poor prognosis of this subtype in advanced CRC. In contrast to advanced CRC, the aggressive mesenchymal subtype (CMS-4) has a very low prevalence in early CRCs which might limit its use for risk stratification in these patients. Our results suggest limited additional value of the Immunoscore for risk stratification in T1 CRC.

Disclosure: Nothing to disclose

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Introduction: Colorectal cancer (CRC) diagnosis at early stages accompanies good prognosis and reduced mortality rates, while detection and removal of premalignant advanced adenomas (AA) result in the reduction of CRC incidence [1]. Invasive approaches for CRC screening, such as colonoscopy, have low participation rates and high cost. On the other hand, non-invasive procedures like fecal immunological test have the advantage of increased acceptance, though sensitivity for proximal colorectal tumours and AA is moderate to low [2]. Thus, there is a clear demand for novel non-invasive tests for the early detection of CRC and AA, to be used in population-wide screening programmes. DNA methylation detected in liquid biopsies, such as serum circulating cell-free DNA (cfDNA), is a promising source of non-invasive biomarkers, because it has been demonstrated that cfDNA reflects the aberrant methylation events occurring in neoplastic and tumour cells [3].

Aims and Methods: In a previous work we reported that, when using cfDNA, a sample pooling strategy offers an affordable approach for methylation biomarker discovery [4]. In this study, applying the sample pooling strategy, we aim to identify novel non-invasive methylation biomarkers for the early detection and screening of colorectal advanced neoplasia (AN: CRC or AA). We extracted cfDNA from serum samples from 130 individuals with no colorectal neoplasia (including individuals with no colorectal findings, benign pathologies and non-advanced adenomas) and from 150 advanced neoplasia cases (comprising patients with proximal AA, distal AA, and CRC stage I–IV). DNA methylation patterns were prepared for each pathological group using equal amounts of cfDNA from 10 individuals, sex-, age- and recruitment hospital-matched. DNA methylation levels of 886,836 CpG positions across the genome were measured with the MethylationEPIC array. Bioinformatics preprocessing and statistical analyses were conducted with methylation specific R/Bioconductor packages.

Results: The epigenome-wide analysis of serum cfDNA revealed 376 differentially methylated positions (DMPs) at 10% false discovery rate, between no neoplasia and pooled serum cfDNA samples (p < 0.02). DMPs were differentially methylated in AN. Some of the differentially methylated CpG sites were found within 49 differentially methylated regions. Unsupervised clustering analyses showed that differential methylation patterns could distinguish advance neoplasia samples from no neoplasia controls.

We applied the Statistically Equivalent Signature algorithm [5] for feature selection and we identified 3,256 combinations of 118 DMPs with statistically equivalent predictive value for “no neoplasia vs advanced neoplasia” classification. We used cross-validation to select a subset of 30 CpG sites as the most robust and predictive candidate set for biomarker validation.

Conclusion: We found a differentially methylated signature between no neoplasia and pooled serum cfDNA samples which could be used as a non-invasive biomarker candidates for colorectal cancer screening. The diagnostic performance of our novel non-invasive methylation candidates should be further evaluated in an independent cohort.

Disclosure: Nothing to disclose

References

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Introduction: Colorectal cancer (CRC) causes over 16,000 deaths every year and it is the second most common cause of cancer death. NICE guideline DG27 recommends universal testing for Lynch Syndrome (LS) at diagnosis of colorectal cancer, by testing the CRC for mismatch repair (MMR) status, a hallmark of the syndrome.

Aims and Methods: We collected data prospectively from Nov 2016 to December 2017 of consecutive newly diagnosed CRC patients at West Middlessex University Hospital (WMUH) in London. CRCs were universally screened for tumour features suggestive of LS (Defective MMR, or dMMR) with immunohistochemistry. We also collected clinicopathological data including age at diagnosis, stage, tumour site, histological findings and MMR tumour-status. Statistical analysis was performed using chi-square test and 2 tailed T test for binary and continuous variables respectively.

Results: A cohort of 123 consecutive CRC patients were universally tested for dMMR. Twelve patients (9.8%) were MMR-deficient of which only 6 (50%) were predicted by the Bethesda Criteria. 11/12 dMMR CRCs were early stage tumours, 6 and 2 (50%) and 5 and 1 (42%) in Dukes’ A or B, p=0.002, and in 20 Duke’s B CRCs in patient under 70 years of age, the result was directly relevant to personalised treatment with 5-FU based chemotherapy. The median age in patients with normal or abnormal MMR IHC was 64.6 years and 68.3 years respectively (p=0.41). With regard to histological features: mucinous tumours were more frequently manifested in dMMR CRCs (p=0.012), with the presence of this, signet ring cells or a lymphocytic response predictive of dMMR CRC (p=0.023). In all 12 patients with dMMR the cancer was located in the right colon (p=0.0001). MMR germline mutations were
Disclosure: | Nothing to disclose
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P1041 | SOX21 GENE PROMOTER METHYLATION ANALYSIS IN PERIPHERAL BLOOD MONONUCLEAR CELLS IS SENSITIVE PREDICTOR OF COLORECTAL CANCER

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Introduction: Early detection of colorectal cancer (CRC) has considerable value in treatment and prognosis. The aim of this study was evaluating predictive value of methylation SOX21 gene’s promoter testing for diagnosis of CRC.

Aims and Methods: This cross-sectional study was done on 64 eligible patients with colorectal cancer (case group) and 64 healthy volunteers. Then 5ml of blood sample was taken and DNA was extracted. DNA was extracted using GeNet Bio DNA extraction kit. The quality and quantity of extracted DNA assessed by spectrophotometry method in 260 and 280 nm wavelength and electrophoresis in agarose gel. %100 primer design methylation-quantification was assessed using Real-time PCR, and expressed in two groups. The Chi-square test performed on both groups using SPSS V.20 software.

Results: There were 32 (50%) and 28 males (43.8%) in case and control group respectively (p-value =0.62). The mean age of case and control group were 55.9± 16.6 and 56.7± 10.7 years respectively (p-value= 0.8). The value of methylation of SOX21 gene’s promoter in cancer case and control group were 71.6± ±20.1% and 31.9± ±11.3% respectively (p< 0.001) with sensitivity and specificity of %81.3 and %71.9 respectively. Predictive positive value and negative predictive value were %74.3 and %79.3 respectively.

Conclusion: The quantity of SOX21 gene promoter methylation in the genomic DNA of peripheral blood samples can be used as a good screening test for early diagnosis of CRC.

Disclosure: Nothing to disclose

P1043 | THE VALIDITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITH SMALL-CALIBER ENDOSCOPE FOR THE LESIONS SPREADING TO APPENDIX ORIFICE

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Introduction: The difficulty of colorectal endoscopic submucosal dissection (ESD) sometimes depends on the location. The lesion spreading to the appendix orifice is one of the most difficult location, because the working space during ESD is very narrow and it is hard to confirm a distal border of the lesion invading the vermiform appendix. From the view point of the tip diameter size, we consider small-caliber endoscopes (GIF-Q60J, tip diameter 9.9mm or PCF-PQ260L, tip diameter 9.2mm), which can go into the vermiform appendix easier, are more efficient than conventional therapeutic colonoscopes (PCF-Q260J, tip diameter 10.5mm). In this study, we evaluated the efficacy and the safety of small-caliber endoscope for ESD of lesions spreading to appendix orifice.

Aims and Methods: We retrospectively reviewed 341 lesions in cecum performed ESD at Omori Red Cross Hospital and NTT Medical Center Tokyo from May 2011 to December 2017. Among them, 36 lesions were spreading to appendix orifice. We classified according to the scope and compared the treatment results.

Results: 17 cases treated by conventional scope (PCF-Q260J) (C group) and 19 cases treated by small-caliber scope (GIF-Q60J or PCF-PQ260L) (S group) were enrolled. There was no significant differences between C group and S group in morphological type (Is/ IIa/ LST-G/ LST-NG respectively 12/5/11/ 5 in C group vs. 14/5/11/ 5 in S group, p=0.96). The value of Vaizey-score was 4.7 for the minimal fibrosis patients versus 6.5 for the other patients (p = 0.198).

Conclusion: Rectal cancer patients with a clinical complete response after CRT who present a normalised rectal wall without any signs of fibrosis on MRI appear to have a more favourable functional outcome in terms of incontinence and bowel function compared to patients with visible fibrosis, although results did not reach statistical significance in this small patient cohort.

Disclosure: Nothing to disclose

P1044 | THE PREDICTORS OF SEVERE SUBMUCOSAL FIBROSIS IN PATIENTS UNDERGOING COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION

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Introduction: Although colorectal endoscopic submucosal dissection (CESD) has been spread as an effective therapy for epithelial neoplasms, its application to lesions with severe fibrosis is difficult because of technical difficulties and risks of complications.

Aims and Methods: This study aimed to investigate the predictors of severe submucosal fibrosis in CESD. From April 2012 to February 2018, consecutive 457 lesions were performed CESD at Omori Red Cross Hospital. Submucosal tumors and non-neoplastic tumors were excluded and 399 lesions were evaluated retrospectively.

Results: 42.8% of the lesions were spreading to appendix, especially for the lesions of that we could not confirm the border, can be confirmed with PCF-Q260J and succeed the procedure with PCF-PQ260L. The lesion with severe fibrosis is difficult because of technical difficulties and risks of complications.

Conclusion: The predictors of severe submucosal fibrosis were investigated using the Vaizey-score and the complication rate. The predictors were a clinical complete response after CRT, the number of lesions spreading to appendix orifice, especially for the lesions of that we could not confirm the border, can be effective and safe.

Disclosure: Nothing to disclose
preoperative procedures (biopsy, local injection, tattooing), and analyzed the predictive factors of severe submucosal fibrosis. We also evaluated the safety of performing ESD to lesions with severe fibrosis by reviewing the postoperative courses and outcomes of the patients. We defined that lesions step over folds were called “over the fold lesions” and Ip or Ip lesions exceeding 30mm were called “large protrusions.” In addition, recently we proposed Double Tunnel Method (DTM) which could resect lesions with severe fibrosis or with muscle retraction sign (Chiha H et al. Endoscopy, 2018 in press) and we evaluate the feasibility of the new method.

Results: 19 lesions (4.8%) were assigned to group F (66.9±12.1 years old), and 380 lesions (95.2%) were assigned to group N (69.5±11.2 years old). Characteristics of the patients (age, sex, BMI and comorbidities) were similar. With respect to the features of the lesions, over the fold lesions were 12 (63.2%) in group F and 107 (28.3%) in group N (p = 0.003). Lesions with tattooing before ESD were 3 (15.8%) / 2 (0.5%), large protruded lesions were 7 (36.8%) / 7 (1.8%), lesions over 50mm in size were 5 (26.3%) / 22 (5.8%), and cancers with submucosal invasion were 9 (47.4%) / 30 (7.9%) in group F and N respectively (p < 0.01). On the other hand, the rate of lesions performed biopsy or local injection, and local recurrence were similar. The lesion size was 36.2 ± 15.9 mm in group F, and 28.2 ± 14.0 mm in group N. Multivariate analysis (Variables were included in the multivariate model if the p value was <0.10 on univariate analysis) showed the predictors were lesions over the fold, lesions with preoperative tattooing, and large protruded lesions. Postoperative courses were similar between two groups. ESD procedure time was 134.2 ± 69.0 min in group F, and 42.1 ± 32.1 min in group N (p < 0.01). En bloc resection rate and curative resection rate (%) were 94.7 / 57.9 in group F, and 100 / 96.6 in group N (p < 0.05), but there were no differences in complication rate between two groups. DTM was done for two cases safely. Conclusion: Lesions over the fold, lesions with preoperative tattooing, and large protruded lesions might be the predictors of severe submucosal fibrosis. DTM could be an effective treatment for them. Disclosure: Nothing to disclose

P1046 RECURRENT AND SECOND PRIMARY CANCERS AT THE ONE YEAR SURVEILLANCE COLORECTOSCOPY FOLLOWING CURATIVE COLORECTAL CANCER RESECTION

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Introduction: After curative resection of colorectal cancer (CRC), postoperative surveillance is aimed at reducing disease specific morbidity and mortality by early detection of recurrent or second primary cancers. Even though endoscopic surveillance has become a routine part of clinical practice, controversy exists on the timing of the first postoperative colonoscopy. Several studies have reported the highest incidence of CRC within two to three years after surgery, reason why most guidelines now recommend a one year surveillance interval after resection. Aims and Methods: To assess the yield of CRC at the one year surveillance colonoscopy after CRC resection. Results: Respectively, files of patients having undergone a curative surgical resection of a first CRC between June 2013 and April 2016 were checked for eligibility in four hospitals. Patients were included in the database when a complete clearing colonoscopy was performed prior to surgery and when the interval between the pre- and postoperative colonoscopy was 6–20 months. Patients with hereditary CRC or inflammatory bowel disease were excluded. Data were collected on patient demographics, quality of colonoscopy, baseline characteristics, adenomas and serrated polyps detected during the preoperative colonoscopy and one year surveillance colonoscopy. A sample size of 571 individuals was needed to assess whether the CRC yield exceeded the 0.5% yield of CRC of primary colonoscopy screening. A multivariable logistic regression was performed to identify risk-factors associated with finding advanced neoplasia (i.e. CRC, advanced adenomas or advanced serrated lesions) at follow-up. Results: Five-hundred seventy-two patients (54.9% male, mean age 66.2 ± (9.9) years) met the inclusion criteria and were enrolled in the study. After a mean surveillance interval of 13.7 ± (2.8) months, 10,572 (1.7%, 95% CI: 0.7–2.8%) were diagnosed with CRC. Of these, five were second primary cancers and five were recurrences at the anastomosis. The second primary CRCs encompassed mostly T3 and T4 tumours (4/5, 80%), of which 4/5 qualified for palliative treatment only. In two of these five patients a polyp had been resected at the preoperative colonoscopy in the same segment as the second primary cancer (i.e. 25mm tubulovillous adenoma with low-grade dysplasia (clear resection margin) and 8 mm hyperplastic polyp). Of the recurrent CRCs, 4/5 (80%) were either T3 or T4, and one of these qualified for palliative treatment only. Resection margins of the primary CRC were clear in all five patients with recurrent CRC (4/5, 95% CI: 8.9–13.8%) of all patients included in the study advanced neoplasia was detected at the one-year surveillance colonoscopy. Synchronous baseline advanced neoplasia was a risk-factor for finding advanced neoplasia at follow-up. Conclusion: The yield of CRC at the one year surveillance colonoscopy after CRC resection was 1.7% (95% CI: 0.7–2.8%). This concerned recurrences as well as second primary tumours, which were often of advanced stage. The high yield justifies the increased colonoscopy demand of one-year surveillance interval. Disclosure: G.A. Meijer: Exact Sciences and Sysmex: provision of materials, equipment or (sample) analyses. E. Dekker: Fujifilm: equipment on loan, research grant, personal consultation-fee; Olympus: equipment on loan, research-grant. Other authors: nothing to disclose.

P1047 ENDOSCOPIC RESECTION OF T1 COLORECTAL CANCER—INFLUENCE OF THE RISK FACTORS ON DECISION-MAKING AND PROGNOSIS

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Introduction: Colon lesions diagnosed as T1 colorectal cancer (CRC) might be treated only with an endoscopic approach. Additional surgery or surveillance depends on the presence of high-risk factors for lymph node metastasis (LNM). The follow-up strategy for these patients remains controversial. Aims and Methods: We intend to know the influence of histopathological risk factors on therapeutic offering and the overall prognosis of patients with resected T1 CRC at our unit. Prospective cohort study of T1 CRC lesions endoscopically removed between January/2013 and January/2018 and in follow-up at our unit. “High-risk lesion” if at least 1 of the criteria: histological high grade, lymphovascular invasion,
budding, Kikuchi-sm2/3 or Haggitt-4, deep submucosal invasion > 1000μm, distance to margin ≥ 1 mm

Results: Resected 92 lesions in 92 patients (67% male, age 65.5±10.5 years). Mostly pedunculated (65.2%), mean size 19.1±1 mm; Left colum in 89%, particularly in sigmoid colon (n = 53); Histological high grade -11%; lymphovascular invasion - 16%; Haggitt-4 in 4 lesions; Kikuchi-sm2/3 in 15 lesions; Median distance to margin - 1.5 mm.
Median follow-up time of 36 months. 56.5% (n = 52) categorized as “High-risk lesion”, with 30 patients undergoing surgery and 22 surveillance due to patient choice or relevant comorbidities. In the patients intervened surgically residual tumor in 13% (n = 4). Disease progression confirmed in 6 cases (6.5%), all “High-risk lesion” (11.5% vs. 0%; p = 0.03); From those, 4 had surgery and 2 were on endoscopic surveillance (13% vs. 9%; p = 0.08). Two deaths reported, 1 “high-risk” patient (2% vs. 2.4%, p = 1). On multivariable analysis lymphovascular invasion presented as the only statistically significant criterion for disease progression (OR 6.2, IC 95% 1.1–34.2).

Conclusion: Endoscopic resection appears to be effective on treating low-risk lesions and we confirm the risk of disease progression on high-risk lesions. In our sample, lymphovascular invasion has a major influence in the prognosis. More studies are needed to optimize decision-making and follow-up strategy to offer based on patients risk profile.

Disclosure: Nothing to disclose.

References:
**P1050** APOPTOSIS INDUCTION IN COLORECTAL CANCER BY NEWLY DEVELOPED ENDOSCOPIC IRREVERSIBLE ELECTROTHERAPY ABLATION DEVICE


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Introduction: Irreversible electroporation (IRE) effectively removes unwanted cells without thermal damage of surroundings. We used multiphoton microscopy (MPM) to evaluate IRE ablation response to cancer cell. By using MP (multiphoton) probe, we focused on two vital intracellular organelles, nucleus and mitochondria, and could get real-time image of IRE-induced apoptosis.

Aims and Methods: Colon cancer cell lines (normal & neoplasm tissues) obtained from 10 patients were stained with MP probes, ABI-Nu for nucleus and PMT for mitochondria respectively. To observe IRE response using MPM, we first compared the states of colon cancer cell lines before and after the IRE with electrical pulses administered in a Harvard apparatus. Then, compared those of normal colon and colon cancer tissue in the same manner. 3-D images, co-labelled with ABI-Nu and PMT were reconstructed. To assess apoptosis, colon cancer cells were stained with the fluorescent dye Annexin V or propidium iodide (PI). To determine whether IRE induces apoptosis, membrane blebbing was examined after applying.

Results: MPM images of cancer cells stained with MP probes revealed that ABI-Nu stained quicker after IRE ablation. Nuclear staining was present earlier and more prominent after IRE application. IRE had a relatively stronger effect on cancer. We obtained MPM images of each tissue slice, including 4 images for every 150 section at a depth of 90-150 µm along the z-direction. Staining was positive for Annexin V and PI, providing the evidence of apoptosis. Blebs, which are distinctive of apoptosis were developed after IRE in the colon cancer cell.

Conclusion: Using MPM, we observed that nuclear staining due to increased cell membrane permeability and bleb was formed after electrical pulse exposure. Those real time images may help us to understand the process of IRE more. MPM can replace other apoptosis assessment methods, including Annexin V-FITC and PI staining by providing in vivo images.

Disclosure: Nothing to disclose.

**P1052** COMPARISON OF INCIDENCE AND SURVIVAL OUTCOMES IN MUCINOUS AND SIGNET-RING CELL COLORECTAL CANCERS WITH CLASSICAL ADENOCARCINOMA: A SEER ANALYSIS

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Introduction: Besides classical adenocarcinoma (AC), mucinous adenocarcinoma (MAC) and signet-ring cell carcinoma (SRCC) are less frequent subtypes of colorectal cancer, and their recent epidemiologic data are lacking. The current study was designed to explore the evolving epidemiology and prognosis of patients with colorectal MAC and SRCC, compared with AC.

Aims and Methods: The Surveillance, Epidemiology and End Results (SEER) registry database was adopted for patients with pathologically confirmed colorectal neoplasms as their first malignancy. Incidence and survival trends were estimated by age and histologic subtype. 5-year cancer specific survival (CSS) were evaluated for entire cohort, and compared in subgroups by age, grade and stage. Multivariate analysis of CSS was conducted for entire cohort.

Results: AC incidence (per 100,000) declined slightly from 6.1 in 1975 to 5.6 in 2001, and fell to 2.5 in 2012 with an APC of −7.8% (95% CI = −8.8%–6.8%, p < 0.001), then reached a plateau. SRCC incidence gradually climbed from 0.1 in 1975 to 0.6 in 1999 with an APC of 8.3% (95% CI = 7.2%–9.4%, p < 0.001) and went down to 0.4 in 2014 with an APC of −3.0% (95% CI = −5.0%–1.0%, p < 0.001). Among patients younger than age 50 years, MAC incidence decreased at an APC of −2.6% (95% CI = −3.6%–1.6%, p < 0.001), and SRCC remained stable, whereas AC incidence increased greatly at an APC of 1.9% (95% CI: 1.6%–2.2%, p < 0.001). Survival of both MAC and AC increased over time, while the survival of SRCC fluctuated without evident improvement. The 5-year CSS of SRCC was 31.3%, significantly lower than AC (66.6%) and MAC (60.4%). For AC and MAC Survival rate of patients aged below 50 years was superior to those aged 50 years or over through time, while in SRCC, after follow-up of approximately 20 months, the survival rate of younger patients dropped and became lower than older patients. Histologic subtype was an independent factor for CSS of CRC.

Conclusion: The incidence and survival of colorectal MAC and SRCC differs from traditional AC. Despite the low incidence of SRCC, the survival is significantly worse than AC and MAC, especially for patients aged younger than 50 years. Further studies of the etiologies and treatment for rare subtypes of CRC are needed.

Disclosure: Nothing to disclose.

**P1051** EFFECT OF ORAL ANTICOAGULANTS AND NSAIDS ON THE ACCURACY OF FECAL IMMUNOCHEMICAL TESTS (FIT) WITHIN A COLORECTAL CANCER SCREENING PROGRAMME – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Most colorectal cancer (CRC) screening programmes globally are now based on faecal immunochemical testing (FIT). The positive predictive value for advanced neoplasia (PPVAN) of FIT has been reported to range between 35 and 55%. The PPVAN is known to depend on gender, FIT cut-off, and screening participation. In contrast, these drugs could increase the tendency of non-neoplastic lesions to bleed too, and cause a decrease in PPVAN. In previous studies into the effect of OAC and NSAID use on FIT performance was inconclusive.

Screening guidelines thus lack recommendations on FIT screening in NSAID / OAC users. The aim of this meta-analysis was to study the effect of OAC and NSAID use on FIT performance.

Aims and Methods: A systematic search was conducted until June 2017 to retrieve studies from Pubmed, Embase, Medline, Web of science, Cochrane central and Google Scholar. Studies were included when reporting on FIT results in users versus non-users of OAC and/or NSAID in average risk FIT-based CRC screening populations. Primary outcome was PPVAN of FIT in relation to NSAID / OAC use. Values were obtained by conducting analysis for pooled OAC use and also separately for NSAIDs (including aspirin) by random-effect forest plots.

Results: Our literature search identified 2022 records, of which 8 studies were included in total. Four studies provided data on OAC use and six studies on NSAID use. A total of 3563 FIT positive screening participants were included for OAC analysis and a total of 2901 for NSAID analysis. Pooled PPVAN of FIT in OAC users vs. non-users was 37.6% (95% CI 33.9–41.4) vs. 40.3% (95% CI 38.5–42.1) (p = 0.75). Pooled PPVAN in NSAID users vs. non-users was 38.2% (95% CI 33.8–42.9) vs. 39.4% (95% CI 37.5–41.3) (p = 0.59). Subgroup analysis of one included study showed that the detection rate of advanced neoplasia significantly decreased with long-term aspirin use (>5 years) compared to short-term use (<5 years); 38.3% vs. 61.2%, respectively (p = 0.03).

Conclusion: Accuracy of FIT is not affected by OAC and NSAID use at time of screening. Based on the current literature, withdrawal of OACs or NSAIDs before FIT screening is not recommended. Future studies should focus on duration of use and drug specifics in association with accuracy of FIT to conduct specific guideline recommendations.

Disclosure: Nothing to disclose.
Aims and Methods: The aim of this single center retrospective observational study was to assess medium-term outcomes of endoscopic removal of early malignant colorectal polyps at the University of Szeged between 2012 and 2016, and to compare them with that of surgical resection. For endoscopic removal (group I), inclusion criteria consisted of histopathological diagnosis of pT1 adenocarcinoma after endoscopically completed (based on the endoscopist’s opinion) polypectomy without additional surgical resection. For surgical removal (group II), inclusion criteria included surgical resection of pT1 adenocarcinoma with superficial submucosal invasion with or without previous endoscopic polypectomy attempt. Recurrence (primary outcome; including local recurrence and distant metastases) was compared between the two. Secondary outcome was nodal involvement in those underwent surgical resection (with vs. without prior endoscopic polypectomy). Mean follow-up was 24.2 ± 7.6 months (7–67 months), follow-up endoscopy was available in 69% of the cases. 

Results: In the analysis of the SEER 9 registries database, 5-year CSS of patients aged <54, 55-64, and 65-74 years showed robust increase since 1975; however, survival of patients aged 75–84 years remained low despite modest improvement, and patients aged 85 or older even showed no survival gains since 1990. Same trend exists after stratifying the disease as localized, regional, and distant. In the analysis of the SEER 18 registries database, there has been a steady increase in the survival of patients aged ≤54, 55–64, 65–74 and 75–84 years as time period advanced; however, for CRC patients aged 85 years and older, the survival curves of the period 1980–2002 couldn’t be distinguished from each other and presented with a negligibly small gap from the survival curve of 1980–1989.

Conclusion: The strong interaction between age and year of diagnosis implies that older patients have benefited less over time than younger patients, especially for early CRC cases. Future studies are needed to determine the cause for these trends and identify potential strategies.

Disclosure: Nothing to disclose.

P1054 IMPACT OF OBESITY AND VISCERAL FAT DISTRIBUTION ON SURVIVAL AND PERITONEAL SEEDING METASTASIS OF STAGE III COLORECTAL CANCER

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Introduction: There has been studies about the relationship between increased body mass index (BMI), and risk of colorectal neoplasia. Obesity may affect outcome of colorectal neoplasia.

Aims and Methods: This study aimed to investigate the associations between visceral fat and oncologic outcomes in stage III colorectal cancer (CRC). 472 patients were identified with stage III CRC (2007.01–2009.12:31). BMI, subcutaneous fat and visceral fat were measured volumetrically via CT scan for each patient at three levels, lumbar spine 3 to 4 (L3-4), 4 to 5 and lumbar spine 5 to sacrum. Adjusting age, sex, medication and underlying condition, the effect of visceral fat volume on mortality and recurrence were evaluated using Cox proportional hazard regression.

Results: Total 111 deaths and 114 cases of recurrence were noted and among recurrent cases, 25 cases were peritoneal seeding recurrence. Higher visceral fat volume was associated with worse progression-free survival. However, higher visceral fat to total fat volume ratio (HR 1.069, 95% CI 1.01-1.131, p = 0.02) and higher visceral fat to subcutaneous fat volume ratio (HR 1.024, 95% CI 1.003-1.045, p = 0.023) were both related to higher risk of peritoneal seeding recurrence. Moreover, among each level, higher visceral to total adipose tissue ratio of L3 showed higher risk of peritoneal seeding recurrence (HR 4.969, 95% CI 1.303-18.949, p = 0.019). In the additional survival analysis, patients with BMI under 18.5 were associated with higher risk of cancer-specific mortality (HR 3.236, 95% CI 1.022-8.555, p = 0.042).

Conclusion: Visceral obesity is closely related with increased risk of peritoneal seeding recurrence in patients with stage III colorectal cancer. Furthermore, underweight patients are associated with higher risk of cancer-specific mortality.

Disclosure: Nothing to disclose.

P1055 QUANTITATIVE FLUORESCENCE ENDOCOSCOPY: A NEW AND PROMISING TOOL TO PREDICT AND EVALUATE RESPONSE TO PREOPERATIVE CHEMORADIOTherapy IN LOCALLy ADVANCED RECTAL CANCER PATIENTS

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Introduction: Patients with locally advanced rectal cancer (LARC) are treated with neoadjuvant chemoradiotherapy (nCRT) followed by surgery. To date, there is a growing interest in the non-operative ‘watchful waiting’ management of patients with a clinically complete response to nCRT, as this is associated with good survival rates and reduced long-term morbidity. However, current staging techniques are suboptimal to identify patients that might benefit from watchful waiting. Therefore, we investigated if quantitative molecular fluorescence endoscopy (Q-MFE) can improve clinical response assessment after nCRT in LARC patients.

Aims and Methods: We evaluated Q-MFE with 4.5mg of the near-infrared (NIR) tracer bevacizumab-800CW targeting vascular endothelial growth factor A in 30 patients with LARC. Q-MFE procedures were scheduled at two different time points during neoadjuvant treatment: 1) at baseline, prior to the start of nCRT; 2) following completion of nCRT. At both time points, fluorescence was visualized using a NIR molecular fluorescence endoscopy platform. Additionally, fluorescence signals were quantified in vivo and ex vivo using multi- dimensional single fiber reflectance and single fiber fluorescence (MDFSR/FFF) spectroscopy. Results were correlated with current clinical standards.

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Disclosure: Nothing to disclose.
radiological restaging, white-light endoscopy and the pathological outcome of the surgical specimen with for Q-MFE and white-light endoscopy respectively a positive predictive value after nCRT of 92% vs. 90% and negative predictive values of 100% vs. 20%. Overall, Q-MFE correctly changed restaging diagnosis in 4 (16%) of the LARC patients.

Conclusion: VEGFA-targeted Q-MFE showed to be a promising new tool for the prediction of tumor response to nCRT already at radiotherapy planning. The findings on Q-MFE results showed a promising correlation to pathological staging of the surgical specimen with for Q-MFE and white-light endoscopy respectively a positive predictive value after nCRT of 92% vs. 90% and negative predictive values of 100% vs. 20%. Overall, Q-MFE correctly changed restaging diagnosis in 4 (16%) of the LARC patients.

Results: Compared with the current guidelines, AI significantly reduced unnecessary additional surgery after endoscopic resection of T1 CRC without missing LNM positivity. AI will help in making decisions as to whether additional surgery is indicated after endoscopic resection of T1 CRCs.

Disclosure: Nothing to disclose

References
M-BLI), we could observe the presence or absence of residual lesions instantly without a pathological diagnosis. This allowed us to resect the residual part of poly as required. Therefore, our ability to completely resect the lesion improved.

**Conclusion:** To prevent residual lesions in cold polypectomy, local injection of a water jet and magnified endoscopic observation using a special light are useful. This should therefore be performed as a routine procedure.

**Disclosure:** Nothing to disclose

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**P1060 SYSTEMATIC REVIEW AND META-ANALYSIS: CONDITIONED PAIN MODULATION IN IRRITABLE BOWEL SYNDROME**

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**Introduction:** Irritable bowel syndrome (IBS) is common and is characterised by recurrent abdominal pain, which is a major contributor to healthcare seeking. The neurobiological basis of this pain is incompletely understood. Conditioned pain modulation (CPM) is a measure of descending pathways, has been implicated in the pathophysiology of IBS, although to date only in studies with relatively small sample sizes. We aimed to clarify this relationship by undertaking a systematic review and meta-analysis.

**Aims and Methods:** A systematic review of MEDLINE and Web of Science databases were searched (up to April 2017). Studies examining CPM in adults with IBS and healthy subjects were included. Data were pooled for meta-analysis to calculate the odds ratio of abnormal CPM in IBS, with 95% confidence intervals (CI).

**Results:** The search strategy identified 645 studies, of which 24 were relevant and 12 met the inclusion criteria. CPM was reduced in IBS patients versus healthy subjects, odds ratio 4.84 (95% CI 2.19–10.71, p = 0.0001). There was significant heterogeneity in effect size (Q-test = 52, p < 0.001, I² = 78.8%) in the absence of publication bias. Numerically, the Rome III criteria was associated with more deficient CPM than Rome II odds ratio 5.65 (95% CI 1.87–17.04) vs 3.44 (95% CI 1.76–6.70), respectively.

**Conclusion:** CPM is significantly reduced in patients with IBS when compared to healthy subjects. These data provide evidence that abnormal descending pathways are an important pathophysiological facet in IBS, which could represent a novel investigation target to allow personalization of neuromodulatory therapy.

**Disclosure:** Nothing to disclose

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**P1061 ASSOCIATIONS BETWEEN SYMPTOMS AND GAS PRODUCTION DURING FODMAP BREATH TESTS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS**

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**Introduction:** Functional gastrointestinal disorders (FGID) are characterized by a broad range of gastrointestinal (GI) and extra-GI symptoms, and an absence of recognizable disease. Mechanisms underlying these phenotypes are unclear, but may be linked to host or microbiome metabolism.

**Aims and Methods:** We investigated underlying mechanisms by studying associations between gas production and symptom genesis during fructose and lactose breath tests in 2042 successive patients with FGID. Breath hydrogen and methane gas concentrations and evoked GI and extra-GI symptoms were assessed for 5 hours following sugar ingestion. Symptom and gas time profiles were compared, Treadlet Transforms were used to derive data-driven symptom clusters, and the symptom severities of the clusters were analyzed for their association with breath gas characteristics.

**Results:** The time profiles of eleven symptoms, as well as of hydrogen and methane gas concentrations, showed significant changes over time following fructose and lactose ingestion (p < 0.0001). Treadlet Transform analysis identified two distinct sugar-evoked GI and CNS symptom clusters. The intensities of the GI and CNS symptoms were closely correlated following both fructose and lactose (all p < 0.0001). The GI symptoms were significantly associated with the production of hydrogen and methane gases (all p < 0.0001), while this was not the case for the CNS symptoms.

**Conclusion:** Clearly defined clusters of GI and CNS symptoms were evoked by fructose and lactose ingestion in patients with FGID. The GI and CNS cluster time profiles correlated significantly, but only the GI symptoms were related to breath gas concentrations. This implies distinct underlying mechanisms likely relating to microbiome metabolism, such as mechanical and chemical interactions.

**Disclosure:** Nothing to disclose

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**P1062 FAECAL METABOLIC PHENOTYPING IN IRRITABLE BOWEL SYNDROME**

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**Introduction:** The complex pathophysiology of Irritable Bowel Syndrome (IBS) is based on incompletely understood disturbances in the microbiota-gut-brain interaction. Faecal microbiota profiles have been associated with IBS and severity of symptoms in IBS patients. However, while the composition of the intestinal microbiota may be altered, the available data on the metabolic activity in the intestinal lumen of IBS patients, which is modulated by diet, microbiota composition and microbial activity, use of medication and host metabolism, is limited.

**Aims and Methods:** The aims of the present study were to identify profiles of faecal metabolites associated to IBS, IBS subtypes and gastrointestinal (GI) symptom severity in IBS.

In a cross-sectional analysis we included 163 extensively phenotyped and clinically diagnosed IBS patients (all according to ROME III criteria) and 121 age and gender matched healthy controls (HC); a subset of the Maastricht IBS cohort. The neurobiological basis of this pain is incompletely understood. Conditioned pain modulation (CPM) was reduced in IBS patients versus healthy subjects. These data provide evidence that abnormal descending pathways are an important pathophysiological facet in IBS, which could represent a novel investigation target to allow personalization of neuromodulatory therapy.

**Disclosure:** Nothing to disclose

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**P1063 PROTEASE ACTIVATED RECEPTOR-2 INDUCES IMMUNE ACTIVATION AND VISCERAL HYPERSENSITIVITY IN POST-INFECTIOUS IRRITABLE BOWEL SYNDROME**

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**Introduction:** Protease-activated receptor-2 (PAR-2), a G-protein-coupled receptor of mast-cell tryptase and trypsin, is highly expressed in the intestine. Role of PAR-2 in the pathogenesis of abdominal pain in irritable bowel syndrome (IBS) is not well defined.

**Aims and Methods:** We aimed to investigate the role of PAR-2-mediated visceral hypersensitivity by using a post-infectious IBS (PI-IBS) mouse model. T. spiralis...
infected PI-IBS mouse model was used. Fecal serine protease activity and intesti- nal immune function was assessed. For outcomes, an intraperitoneal PAR-2 antagonist (FSLRLY-NH2) or normal saline, and control mice received intra- colonically PAR-2 agonist (SLIGRL-NH2) or normal saline. Intestinal perme- ability was assessed by urine lactulose/mannitol ratio, and colonic expressions of PI-IBS. T. spiralis (TJ) proteins were examined by Western blot. Intestinal immune profile was assessed by measuring Th (T helper) 1/Th2 cytokine expression. Visceral sensitivity was evaluated by abdominal withdrawal reflex (AWR) in response to colorectal distension (CRD).

Results: T. spiralis induced visceral hypersensitivity after 8 weeks. PI-IBS mice had higher AWR scores for all levels of distention (20, 40, 60, and 80 mmHg) and lower pain and volume thresholds compared to the control mice (all P < 0.05). Colonic PAR-2 expression (19.4 ± 6.4 vs. 0.23 ± 0.1, P < 0.05) as well as fecal serine protease activity (127.2 ± 39.1 U/mg vs. 25.6 ± 15.8 U/mg, P = 0.02) and intestinal mast cell counts (191.2 ± 2.7 vs. 2.8 ± 0.7, P < 0.001) were elevated in PI-IBS compared to the control mice. Decreased colonic TJ proteins (occludin: 0.45 ± 0.16 vs. 0.49 ± 0.28, P = 0.009; ZO-1: 0.48 ± 0.23 vs. 1.94 ± 1.06, P = 0.015) expression, increased lactulose/man- nitol ratio (0.35 ± 0.04 vs. 0.15 ± 0.03, P < 0.001), and elevated colonic Th1/Th2 cytokine ratio (3.5 ± 0.4 vs. 1.4 ± 0.1, P < 0.001) were observed in PI-IBS com- pared to the control mice. Administration of PAR-2 agonist in control mice demonstrated similar changes observed in PI-IBS mice, while PAR-2 antagonist normalized intestinal hyper-permeability (0.15 ± 0.02 vs. 0.35 ± 0.04, P < 0.001), led a trend towards decreased Th1/Th2 ratio (2.4 ± 0.3 vs. 3.5 ± 0.4, P = 0.07) and reduced visceral hypersensitivity (decreased AWR scores and higher pain and volume thresholds) in PI-IBS mice.

Conclusion: PAR-2 activation induces intestinal hyper-permeability leading to immune activation and visceral hypersensitivity in PI-IBS mouse model. PAR-2 plays an important role in the pathogenesis of PI-IBS.

Disclosure: Nothing to disclose.
Introduction: Although previous studies show conflicting results, colonic mast cell (MC) numbers and increased proportions of MC in close proximity to intestinal nerves have been proposed to be associated with more severe Irritable Bowel Syndrome (IBS) symptoms, altered intestinal barrier properties and visceral hypersensitivity.

Aims and Methods: This study aimed to determine if IBS patients displayed an altered MC profile compared with healthy subjects and if MC profiles correlated with IBS symptoms, barrier integrity or visceral sensitivity.

Biopsies from the sigmoid colon (25–35 cm from the anus) were collected from a Swedish cohort of IBS patients meeting the Rome III criteria and from healthy subjects. Mucosal MC profile was determined using anti-tryptase antibody, immunofluorescence and blinded quantification with a computer-assisted analysis system. The IBS Severity Scoring System (IBS-SSS), Gastrointestinal Symptom Rating Scale-IBS (GSRS-IBS), Visceral Sensitivity Index (VSI) and Hospital Anxiety and Depression Scale (HADS) questionnaires were used to evaluate the symptom profile. Expression of mucosal barrier proteins CLD-1, MUC, TJP1 and OCLN was measured with Real-time quantitative PCR and normalised to housekeeping genes 18S, POLR2Y and RPLPO. Fecal protease activity was detected using azocasein or tryptase substrate protease assays and AEBSF inhibitor. Visceral sensitivity was determined with a rectal balloon distension procedure (HCAS) and multi-variate orthogonal partial least squares-discriminant analysis (OPLS-DA) were performed. Data are presented as median (25th-75th percentiles).

Results: This study included 43 IBS patients (30 females; 32 (25–44) years of symptom onset) and 18 healthy subjects (11 females; 27 (24–38) years). Total HAD scores were 13 (9–19) in IBS patients and 7 (3–13) in healthy subjects (p = 0.0002). MC frequencies were 2 (0–6) cells in IBS patients and 3.5 (1.1–9.1) cells in healthy subjects (p = 0.026, univariate analysis). MC in close proximity to nerve fibres were 0 (0–20) % in IBS patients and 3.1 (1.7–16.7) % in healthy subjects (p = 0.76). There were no differences between the different IBS subtypes concerning MC numbers and location. HCA identified two distinct groups among IBS patients, based on MC numbers and location. These groups were characterized by higher MC numbers and proportions of MC in close proximity to nerves (MC high), or by lower MC numbers and proportions of MC in close proximity to nerves (MC low). Univariate analysis showed no differences in total IBS-SSS, VSI and HAD scales between MC high and MC low IBS patient groups. OPLS-DA showed that MC high and MC low groups could not be discriminated with regards to IBS symptoms (GSRS, IBS-SSS, VSI and HAD) or barrier properties (mucosal expression of CLD-1, MUC, TJP1 and OCLN, and activity of fecal serine proteases). Finally, parameters of visceral sensitivity were equivalent in MC high and MC low groups when investigated by OPLS-DA.

Conclusion: This study was not able to identify any differences in mast cell frequencies or proportions of mast cells in close proximity to nerves, between IBS patients and healthy subjects. Furthermore, there were no links between mast cell profile to individual or global IBS symptoms, expression levels of barrier proteins or degree of visceral sensitivity in IBS patients. These findings illustrate that quantity and location of mucosal mast cells are factors not involved in the pathophysiology of IBS.

Disclosure: Boris Le Neve is an employee of Danone Nutricia Research.
**P1060 IR RIBBLES BOWEL SYNDROME, CHRONIC FATIGUE AND PAIN IN A NORWEGIAN PRIMARY CARE POPULATION**

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**Introduction:** Irritable bowel syndrome (IBS) is a highly prevalent functional gastrointestinal disorder associated with chronic widespread pain and fatigue. Several studies have shown that a large proportion of patients with IBS also reported chronic fatigue or pain. The prevalence varies depending on the year and geographic location of the study, method for data-collection and the criteria used (1). In 2016 the new Rome IV criteria for the diagnosis of IBS were announced (2). No studies on the prevalence of IBS based on the Rome IV criteria have been published, but it has been reported that Rome IV criteria will identify a smaller patient population with more severe IBS compared to the previous Rome III criteria (3).

**Results:** During the sixth year of their studies, all medical students at the University of Bergen have a four-week placement in general practice. Each student was asked to distribute a one-page questionnaire to 20 consecutive patients aged 18 and above who visited the practice. The data collection for this study took place in the fall of 2017 and winter of 2018.

The main outcome was IBS based on questions composed to fit Rome IV criteria. Secondary outcomes were the symptoms ‘chronic fatigue’ based on two questions from Chalder’s Fatigue Questionnaire that corresponded best with chronic fatigue in the control group of a previous study (4), and ‘pain’-based on questions about back pain and musculoskeletal pain. Explanatory variables were age, sex, education and country of birth.

**Conclusion:** The prevalence of IBS in Norwegian primary care was 5.9%. IBS was associated with chronic widespread pain and fatigue. Several studies have shown an overlap of IBS with other syndromes and symptoms, such as chronic fatigue, fibromyalgia, and widespread pain (4). Mostly, these studies are small, with patients in secondary or tertiary care.

**Aims and Methods:** The aims of this study were to estimate the prevalence of IBS according to Rome IV criteria in a primary care population, and to establish the association with chronic widespread pain and fatigue.

**Disclosure:** Nothing to disclose.

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**P1070 THE SOCIOECONOMIC BURDEN OF IRRITABLE BOWEL SYNDROME IN A DUTCH POPULATION**

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2 University of Bergen, Department of Global Public Health and Primary Care, Bergen, Norway

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**Introduction:** Irritable Bowel Syndrome (IBS) is a highly prevalent functional disorder that carries a substantial socioeconomic burden due to increased healthcare utilization and productivity losses. Actual data on this topic for the Dutch situation is lacking.

**Aims and Methods:** This study aimed to determine the socioeconomic cost of IBS and 2) to identify sociodemographic and clinical characteristics associated with direct and indirect costs in a Dutch IBS population.

Baseline data from patients enrolled in the PERSUADE trial (peppermint oil versus placebo) was used. IBS patients (ROME IV), aged between 18 and 75 years old, were included via primary and secondary/tertiary care recruitment or self-referral and completed questionnaires regarding demographics and life style, symptom severity, Quality of Life, and anxiety and depression. Direct and indirect health related costs were measured using the iMTA/Trimbos Medical Cost Questionnaire (MCQ, recall period 3 months) and Productivity Cost Questionnaire (PCQ, recall period 4 weeks) respectively. Costs were calculated by multiplying resource use by the cost price per resource unit, adjusted for reference prices derived from the Dutch guidelines for cost calculations in health care. The friction cost method was applied for the determination of long term absenteeism costs. Data regarding short-term absenteeism was extrapolated to estimate costs for a 3-month period.

**Results:** 111 patients (86% female, mean age 33 years old; Sd 13) were included in the current analysis. Data was highly skewed. Table 1 shows the total direct and indirect costs.

**Disclosure:** Nothing to disclose.

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**P1071 STRONG EVIDENCE SOMATISATION MEASURES BASED ON PSYCHIATRIC CHECKLISTS ARE MORE REFLECTIVE OF PSYCHOLOGICAL RATHER THAN PHYSICAL HEALTH: IMPORTANT CONSEQUENCES FOR GASTROENTEROLOGY RESEARCH AND PRACTICE**

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**Introduction:** Functional gastrointestinal disorders (FGIDs) have been strongly associated with psychological disorders, including somatisation (1). Somatisation in gastrointestinal (GI) research is typically defined as a physical expression of psychological distress and a number of scales are commonly used to measure it, including somatic symptom checklists (SSC-Ls) (2) and measures centred around psychological distress [e.g. DSM]. Some of these have been criticised as not truly measuring somatisation as they can be confounded with actual organic co-morbidities, especially in the absence of clinical examination or structured interview (3). Consequently neither researchers nor clinicians can be certain whether they are reflecting psychological distress or somatic illness burden.

**Aims and Methods:** We aimed to determine whether somatisation as measured through an SSCL was primarily driven by measures of psychological state or measures of physical health in a large, longitudinal study of women’s health.

**Disclosure:** Nothing to disclose.

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**References**


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**Category**

<table>
<thead>
<tr>
<th>Category</th>
<th>Total direct and indirect costs, sum in € (%); mean (Sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 111</td>
<td>45.619 (39.8); 205 (1.150)</td>
</tr>
<tr>
<td>Abstinence</td>
<td>Mental health care</td>
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<tr>
<td>Outpatient consultation</td>
<td>11.439 (10); 122 (39)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>8.775 (7.7); 79 (142)</td>
</tr>
<tr>
<td>Diagnostics or treatment without hospitalization</td>
<td>7.931 (6.9); 36 (268)</td>
</tr>
<tr>
<td>Impaired unpaid work</td>
<td>5.291 (4.6); 48 (135)</td>
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<tr>
<td>General Practice</td>
<td>5.276 (4.6); 48 (58)</td>
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<td>Medication</td>
<td>3.416 (3.0); 31 (249)</td>
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<tr>
<td>Other costs</td>
<td>9.794 (8.6); 12 (77)</td>
</tr>
</tbody>
</table>

**Total**

114.513 (100); 1031 (2022)

**Disclosure:** Nothing to disclose.
Two waves (3 and 4) of data collected from the cohort born 1973-1978 of the Australian Longitudinal Study of Women’s Health (n = 4366) were analysed to determine whether somatisation as measured in wave one was better predicted by psychological traits or physical health and lifestyle 3 years earlier. The same analysis was repeated cross-sectionally to determine whether the SSC1 was more influenced by concurrent psychological state or physical health. To reduce optimism bias in model development predictors were chosen on Bayesian Information Criterion (BIC) rather than conventional tests.

Results: As shown in the table below, almost the same number of psychological and physical health measures were found to be longitudinal predictors of SSC1. However the psychological predictors accounted for approximately twice as much of the variance in SSC1 as did physical health predictors. Cross-sectionally, a much larger list of concurrent physical health predictors were identified (Table 1) and slightly fewer psychological predictors were involved. However the variance in SSC1 explained by concurrent psychological predictors was again approximately twice the variance explained by physical health and lifestyle predictors.

Conclusion: Despite being a list of potential health complaints, the SSC1 utilised in this large, population-representative longitudinal study of women appears to be more a reflection of psychological distress than physical health.

<table>
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<tr>
<th>Predictor</th>
<th>Longitudinal</th>
<th>Cross-sectional</th>
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</thead>
<tbody>
<tr>
<td>SEHA (SES)</td>
<td>−0.04 (.02)</td>
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</tr>
<tr>
<td>CESD (depression)</td>
<td>0.05 (.02)</td>
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</tr>
<tr>
<td>Socioeconomic status</td>
<td>0.149 (.199)</td>
<td>0.139 (.199)</td>
</tr>
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<td>SF-36 mental</td>
<td>−0.173 (.025)</td>
<td>−0.279 (.025)</td>
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<tr>
<td>Satisfaction with GP</td>
<td>−0.032 (.014)</td>
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<tr>
<td>Experienced violence</td>
<td>0.020 (.013)</td>
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<tr>
<td>SF-36 physical</td>
<td>−0.256 (.020)</td>
<td>−0.343 (.020)</td>
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<tr>
<td>Major illness</td>
<td>0.051 (.014)</td>
<td>0.040 (.013)</td>
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<td>Medications for nerves</td>
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<td>Other medication</td>
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<td>Smoking: ex v never</td>
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<tr>
<td>Smoking: current v never</td>
<td>0.020 (.014)</td>
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<tr>
<td>Marijuana: ever v never</td>
<td>0.021 (.015)</td>
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<tr>
<td>Other drugs: ever v never</td>
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</tr>
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<td>Exercise: moderate v low</td>
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</tr>
<tr>
<td>Exercise: high v low</td>
<td>0.032 (.014)</td>
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</tr>
<tr>
<td>Other exercise</td>
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</tr>
<tr>
<td>R² (total)</td>
<td>0.188</td>
<td>0.249</td>
</tr>
<tr>
<td>R² (psych)</td>
<td>0.138</td>
<td>0.174</td>
</tr>
<tr>
<td>R² (physical)</td>
<td>0.068</td>
<td>0.098</td>
</tr>
</tbody>
</table>

References

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P1073 PREVALENCE AND IMPACT OF SELF-REPORTED VERSUS ROME IV CRITERIA-BASED IRRITABLE BOWEL SYMPTOMS IN THE GENERAL POPULATION

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The symptom-based diagnostic criteria for IBS have recently been revised in the Rome IV consensus. In a tertiary care cohort, compared to Rome III, Rome IV identifies a subgroup with more severe symptoms, co-morbidity and quality of life impact (Vork 2018). On the other hand, with rising public awareness of IBS, self-diagnosis and self-management are likely to increase as well. The prevalence and impact of Rome IV-based IBS versus self-diagnosed IBS was compared in the general population.

Aims and Methods: An internet panel filled out an online survey on bowel symptom burden and its impact. Questionnaire-based demographics and self-reported symptoms based on Rome IV criteria, their frequency, and their impact on healthcare utilization and daily activities.

Results: A representative internet panel of 1,012 subjects, which reflected the Belgian population in terms of educational level, professional activity, and regional distribution, completed the online survey. Rome IV IBS criteria were fulfilled by 5.5% of the Belgian population who were younger and more likely to be female (7% of women vs. 3.9% of men, 42.4 ± 1.9 vs. 45.4 ± 0.3 years, p < 0.001). Thirty-seven percent consulted a physician for IBS symptoms (27% primary care, 15% a specialist) over the last year, with an average of 41 ± 2.2 doctor visits per patient; colonoscopy was performed in 12% and radiological examination in 15%. Rome IV IBS subjects reported a consequence of their symptoms such as somatisation (88%), irritability (85%), insomnia (65%), anxiety (69%), loss of appetite (69%), depressive mood (54%), shame (58%), staying home from social activities (54%), anger (54%) and interference with ability to work (27%). Sixty-one percent of these subjects were employed, and 7% reported absence from work due to IBS symptoms, leading to 14 days of absence from work due to bowel symptoms over the last year.

Conclusion: Despite being a list of potential health complaints, the SSC1 utilised in this large, population-representative longitudinal study of women appears to be more a reflection of psychological distress than physical health.

Disclosure: Nothing to disclose

Reference

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Introduction: The fructose breath test is widely used for the investigation of fructose intolerance and malabsorption as contributing factors to symptoms of functional gastrointestinal disorders (FGID). Additionally, it is useful in predicting responders to a dietary reduction of fermentable sugars (low FODMAP diet). Patients with FGID are, however, well known to have high placebo response susceptibility. As the breath test is normally applied in open fashion, it is unknown what the contribution of knowledge of the substrate is to the test outcome.

Aims and Methods: The aim of this single-centre, placebo-controlled prospective trial was to compare the outcome of breath tests when fructose is given in open versus blinded fashion in successive patients with FGID. Identical breath tests were performed in randomised sequence at least one week apart with either a) water (neutral placebo), b) artificial sweetener (Aspartin®: cyclamate/saccharine, sweet placebo), c) fructose given double-blind or d) fructose given open. Breath samples were collected in 30 male and female patients with FGID (defined by Rome III criteria, mean age 29.4 ± 9.9 years) for measurement of hydrogen and methane concentrations, and GI symptom intensities (abdominal bloating, flatus, fullness, nausea, diarrhoea, abdominal cramps or pain, borborygmi, and gasoroosophageal reflux) were each scored on a 3-point Likert scale for 5 hours after substrate ingestion. Patients were not selected based on symptom or gas responses. The areas-under-the-curve (AUC) of the individual and aggregate GI symptom scores and of the breath hydrogen and methane concentrations were compared between substrate arms.

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P1074 DOES BLINDING AFFECT THE OUTCOME OF FRUCTOSE BREATH TESTING IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS?

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2. Brain-Gut Research Group, UZ Leuven, Belgium
3. Brain-Gut Research Group, Bern, Switzerland

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Introduction: The fructose breath test is widely used for the investigation of fructose intolerance and malabsorption as contributing factors to symptoms of functional gastrointestinal disorders (FGID). Additionally, it is useful in predicting responders to a dietary reduction of fermentable sugars (low FODMAP diet). Patients with FGID are, however, well known to have high placebo response susceptibility. As the breath test is normally applied in open fashion, it is unknown what the contribution of knowledge of the substrate is to the test outcome.

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Abstract No: P1074
Table: Baseline-corrected means and standard deviations are shown.

<table>
<thead>
<tr>
<th></th>
<th>fructose open</th>
<th>fructose blind</th>
<th>artificial sweetener</th>
<th>p-value across all arms (Dunn’s test, Bonferroni corrected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC GI aggregate symptom score</td>
<td>1.42 ± 5.17</td>
<td>6.47 ± 9.04</td>
<td>4.37 ± 8.27</td>
<td>1.81 ± 3.98</td>
</tr>
<tr>
<td>AUC hydrogen concentration</td>
<td>-8.92 ± 18.94</td>
<td>23.39 ± 50.16</td>
<td>25.04 ± 53.09</td>
<td>-6.05 ± 26.12</td>
</tr>
<tr>
<td>AUC methane concentration</td>
<td>-1.16 ± 4.54</td>
<td>8.83 ± 21.74</td>
<td>3.52 ± 13.10</td>
<td>0.08 ± 9.22</td>
</tr>
</tbody>
</table>

Results: There were no significant differences between the open fructose and blinded fructose arms in the AUCs of any of the individual or aggregate GI symptom scores (see Table). However, the AUCs of the aggregate GI symptom scores were greater following open fructose than water (p = 0.003). There were no significant differences in the AUCs of either hydrogen or methane concentrations between open and blinded fructose breath tests, but hydrogen gas concentration AUCs were greater following open and blinded fructose than after water and artificial sweetener (all p < 0.05). A similar trend towards higher methane breath gas concentrations following open and blinded fructose than after water and artificial sweetener was seen. Blinding was maintained very effectively, as only 5 of 120 (4%) treatment substrates were attributed correctly by the patients.

[Baseline-corrected means and standard deviations are shown.]

Conclusion: The absence of significant differences in symptom scores and gas concentrations between breath tests with fructose given open or blinded clearly indicates that clinical breath testing can be performed in open fashion in patients with FGID. The comparisons of GI symptoms and breath gas concentrations between the neutral and sweet placebos and the fructose arms are marked by wide variability due to the inclusion of patients across the entire spectrum of responses, i.e. with and without fructose intolerance or malabsorption.

Disclosure: Sponsored by Forschungsstiftung Hirslanden, Zurich, Switzerland.

Reference

**P1075 BLOATING IN A LARGE OUTPATIENT POPULATION: DISCHARGE OR INVESTIGATE?**

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Introduction: Bloating is a common presenting complaint and affects approximately up to 20% of the population. Though objective abdominal distension only occurs in half of the cases. It can have a significant impact on the patient’s everyday activities. Its severity may vary from transient without the need for treatment, to severe and debilitating symptoms that cause multiple outpatient clinic visits or even to the emergency department. However, its evaluation and management may be difficult, thus necessitating multiple medical appointments and investigations.

Aims and Methods: The aims of this study were to determine the prevalence of this symptom among patients presenting to a gastroenterology out-patient clinic and the pathologies that were diagnosed in this group of patients. This was a retrospective analysis of patients presenting to a single consultant gastroenterology secondary care out-patients clinic (2013–2015) where one of the symptoms being investigated was bloating. The clinical case notes and investigations (blood tests, faecal cal-

Results: From an overall cohort of 840 patients, 256 patients with bloating (30.9%) were identified. The mean patient age was 42.4 (SD 14.1) years. The mean time of follow up for these patients was 47.5 months (range: 20.5–71.3) years. Other symptoms were: abdominal pain (73.8%), dyspepsia (32%), nausea (14.8%), vomiting (4.7%), bloating (7%), change in bowel habit to diarrhoea (29.7%), change in bowel habit to constipation (17.6%) and weight loss (9%). In 9.4% of the patients following pathologies were diagnosed: colicel disease (n = 6), small bowel intussusception (n = 1); renal cell carcinoma (n = 2); endo-

Conclusion: This data demonstrates that bloating contributes to a significant patient load in an out-patient setting as 30.5% of patients had this symptom. Routine blood investigations, a faecal calprotectin and abdominal ultrasonography are initial baseline investigations that should be considered in all such patients as approximately 10% of these patients had significant pathologies diagnosed.

Disclosure: Nothing to disclose

**P1076 EFFECTS OF ALOE BARBADENSIS MILL. EXTRACT ON SYMPTOMS AND FAECAL MICROBIOTA PROFILE IN PATIENTS WITH IRITRABLE BOWEL SYNDROME**

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Introduction: Aloe barbadensis Mill. has been suggested to reduce symptoms in patients with irritable bowel syndrome (IBS).

Aims and Methods: We aimed to determine the effects of a commercially available Aloe barbadensis Mill. (Aloe) extract AHY2008, on symptoms and fecal micro-

Results: In total, 160 IBS patients completed the study. The overall severity of IBS symptoms was reduced in patients receiving active treatment (n = 84; 242 (199–291) vs. 218 (138–281), P < 0.001) and placebo (n = 76; 236 (171–289) vs. 226 (101–308), P = 0.003) but not placebo (n = 22; 229 (138–259) vs. 196 (118–238), P = 0.17), although without difference between the groups (P = 0.21). Further, pain severity, pain frequency, bloating and daily life were similarly reduced in both groups (data not shown). However, bowel habit was improved by active treatment (70 (52–88) vs. 60 (41–81), P = 0.001), but not placebo (70 (46–85) vs. 66–64–80, P = 0.17), without difference between the two groups (P = 0.43). The frequency of responders did not differ between active treatment (n = 27, 32%) and placebo (n = 31, 41%) (P = 0.26).

In the active treatment group, faecal microbiota profiles differed between responders (n = 10) and non-responders (n = 14) both before (R2 = 0.96, Q2 = 0.55) and after intervention (R2 = 0.94, Q2 = 0.73). The abundance of Akkermansia muci-

Conclusion: Aloe and placebo were similarly effective in reducing overall symptoms of IBS patients, but a tendency towards better effect of aloe extract were seen in IBS-D patients. Further, faecal microbiota profiles may help predict IBS patients’ responsiveness to aloe extract.

Disclosure: Presenting Author – Bani Ahluwalia is employed by Calmino Group AB while carrying out her Industrial PhD studies at the University of Gothenburg.

**P1077 EFFICACY AND SAFETY OF EULAXODINE IN IBS-D PATIENTS WHO REPORT INADEQUATE SYMPTOM CONTROL WITH PRIOR LOPERAMIDE USE: A PHASE 4, MULTICENTER, MULTINATIONAL, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY (RELIEF)**

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Introduction: Irritable bowel syndrome with diarrhea (IBS-D) is a functional gastrointestinal disorder with limited treatment options. We evaluated the efficacy and safety of eulaxodine, an FDA-approved mixed α-μ-opioid receptor (OR) and δ-OR agonist and δ-OR antagonist compared to placebo in IBS-D patients

References
who reported inadequate symptom control with prior use of loperamide, an over-the-counter laxative generally used for mild-to-moderate watery diarrhoea.

**Aims and Methods:** Adults with IBS-D (River Island criteria) who reported inadequate symptom control subsequent to loperamide use within the preceding 12 months were randomized 1:1 to placebo or eluxadoline 100 mg twice daily taken with food. Patients received daily IBS-D symptoms, including worst abdominal pain (WAP) on a 0 to 10-point scale and stool consistency (evaluated by Bristol Stool Scale [BSS]). The primary efficacy endpoint was the proportion of composite responders, defined as patients who met daily composite responder criteria (WAP improvement by ≥40% and BSS score ≤5 or absence of bowel movement accompanied by ≥40% WAP improvement compared to baseline) for at least 50% of treatment days, and had ≥60 days of diary entries over the 12-week treatment period.

**Results:** 346 patients were enrolled. The majority (70%) were female, and mean age was 44 years. A significantly greater proportion of patients receiving eluxadoline achieved the primary composite responder endpoint compared to placebo (22.7% [39/172] vs. 10.3% [18/174]; p = 0.0022). Additionally, a higher proportion of patients achieved the secondary endpoints of improvements in stool consistency (27.9% [48/172] vs. 16.7% [29/174]; p = 0.0119) and WAP (43.6% [75/172] vs. 31.0% [54/174]; p = 0.0174) with eluxadoline than placebo, respectively. Throughout the 12-week study, a greater proportion of eluxadoline patients met the monthly composite responder endpoint compared with placebo (Weeks 1–4: 14.0% vs. 6.9%, p = 0.0336; Weeks 5–8: 26.7% vs. 14.9%, p = 0.0063; Weeks 9–12: 30.8% vs. 16.7%, p = 0.0018). A comparable number of patients reported treatment-emergent adverse events (TEAEs) with eluxadoline (124 events; 37.4% [64/171] and placebo (112 events; 35.3% [61/173]). More patients discontinued treatment due to TEAEs with eluxadoline compared with placebo (10 vs. 3). No treatment-related serious AE was reported.

**Conclusion:** Eluxadoline appears safe, effective, and well tolerated for treating IBS-D symptoms in patients who report inadequate symptom control with prior loperamide use.

**Disclosure:** This study was funded by Allergan plc. Darren Brenner is a consultant and speaker for Allergan plc. Catherine Gutman is an employee of Allergan plc. Esther Jo is an employee of Allergan plc.

### Table 1: Intervention timecourse.

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Weeks 4–7</th>
<th>Week 8</th>
</tr>
</thead>
</table>

**References**


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**P1078 MULTIDISCIPLINARY SHARED MEDICAL APPOINTMENTS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS: PRELIMINARY RESULTS OF A NON-PHARMACOLOGICAL PILOT STUDY**

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**Introduction:** Functional gastrointestinal disorders (FGIDs) are prevalent and resource consuming. Biopsychosocial interventions have proven useful for symptom control. Shared medical appointments have been successfully used in other diseases to reduce waiting times, limit costs and increase patient satisfaction, but their use in FGIDs is limited. No specific multidisciplinary programmes have been developed for FGIDs.

**Aims and Methods:** A multidisciplinary (Gastroenterology, Dietetics, Psychiatry) approach was provided to 10 patients diagnosed with FGIDs attending shared medical appointments. Efficacy of a series of non-pharmacological interventions (dietary modifications, psychoeducation, stress and anxiety control) over a 4-month period was assessed on several health indicators (presence and absence of bowel movement accompanied by 40% WAP improvement, baseline and waist circumference). The severity of the GI symptoms improved from a baseline score of 60.4 (mild) to 40.8 (mild) (p < 0.00005).

**Results:** 25 patients have been included so far. 80% were women. Mean age was 46.2 years (range 29–68). Initial diagnoses were as per the ROME IV criteria (1, 2): 36% irritable bowel syndrome, 12% functional diarrhea, 32% functional abdominal distension, and 88% dyspepsia. 96% of patients attended at least once formative session. The severity of the GI symptoms improved from a baseline score of 42.8 ± 16.7 points (severe) to 104 ± 28.4 (mild) (p < 0.00005). Adherence to low fodmap diet was good (7.3 ± 1.4 vs 1.4 ± 1.1 servings of high fodmap foods per day, p = 0.025). A trend towards a reduction in waist circumference (97.4 ± 8.9 vs 92.8 ± 8.3 cm, p = 0.076) in the absence of significant changes in body mass index suggests an improvement in abdominal bloating. The number of drug groups used during the 6 months prior to the intervention was 2.7 ± 0.4, and it was reduced to 0 ± 0 (p = 0.0037). Baseline anxiety and depression scores (4) were within the pathological and borderline range respectively and did not improve significantly after the intervention (11.4 ± 0.8 vs 10.2 ± 2.3; 7.2 ± 1.1 vs 6.6 ± 2.8 for depression).

**Conclusion:** A multidisciplinary shared medical appointment approach to implement non-pharmacological measures in the treatment of FGIDs is useful to alleviate GI symptoms in these patients. A stronger psychological intervention might be needed for adequate control of anxiety. A dietary reintroduction phase is currently being implemented to tailor the individual needs and prevent nutritional deficits. A 6 and 12-month post intervention assessment will be needed to see whether improvement persists.

**Disclosure:** Nothing to disclose.

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**P1079 HYPNOTHERAPY FOR IRRITABLE BOWEL SYMPTOMS: THE PATIENT’S PERCEPTION**

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**Introduction:** Numerous studies have shown that hypnotherapy (HT) improves the symptoms of irritable bowel syndrome (IBS) using clinical outcome measures. In light of the increasing interest in capturing the patient’s perception of their illness and treatment, it was felt it would be helpful to record how patients perceive the hypnotherapeutic process, on which there is currently little information.

**Aims and Methods:** In addition to measuring symptom change, we have recently started to record the patient’s perception of hypnotherapy for their IBS, including their expectations, and now report the results for the first 50 patients. 50 consecutive IBS patients (38 females and 12 males, age range 18–76) attending for hypnotherapy were asked to complete questionnaires recording their beliefs about the efficacy of HT. Their perceptions about the hypnotherapeutic process were assessed quantitatively and also qualitatively using patient descriptions. Furthermore, the analysis compared the characteristics of responders and non-responders.

**Results:** Out of 50 patients (78%, P < 0.001) responded to treatment (50 point or more reduction in IBS SSS), which is exactly consistent with our previously published data. Pain scores, non-colonic symptoms, quality of life, anxiety and depression also significantly improved after HT (all P < 0.01). When asked how they felt before treatment, 52% of responses portrayed hypnotherapy negatively compared to 3% after treatment. The relatives and doctors of patients were generally supportive of HT although one cognitive behavioral therapist advised against it. 9 of 11 non-responders (82%) considered treatment worthwhile despite no significant effect on their symptoms. This may be because 46 patients (92% of all patients) had found HT helped them with other issues, such as dealing with stressful situations or poor sleep.

**Conclusion:** Although initially being perceived negatively, hypnotherapy significantly improved symptoms and resulted in other benefits not related to the gastrointestinal system. Interestingly, those with greater expectation about treatment did not seem to do quite so well, suggesting that high expectations are not necessary for a good outcome.

**Disclosure:** Nothing to disclose.

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**Abstract No:** P1078

**Table 1: Intervention timecourse.**
P1080 RANDOMIZED CLINICAL TRIAL: EFFECT OF BIO-25 ON MICROBIOTA COMPOSITION OF PATIENTS WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME

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Introduction: The pathogenesis of IBS is multifactorial and not completely understood. Epidemiological observations have demonstrated the development of IBS symptoms following disruption of the individual ‘normal’ microbiota and multiple studies have described differences between the microbiome in IBS patients and healthy cohorts. While probiotic therapy for IBS is the subject of intense investigation, its mechanisms of action are not clear.

Aims and Methods: We aimed to evaluate the impact of a multifaceted probiotic on the enteric microbiota composition in women with diarrhea-predominant irritable bowel syndrome (IBS-D) and to determine whether these effects are associated with changes in IBS symptoms or inflammatory markers.

In this double blind, placebo-controlled study, Rome III IBS-D women completed a two-week run-in period. Eligible women were then assigned at random to a probiotic capsule (BIO-25) or an indistinguishable placebo, twice daily for 8 weeks. IBS symptoms and stool consistency were rated daily by visual analogue scales and the Bristol stool scale. High-sensitive C-reactive protein was tested at baseline and 4 and 8 weeks. Fecal calprotectin and microbial composition (diversity and taxa) were tested at baseline and 8 weeks. Microbial sequencing of the 16S rRNA was performed using PCR pyrosequencing platform. Data was analyzed to compare patients who responded to treatment and those who did not using QIIME and Linear discriminate analysis with effect size estimation (LEfSe).

Results: One-hundred and seventy-two IBS-D patients were recruited, and 107 eligible patients were allocated to the intervention (n=54) or placebo (n=53) group. Compared to placebo, BIO-25 did not result in significant fecal microbial alterations, except for higher Lactobacillus levels in the BIO-25 group (P=0.002). Among patients receiving BIO-25, the prevalence of specific microbial groups at baseline was predictive of the response to probiotic therapy: higher proportions of Bilophila at baseline were associated (P=0.003) with symptomatic relief (clinical response) and higher proportions of Hemophilus (P=0.01), Enterobacter (P=0.05), Slackia (P=0.03), Faecalibacterium (P=0.03) and Odoribacter (P=0.05) were associated with a decrease in CRP/calprotectin levels (inflammatory response) compared to the non-responders (Table 1).

Conclusion: This study demonstrates that patient education for patients with IBS can both give effects comparable to patient education in a group format. This study shows that patient education for patients with IBS can both give effects comparable to patient education in a group format.

Disclosure: Nothing to disclose

Table 1 – Proportions of fecal bacterial genera associated with IBS response to the probiotic Bio-25.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Genus</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bristol stool scale</td>
<td>Bilophila</td>
<td>0.0006</td>
<td>0.022</td>
<td>0.02</td>
</tr>
<tr>
<td>Abdominal pain reduction</td>
<td>Bilophila</td>
<td>0.0014</td>
<td>0.025</td>
<td>0.03</td>
</tr>
<tr>
<td>hs-CRP</td>
<td>Haemophilus</td>
<td>0.0013</td>
<td>0.027</td>
<td>0.01</td>
</tr>
<tr>
<td>Fecal calprotectin</td>
<td>Enterobacter</td>
<td>0.0006</td>
<td>0.026</td>
<td>0.05</td>
</tr>
<tr>
<td>Faecalibacterium</td>
<td>Slackia</td>
<td>0.0026</td>
<td>0.016</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 1 Outcome: Mean (SD)

Outcome | Baseline | 6-months follow-up |
---------|----------|--------------------|
Group    | Internet | Internet           |
IBS-SSS  | 297.5 (103.4) | 288.9 (77.3) | 243.3 (102.2) | 246.1 (101.1) |
GSRS-IBS | 51.3 (14.3) | 50.4 (10.3) | 45.1 (14.5) | 43.5 (13.5) |
VSI      | 40.3 (20.0) | 39.2 (18.8) | 34.2 (20.8) | 30.8 (18.5) |
Knowledge (VAS 0–100) | 48.3 (21.8) | 49.0 (22.6) | 71.5 (17.2) | 66.0 (19.0) |
HADS (Depression) | 8.2 (4.3) | 7.6 (4.4) | 7.4 (4.9) | 6.2 (4.2) |
HADS (Anxiety) | 5.3 (3.9) | 5.0 (4.2) | 4.9 (3.5) | 4.9 (3.7) |

P1081 STRUCTURED PATIENT GROUP EDUCATION VERSUS STRUCTURED PATIENT EDUCATION VIA THE INTERNET FOR PATIENTS WITH IBS: A RANDOMIZED, CONTROLLED TRIAL

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Introduction: Structured patient group education (IBS School), has previously been evaluated and found efficacious for symptom improvement in patients with irritable bowel syndrome (IBS) (Ringstrom et al 2012). In this randomized controlled study we compared the effects with a similar education provided via the internet. We hypothesized that patient education provided via the internet would give effects comparable to patient education in a group format.

Aims and Methods: The study population consists of IBS patients >18 years, referred to our unit to participate in the IBS School. Patients were included in blocks of 20 and were then randomized 1:1 to IBS School in group-format or via Internet. A total number of 120 patients were included in the study (57 in the group format and 63 in the internet condition). The IBS school in group-format consisted of three, two-hour sessions held once per week with eight to ten patients in each group. A nurse and a dietician lead the sessions. At the first session, general information was provided about IBS, symptoms, pathophysiology and treatment options. At the second session, food-related issues were discussed and at the third the effects of other life style factors like stress, physical activity and relaxation were discussed. The participants in the Internet group received texts in a stepwise fashion over the three weeks, with the same information that were covered in the group condition. The patients were also able to communicate reflections and questions concerning the written information with the nurse and the dietician via e-mail. They were also encouraged to attend a closed online forum where they had the opportunity to discuss and reflect over information material from the last week with other patients. GI symptom severity (IBS-SSS and GSRS-IBS), GI-specific anxiety (VSI), self-rated disease knowledge (VAS 0–100 score), anxiety and depression (HADS) were assessed with validated questionnaires at baseline and 6 months after the intervention.

Results: For the primary endpoint, the IBS-SSS, 90 patients (75%) had provided follow-up data. Taken together, both groups showed significant improvement of GI symptom and GSRS-IBS (p<0.001, respectively), but there were no differences between the groups (p=0.54 and p=0.73, respectively). Both groups showed improvement in GI-specific anxiety (p<0.001), self-rated disease knowledge (p<0.001), and anxiety (p=0.005). There were no differences between the groups in any of these outcomes (p=0.31, p=0.87 and p=0.46, respectively). There was no overall improvement in symptoms of depression (p=0.54) and no differences between the groups (p=0.93). See Table 1 for means and standard deviations for the two groups at the assessment points.

Conclusion: This study demonstrates that patient education for patients with IBS can both be delivered in traditional group format and over the internet with significant improvements in GI symptom severity, GI-specific anxiety, general anxiety, and self-rated disease knowledge and with comparable effects between the two education formats.

Disclosure: Nothing to disclose
P1082 USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE BY PATIENTS WITH ROME IV CRITERIA FOR IRRETTABLE BOWEL SYNDROME: A SINGLE-CENTER ITALIAN SURVEY

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Introduction: Depression symptoms and quality of life (QOL) in patients with BADs. Single-center prospective study that included consecutive patients with BADs evaluated at the Coloproctology outpatient clinic and a group of healthy volunteers (blood donors). Psychological morbidity was assessed using the Hospital Anxiety and the Rome IV Scale (HADS) questionnaire, including anxiety (HADS-A) and depression (HADS-D) subscales. A HADS score greater than 8 was considered abnormal. The QOL was evaluated using the Short Form (36) Health Survey (SF36), summarized in a physical (PCS) and mental (MCS) component score (with lower scores representing a lower QOL).

Results: Fifty-one patients (31 patients and 20 healthy volunteers) were included, 59% women, with a median age of 52 years (IQR 38–62). There were no differences between the two groups regarding gender (p=0.250) but the control group was younger (mean 45 vs. 52 years, p=0.002) and had a higher education (high school 55% vs. 26%, p=0.044). The main BADs were hemorrhoids (32%), pruritus ani (29%) and anal fissure (19%). More than one BAD was present in 23% of patients. In cases of BADs, patients with BADs had a higher mean scores of HADS-A (10 vs. 4 ± 3.3, p<0.001) and HADS-D (7 ± 4 vs. 2 ± 3, p<0.001). In the BADs group the proportion of patients with abnormal scores of HADS-A (77% vs. 10%, p<0.001) and HADS-D (47% vs. 17%, p=0.009) was significantly greater than in control-adenoma of scores of PCS (46 ± 10 vs. 54 ± 6, p<0.001) and MCS (31 ± 22 vs. 48 ± 17, p=0.004) were lower in the BADs group. In the subanalysis of the BADs group the presence of pruritis ani was significantly associated with a higher HADS-A score (13 ± 5 vs. 5 ± 6, p=0.013) and lower MCS (16 ± 20 vs. 35 ± 20; p=0.031). The presence of more than one BAD showed a tendency for a lower PCS (39 ± 7 vs. 48 ± 10; p=0.057) and MCS (16 ± 15 vs. 34 ± 22; p=0.06) but it did not reach statistical significance.

Conclusion: Benign anorectal disorders are associated with a considerable prevalence of anxiety/depression symptoms and a negative impact on quality of life. A high degree of suspicion of an undiagnosed BADs-associated psychological disorder may be important, in order to allow for a timely and adequate therapeutic approach.

Disclosure: Nothing to disclose

P1083 THE MEANING OF BILE ACIDS AND VIOLATIONS OF MICROBIAL METABOLISM IN THE COLON IN THE PATHOGENIC MECHANISMS OF BENIGN ANORECTAL DISORDERS IN PATIENTS THAT SUSTAINED CHOLECYSTECTOMY OR RESECTION OF THE SMALL INTESTINE

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Introduction: Cholecystectomy and resection of the small intestine result in increased risk of bile acid diarrhea due to a large amount of bile acid entering the colon. Long-term presence of BA in the colon may result in violation of microbiota composition and inflammation of its mucous membrane.

Aims and Methods: The aim of this work is to evaluate the influence of BA on colon microbiocenosis in patients with chronic diarrhea that had cholecystectomy or resection of the small intestine, compared to the Rome I criteria. The widespread use of CAM in IBS, the patients’ belief in its safety, and their vocation to re-use it, suggest that knowledge of health-care providers and patient education should be improved.

Disclosure: Nothing to disclose

P1084 PSYCHOLOGICAL MORBIDITY AND IMPACT ON THE QUALITY OF LIFE OF BENIGN ANORECTAL DISORDERS

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Introduction: Benign anorectal disorders (BADs) are very common, with associated symptoms that may have a significant impact on the quality of life. Aims and Methods: The aim of the study was to evaluate the prevalence of anxiety and depression symptoms and quality of life (QOL) in patients with BADs. Single-center prospective study that included consecutive patients with BADs evaluated at the Coloproctology outpatient clinic and a group of healthy volunteers (blood donors). Psychological morbidity was assessed using the Hospital Anxiety and the Rome IV Scale (HADS) questionnaire, including anxiety (HADS-A) and depression (HADS-D) subscales. A HADS score greater than 8 was considered abnormal. The QOL was evaluated using the Short Form (36) Health Survey (SF36), summarized in a physical (PCS) and mental (MCS) component score (with lower scores representing a lower QOL).

Results: Fifty-one patients (31 patients and 20 healthy volunteers) were included, 59% women, with a median age of 52 years (IQR 38–62). There were no differences between the two groups regarding gender (p=0.250) but the control group was younger (mean 45 vs. 52 years, p=0.002) and had a higher education (high school 55% vs. 26%, p=0.044). The main BADs were hemorrhoids (32%), pruritus ani (29%) and anal fissure (19%). More than one BAD was present in 23% of patients. In cases of BADs, patients with BADs had a higher mean scores of HADS-A (10 vs. 4 ± 3.3, p<0.001) and HADS-D (7 ± 4 vs. 2 ± 3, p<0.001). In the BADs group the proportion of patients with abnormal scores of HADS-A (77% vs. 10%, p<0.001) and HADS-D (47% vs. 17%, p=0.009) was significantly greater than in control-adenoma of scores of PCS (46 ± 10 vs. 54 ± 6, p<0.001) and MCS (31 ± 22 vs. 48 ± 17, p=0.004) were lower in the BADs group. In the subanalysis of the BADs group the presence of pruritis ani was significantly associated with a higher HADS-A score (13 ± 5 vs. 5 ± 6, p=0.013) and lower MCS (16 ± 20 vs. 35 ± 20; p=0.031). The presence of more than one BAD showed a tendency for a lower PCS (39 ± 7 vs. 48 ± 10; p=0.057) and MCS (16 ± 15 vs. 34 ± 22; p=0.06) but it did not reach statistical significance.

Conclusion: Benign anorectal disorders are associated with a considerable prevalence of anxiety/depression symptoms and a negative impact on quality of life. A high degree of suspicion of an undiagnosed BADs-associated psychological disorder may be important, in order to allow for a timely and adequate therapeutic approach.

Disclosure: Nothing to disclose

P1085 ANATOMICAL AND FUNCTIONAL FEATURES OF THE INTERNAL RECTAL DETUMESCENT SYNDROME (IRDS) AS A FUNDAMENTAL ELEMENT IN PATIENTS WHO SUFFER FROM ANORECTAL INJURIES: ENDORECTAL ULTRASONOGRAPHY AND HIGH-RESOLUTION ANORECTAL MANOMETRY. AN OBSERVATIONAL CASE-CONTROL STUDY

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Introduction: Approximately half of constipated patients suffer from obstructed defecation. Obstructed defecation syndrome (ODS) is the inability to empty the rectum satisfactorily during defecation and is well defined in the Rome IV. Internal anal sphincter hypertrophy (IRDS) is a condition of impaired anorectal emptying that is often associated with rectocele, plays an important role in the pathophysiology of ODS. Furthermore, there are scarce data on rectal anatomical evaluation and its relationship with a possible impairment of rectal function.

Aims and Methods: The aim was to analyze the correlation between rectal wall thickness (RWT) and rectal pressure (RP), determined by means of 3D endorectal ultrasound (EUS) and high-resolution anorectal manometry (HRAM), can offer new insights in the pathophysiology of patients with ODS caused by IRDP.

Results: Twenty-five ODS patients and 25 HVs were enrolled. HVs showed 68.45 cm3 median TRWV compared with 57.32 cm3 (p<0.001) and 57.32 cm3 (p<0.001), and 10 had severe pathological TRWV (p<0.001). Eight patients had normal PEP, 22 had slightly hypotonic PEP (p<0.013) and lower MCS (16 ± 20 vs. 35 ± 20; p=0.031). The presence of more than one BAD showed a tendency for a lower PCS (39 ± 7 vs. 48 ± 10; p=0.057) and MCS (16 ± 15 vs. 34 ± 22; p=0.06) but it did not reach statistical significance.

Conclusion: Benign anorectal disorders are associated with a considerable prevalence of anxiety/depression symptoms and a negative impact on quality of life. A high degree of suspicion of an undiagnosed BADs-associated psychological disorder may be important, in order to allow for a timely and adequate therapeutical approach.

Disclosure: Nothing to disclose
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P1087 EFFECTS OF BIOFEEDBACK THERAPY ON CLINICAL AND MANOMETRIC PARAMETERS IN PELVIC FLOOR DYSFUNCTION

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Introduction: Patients with pelvic floor dysfunctions may benefit of biofeedback therapy (BFT), before considering surgical treatment for coexisting anomalies. The efficacy of BFT has been reported to be an effective treatment of fecal incontinence (FI) and dysynergic defecation (DD).

Aims and Methods: To evaluate the effect of BFT in patients with pelvic floor dysfunctions. The population referred to the outpatient Unit of Gastroenterology of two Italian Hospitals (in Rome and Milano) included 1235 patients (M 16%, F 84%), mean age 64 ± 17 s.d. (range 16–95 years) with DD (74.4%) and FI (25.6%). All patients received behavioural treatments such as anal sphincter exercises, pelvic floor muscle training with 8 sessions of BFT, in a month period. Clinical symptom (history of symptoms, frequency and severity of faecal incontinence) and anorectal physiological evaluation (digital examination, manometry, rectal sensory testing, balloon expulsion test) were performed before and after BFT. Improvement of resting/squeezing pressure and reduction in laxatives therapy were considered as clinical improvement of FI and DD, respectively.

Results: In the FI group (F 94%), 44% of patients reported a complete resolution of symptoms, 53% had a considerable improvement, 3% no effect. Resting pressure increased from 42 ± 28 s.mHg to 53 ± 17 s.mHg after BFT, squeezing pressure from 96 ± 28 s.mHg to 117 ± 24 mmHg; the rectal volume for first sensation was 37 ± 12 ml to 34 ± 11 ml. In the DD group (F 81%), 41% of patients reported a complete resolution of symptoms, 52% considerable improvement, 7% no effect. Resting pressure and rectal volume for first sensation were normal at baseline (73 ± 21 mmHg and 41 ± 30 ml, respectively). Before BFT, 46% of patients had no complete relaxation straining, 68% had a failure of balloon expulsion test (EBT). After BFT, 69% of patients had a complete relaxation during straining and 84% were able to expel the balloon.

Conclusion: BFT is considered an effective treatment for DD and FI and is widely used. Our data confirm the ability of BFT to improve manometric parameters and clinical symptoms of pelvic floor dysfunctions.

Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00

Oesophageal, Gastric and Duodenal Disorders II – Hall X1

P1089 PREVALENCE OF AUTOIMMUNE GASTRITIS IN AUTOIMMUNE DISEASES: A POPULATION STUDY BASED ON A NON-INVASIVE TEST

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Introduction: Autoimmune gastritis (AG) is a chronic disease in which parietal cell antibodies cause an inflammatory damage to the gastric mucosa, leading to parietal cell atrophy, reduction of the acid secretion and consequently, hypergastrinemia. Although it is generally associated with few symptoms or none at all, it represents a precancerous condition that warrants an appropriate follow-up due to the increased risk of developing gastric adenocarcinoma and neuroendocrine neoplasms.

Aims and Methods: The aim of the study was to evaluate the prevalence of the following autoimmune diseases in the general population: Hashimoto’s thyroiditis (HT), rheumatoid arthritis (RA), psoriatic arthritis (PA), Sjögren’s syndrome (SS) and vitiligo (VI), and to assess cases of patients with multiple autoimmune diseases.

The secondary aim was to investigate in these patients the prevalence of chronic atrophic AG through a non-invasive test, and to evaluate its usefulness for the diagnosis of AG in patients affected primarily by a different autoimmune disease. The study was performed in a tertiary regional hospital and patients affected by the mentioned autoimmune conditions were enrolled through the specific code, according with Italian Health System rules, obtaining a population sample of 5291 patients (4299 F, mean age 51.9 ± 17.6; 60% of them (3153 F, mean age 52.4 ± 17.3) underwent a non-invasive test by BFT (M 3F, mean age 30 ± 17.7 s.d. mmHg; the rectal volume for first sensation were normal at baseline (73 ± 21 mmHg and 41 ± 30 ml, respectively). Before BFT, 41% of patients had no complete relaxation straining, 68% had a failure of balloon expulsion test (EBT). After BFT, 69% of patients had a complete relaxation during straining and 84% were able to expel the balloon.

Conclusion: BFT is considered an effective treatment for DD and FI and is widely used. Our data confirm the ability of BFT to improve manometric parameters and clinical symptoms of pelvic floor dysfunctions.

Disclosure: Nothing to disclose

TUESDAY, OCTOBER 23, 2018 09:00–17:00

Oesophageal, Gastric and Duodenal Disorders II – Hall X1

P1086 FAECAL INCONTINENCE IN TYPE 2 DIABETICS: COMPARISON WITH NON DIABETIC HEALTHY INDIVIDUALS AND ANALYSIS OF RELATED FACTORS

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Introduction: Faecal incontinence is a complaint that some type 2 diabetic patients frequently refer1,2. The factors involved with are not well known.

Aims and Methods: The aim of this study was to compare the frequency of faecal incontinence between type 2 diabetic patients and non diabetic healthy individuals, and to analyse some factors involved in this perturbation in diabetics. A questioner of Gastrointestinal Symptoms Rating Scale was performed to 140 type 2 diabetics and 132 non diabetic healthy individuals, matched by age and gender.

Results: The frequency of faecal incontinence in diabetics vs. non-diabetics was the follow: minor symptoms, 52% vs. 2.3%; moderate symptoms, 7.9% vs. 0.8%; severe symptoms, 5% vs. 0.6%. The frequency of faecal incontinence between diabetics vs. non diabetics was the follow: minor symptoms, 5.6% vs. 2.3%; moderate symptoms, 7.8% vs. 0.5%; severe symptoms, 5.6% vs. 0.5%. The factors involved with are not well known.

Disclosure: Nothing to disclose

Reference
Gastric atrophy was found in 97 patients (15.9%); only patients affected by CD did show cases of atrophy, neither as a single disease, neither in association. Conclusion: Atrophic gastritis is more frequently found in patients with autoimmune diseases compared to the general population. The serological evaluation of PGI and G17 can be a useful non-invasive method for the assessment of the presence of chronic atrophic AG in asymptomatic patients affected by autoimmune diseases.

Disclosure: Nothing to disclose

P1090 GASTRIC FUNCTION MARKERS: BECAUSE ANTIBODIES ARE NOT ENOUGH IN THE EVALUATION OF AUTOIMMUNE GASTRITIS

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Disclosure: Nothing to disclose

Introduction: Autoimmune gastritis (AG) is a chronic disease that affects the community, and is characterized by the development of two types of auto-antibodies: anti-parietal cells antibodies (APCA) and anti-intrinsic factor antibodies (AIFA). The hypergastrinemia that ensues as a consequence of gastric cell destruction and hypochlorhidria increase the risk of adenocarcinoma and lymphomas; an early diagnosis and an appropriate follow-up are therefore warranted. AG is usually diagnosed using a combination of APCA positivity and histological criteria. However, the latter is an invasive and costly method, and lacks an evaluation of gastric function.

Aims and Methods: The aim of this study was to assess the usefulness of two serological gastric function markers, pepsinogen I (PGI) and gastrin-17 (G-17), in association with APCA determination, in the evaluation of AG.

A cohort of patients with autoimmune gastritis, who are part of our tertiary hospital protocol, underwent routine upper endoscopy with histological evaluation (two antral, one angularis, and two corpus biopsies) for the exclusion of autoimmune gastritis, were considered for this study. All patients were also evaluated from a functional standpoint, with the non-invasive determination of serum pepsinogen I (PGI) and gastrin-17 (G-17). Cut-off values of PGI < 30 µg/l and G17-7 > 7 pmol/l were considered diagnostic for atrophic gastritis of the stomach body and fundus. APCA dosage was also performed in all patients, and a title of > 1/80 was considered positive.

Results: A total of 237 patients (F=111, mean age 54.6±14.8 years) were included in the study. Stomach body atrophy was histologically determined in 97 patients (AG group). PGI and G17 were significantly reduced in patients with body mucosal atrophy (PGI mean value 16.63±15.38; G17 mean value 88.66±99.78), with respect to patients without this histological feature (non-AG group) < p< 0.0001. APCA were more frequently found in the AG group (87.97, 89.69%) than in the non-AG group (78/140, 55.71%) (p < 0.0001).

Conclusion: The positivity of APCA in patients with autoimmune diseases seems to be a consequence of histological and functional features of AG. On the other hand, histological damage well correlates with impaired gastric function. Thus, a gastric function evaluation including determination of PGI and G17 could be a useful and cost-effective method for early stomach body atrophy, especially in asymptomatic patients without indication for performing upper endoscopy. Finally, an evaluation of the isolation presence of APCA is inadequate and should be integrated with gastric functional markers (PGI and G17) to adequately evaluate both disease presence and severity.

Disclosure: Nothing to disclose

P1092 GASTRIC MUCOSAL DAMAGE INDUCED BY ETHANOL CAN BE IMPROVED BY CAFFEIC ACID IN RATS

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Introduction: Peptic ulcer is one of the most common gastrointestinal diseases. Excessive ethanol ingestion results in gastritis characterized by mucosal edema, subepithelial hemorrhages, cellular exfoliation, and inflammatory cell infiltration. Caffeic acid is a natural phenolic compound found in many plants and present in diets as part of fruits, vegetables, tea and wine. It has been reported to have broad spectrum of bioactive activities including anti-inflammatory, antihypertensive, antioxidant, immunomodulatory, anti-inflammatory and neuroprotective properties.

Aims and Methods: Aim of the study is to investigate the anti-ulcerative effects of caffeic acid on ethanol induced ulcer model and to determine the pathways that are involved in the anti-ulcerative action of caffeic acid. Following a 18-h starvation period, ulcer was induced in Sprague-Dawley rats (250-300g) by intragastric administration of absolute ethanol while control group received saline. 60 minutes before ulcer induction, rats were treated with either 1 ml 10% tween-80 as vehicle or caffeic-acid (100, 250 or 500 mg/kg dissolved in 1ml vehicle, per oral). 250 mg/kg of caffeic acid was found to be most efficient dose. To elucidate the roles of nitric oxide (NO) and cholinergic pathway, 10 mg/kg L-NAME or 1 mg/kg atropine was administered 30 minutes before 250 mg/kg of caffeic acid treatment. Ulcers were induced rats were decapitated 60 minutes after ulcer induction and stomach samples were scored macroscopically, and analyzed for myeloperoxidase activity (MPO; index of tissue neutrophil infiltration), malondialdehyde (MDA; an end product of lipid peroxidation) and glutathione (GSH; an important antioxidant) levels. GSH was used as a statistical analyses. Values of p < 0.05 was regarded as significant.

Results: Ethanol administration resulted in an increase in macroscopic damage score (p < 0.001) and in MDA (p < 0.001) activity with concomitant decrease in GSH levels were measured with the ulcer induction. Treatment with 250 mg/kg caffeic acid decreased MDA levels (p < 0.05). Both 250 mg/kg and 500 mg/kg caffeic acid treatment decreased MPO activity (p < 0.05) while gastric GSH was replenished (p < 0.05 and p < 0.01, respectively). Administration of atropine before 250 mg/kg caffeic acid elevated the reduced MDA levels (P < 0.05). Furthermore, increased GSH levels by caffeic acid decreased by L-NAME administration (P < 0.05).

Conclusion: Results showed that caffeic acid ameliorates the ethanol-induced gastric mucosal damage by preventing neutrophil infiltration, tissue damage derived from lipid peroxidation and endogenous anti-oxidant GSH depletion. Moreover, caffeic acid may display these effects via NO and/or cholinergic pathway. Future studies are needed to investigate the mechanism of anti-ulcerative effects of caffeic acid as a therapeutic agent.

Disclosure: Nothing to disclose

P1094 GASTRIC MICROBIOTA ALTERATION FOLLOWING ERADICATION OF H. PYLORI

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Introduction: The human gastric microbiota studies are mainly focused on H. pylori (HP) infection, and few studies focused on bacteria other than HP. Moreover, the results of these studies are controversial. Bik et al. reported that...
the human gastric flora was not affected by HP infection. On the other hand, Maldonado-Conteras et al. reported that HP infection increased the rate of Proteobacteria in the human stomach, and decreased the rate of Firmicutes.

Aims and Methods: The aim of this study is to clarify the composition of the gastric bacterial flora using the next generation sequencer and the changes in gastric microflora before or after HP eradication.

Between December 2012 and July 2016, 24 patients who underwent upper gastros- testinal endoscopy before and after HP eradication were enrolled. Stomach body and antrum biopsy specimens were collected using upper gastrointestinal endoscopy. Bacterial DNA was extracted and purified from the collected samples by the complex enzyme method. After PCR amplification of the 16S rRNA gene V1-2 region of the extracted DNA, barcode sequencing was carried out using MiSeq (Illumina) which is a high-speed sequencer. The stomach bacterial flora was classified through the intergal and intra-gal analysis of the obtained sequence data by using Operational Taxonomic Unit (OTU) analysis.

Results: Twelve pairs of samples obtained from the antrum before and after HP eradication and seventeen pairs of the stomach body samples were PCR amplifi- cation intensities that were performed twice thereafter. There were many kinds of bacterial species other than HP in the gastric environment. In antrum, average OTU is 120.9 and 118.3 before and after eradication, respectively. In gastric body, average OTU is 90.9 and 123.8 before and after eradication, respectively. HP eradication was associated with a significant increase in α-diversity in gastric body microbiome in Shannon’s diversity and there was no significant difference in α-diversity of antrum microbiome before and after eradication. Principal coordinates analysis (PcoA) of weighted and unweighted Unifrac distances of both gastric body and antrum microbiome were significantly different between before and after HP eradication based on Permutational Multivariate Analysis of Variance. While HP is the most dominant species before HP eradication in both gastric body (64%) and antrum (24%), Streptococcus mitis, which is the second dominant bacteria before HP eradication, became the most dominant bacteria species after eradication. The population of many bacteria species were increased and the population of some bacteria species were decreased after HP eradication compared to before eradication.

Conclusion: There were a lot of bacterial species in the gastric environment. HP eradication changes the gastric microbiota dramatically.

Disclosure: Nothing to disclose

P1095 HELICOBACTER PYLORI ANTI BODY AND PEPSINOGEN TESTING FOR PREDICTING GASTRIC MICROBIOME ABUNDANCE

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Introduction: Although the high-throughput sequencing technique is useful for evaluating gastric microbiome, it is relatively expensive and requires gastric mucosal samples (or juice). Therefore, we aimed to develop a predictive model for gastric microbiome using serologic testing.

Aims and Methods: This study was designed to further analyze the Hanyang University Gastric Microbiome Cohort, which was originally established to investigate gastric microbial distribution according to the intragastic environ- ment. We analyzed the relative abundance of the gastric bacteria or type IV secretion system (T4SS) protein gene-contributing bacteria, IgG anti-Helicobacter pylori (HP) antibody, and pepsinogen (PG) levels.

Results: Twelve pairs and 26 participants without and with HP infection, respectively. The relative abundance of nitrosating/nitrate-reducing bacteria was 4.9% and 3.6% in the HP(-) and HP(+) groups, respectively. The relative abundance of TASS gene protein-contributing bacteria was 20.5% and 6.5% in the HP(+) and HP(-) groups, respectively. The relative abundance of both nitrosating/nitrate-reducing bacteria and TASS protein gene-contributing bacteria increased exponentially as PG levels decreased. In the multivariable analysis, advanced age (only for nitrosating/nitrate-reducing bacteria), a negative IgG anti-HP antibody result, low PG I and II levels, and high Charlson comorbidity index were associated with a high relative abundance of nitrosating/nitrate-reducing bacteria and TASS protein gene-contributing bacteria. Adjusted coefficient of determination (R2) was 53.7% and 70.0% in the model for nitrosating/nitrate-reducing bacteria and TASS protein gene-contributing bacteria, respectively.

Conclusion: Negative results of IgG anti-HP antibody and low PG levels were associated with a high abundance of nitrosating/nitrate-reducing bacteria and TASS protein gene-contributing bacteria.

Disclosure: This work was supported by the research fund of Hanyang University (HY-2017).

P1096 CHARACTERIZATION OF MUCOSAL AND FLUID MICROBIOME ACROSS STAGES OF GASTRIC CARCINOMA

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Introduction: Recently a complex microbiota has been uncovered within the stom- ach and the mucosal microbiota dysbiosis is associated with gastric cancer (GC). However, the alterations of mucosal microbiota among stages of GC are inconsistent in different studies. It is also not uncertain the role of fluid bacteria in this process and its difference with mucosal microbiota.

Aims and Methods: The aim of this study was to perform a comparative analysis of the microbiome in both luminal and mucosal niches along the histological stages of gastric cancer. We performed 16S rRNA gene sequencing of gastric mucosal samples from 179 patients including 61 superficial gastritis (SG), 54 intestinal metaplasia (IM) and 64 GC, as well as gastric fluid samples from 96 patients of the same cohort including 42 SG, 26 IM and 28 GC, to determine their alterations across stages of GC.

Results: The composition of gastric mucosal microbiome was different from fluid with lower bacterial diversity. Helicobacter pylori (H. pylori) was observed to dominate the mucosal community strikingly influenced the overall microbial community structure in the stomach that was inconsistent with the fluid. Microbial dysbiosis was shown in mucosa rather than fluid during the progression of GC. Three enterotypes were identified in gastric mucosa with compositional and functional differences and the changes along disease stages varied between enterotypes. The specific taxas consistently altered in IM and GC were identified in each enterotype and their effect for discriminating GC from SG was validated.

Conclusion: The detailed analysis of the whole gastric microbiome along carci- nogenesis demonstrated for the first time that the dysbiosis of mucosal instead of luminal bacteria was associated with GC. The distinct features of gastric mucosal enterotypes in GC development suggest that the potential necessity of enterotype classification before evaluating the correlation between gastric micro- biome and GC.

Disclosure: Nothing to disclose

P1097 COMPREHENSIVE ANALYSIS OF HISTOLOGICAL MICROBNS OF PANCREATIC CANCER COLLECTED BY EUS-FNA

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Introduction: The miRNA is a small RNA molecule whose full length is 18-25 bases, whose biological roles are to regulate its expression by binding to and disrupting target messenger RNA in cells. Recently, it has been reported that these miRNAs are involved in metastasis and expression of various cancers. The aim of this study was to comprehensively analyze the extracted miRNA of cancer tissue obtained by EUS-FNA, which was performed for the definite diagnosis of pancreatic cancer, and to identify miRNA targets related to prediction of metastasis, grade, and prognostic factors.

Aims and Methods: The subjects were 51 patients (21 men and 30 women) with invasive ductal adenocarcinoma diagnosed histologically by EUS-FNA (written informed consent was obtained with approval from the hospital ethics committee). The observation period was from April 2013 to February 2018. MiRNAs extracted from tissues collected by EUS-FNA performed for definitive diagnostic purposes was comprehensively analyzed using a microarray tip equipped with 2555 molecules. MiRNAs comparisons were made using the following three areas of clinical features, clinical stage, sites of recurrences and metastases, and prognosis. The miRNAs of candidates for defining clinical pathology was identified using statistical methods such as cluster analysis.

Results: 1. We identified miRNAs (oncogenic miRNA) with increased expression and miRNAs (tumor suppressor genotype miRNAs) with decreased expression in cancer tissue compared with normal tissues. We focused on miRNAs with higher expression in cancer tissues and miRNAs with lower expression in cancer tissues. 2. There were the increase and decrease of the genes which seemed to correlate in miRNAs and micrornas (tumor suppressor genotype miRNAs) with decreased expression in cancer tissues. 3. The microRNA is a small RNA molecule whose full length is 18–25 molecules. MiRNAs comparisons were made using the following three areas of clinical features, clinical stage, sites of recurrences and metastases, and prognosis. The miRNAs of candidates for defining clinical pathology was identified using statistical methods such as cluster analysis.

Disclosure: Nothing to disclose

References

P1098 ALTERATIONS IN GUT MICROBION COMPOSITION DURING AGING

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Introduction: The gut microbiota have been considered to play an important role in health. Meanwhile aging is a degenerative process that accompanied with a number of diseases and poor health, such as atherosclerosis, dementia, or gastritis.
cancer. Several researchers have reported that gut microbiota were closely related with aging in recent years. However, the distinct species of age-related changes in microbiota composition remains unexplored.

**Aims and Methods:** The present study was conducted to deepen our knowledge on the relationship between the composition of the gut microbiota and host’s age. 116 healthy adults were enrolled for this study in Hangzhou. The 116 healthy adults were divided into 3 groups: young group (n = 36, 20–34 years, 27.89 ± 3.37), middle-aged group (n = 53, 35–55 years, 45.58 ± 5.70) and elderly group (n = 27, ≥ 56 years, 63.00 ± 5.52). Feces were collected and stored at -80°C, total DNA was extracted from frozen samples. The fecal microbiota of the 116 samples was characterized by Illumina sequencing of the V3-V4 region of the bacterial 16S rRNA gene.

**Results:** No significant difference was observed among the three groups with regards to baseline characteristics. Among the detected gut microbes, the cha o index was decreased in middle-aged and elderly groups compared with young group, which represents the community richness. Moreover, the genera Prevotella, Paraprevotella, Veillonella and Klebsiella were enriched with aging. The genera above were mostly the source of common infection. However, the genera Phascolarctobacterium, Faecalibacterium, Bifidobacterium, Streptococcus, Dorea and Bifidobacterium were negatively correlated with age, some of which were well known as beneficial to the gut health. Meanwhile, the presence of Faecalibacterium prausnitzii, Dorea formigenicenens and Bifidobacterium longum were negatively correlated with age, which has a significant difference. The three specific species above were known to have anti-inflammatory or protective properties in gastrointestinal tract.

**Conclusion:** These results suggested the evolving microbial-host associations and relations across the lifespan of a human being. Furthermore, we proved that the microbiota aimed at improving healthy outcomes were decreased with aging. On the other hand, the opportunistic bacteriums were elevated with aging. The genera above were mostly the source of common infection. However, the genera Phascolarctobacterium, Faecalibacterium, Bifidobacterium, Streptococcus, Dorea and Bifidobacterium were negatively correlated with age, some of which were well known as beneficial to the gut health. Meanwhile, the presence of Faecalibacterium prausnitzii, Dorea formigenicenens and Bifidobacterium longum were negatively correlated with age, which has a significant difference. The three specific species above were known to have anti-inflammatory or protective properties in gastrointestinal tract.

**Disclosure:** Nothing to disclose.

### Table: Species Comparison

<table>
<thead>
<tr>
<th>Species</th>
<th>Young group (%)</th>
<th>Middle-aged group (%)</th>
<th>Elderly group (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faecalibacterium prausnitzii</td>
<td>5.23 ± 6.7</td>
<td>3.41 ± 3.92</td>
<td>2.63 ± 2.66</td>
<td>0.0465*</td>
</tr>
<tr>
<td>Roseburia faecis</td>
<td>5.02 ± 13</td>
<td>1.94 ± 2.77</td>
<td>3.00 ± 3.72</td>
<td>0.01335*</td>
</tr>
<tr>
<td>Blautia obeum</td>
<td>0.25 ± 0.39</td>
<td>0.27 ± 0.52</td>
<td>0.08 ± 0.74</td>
<td>0.02314*</td>
</tr>
<tr>
<td>Bifidobacterium longum</td>
<td>0.22 ± 0.35</td>
<td>0.18 ± 0.43</td>
<td>0.07 ± 0.16</td>
<td>0.00597</td>
</tr>
<tr>
<td>Dorea formigenicenens</td>
<td>0.12 ± 0.20</td>
<td>0.11 ± 0.27</td>
<td>0.04 ± 0.05</td>
<td>0.003381*</td>
</tr>
<tr>
<td>Bifidobacterium adolescentis</td>
<td>0.10 ± 0.25</td>
<td>0.05 ± 0.26</td>
<td>0.08 ± 0.32</td>
<td>0.00157*</td>
</tr>
</tbody>
</table>

(Please note: The table format is not perfectly rendered here, as it involves complex formatting and layout.)

**Conclusion:** This study explored the role of gut microbiota in maintaining health and aging.
P1101 EFFECT OF GASTROPROTECTIVE AGENTS ON PREVENTING GASTROINTESTINAL BLEEDING IN PATIENTS RECEIVING DIRECT ORAL ANTICOAGULANTS: A RETROSPECTIVE MULTICENTER STUDY

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Introduction: Direct oral anticoagulants (DOACs) are effective in the prevention and treatment of thromboembolism; however, they are associated with upper gastrointestinal bleeding (UGIB). In this study, we evaluated the efficacy of gastroprotective agents (GPAs) in reducing the risk of UGIB in patients receiving DOACs.

Aims and Methods: We retrospectively reviewed the medical records of 2076 patients who received DOACs for the prevention or treatment of thromboembolic events between January 2008 and July 2016. A cumulative incidence analysis using the Kaplan-Meier method was performed to determine the rate of UGIB and its association with GPAs administration.

Results: Of the 2076 patients, 360 received GPAs. Over the follow-up period (1160 person-years), 1 patient in the GPA group (0.7 per 100 person-years) and 29 patients in the non-GPA group (2.8 per 100 person-years) developed UGIB (P = 0.189). In the multivariate analysis, UGIB was associated with older age (hazard ratio [HR], 1.041; P = 0.048), a history of peptic ulcer or UGIB (HR, 5.931; P < 0.001), and concomitant use of antiplatelet agents (HR, 3.121; P = 0.004). GPAs administration did not reduce the risk of UGIB (HR, 0.200; P = 0.116). However, based on the subgroup analysis of 225 patients with concomitant use of antiplatelet agents or a history of peptic ulcer or UGIB, the GPA group (0 per 100 person-years) showed reduced incidence of UGIB compared with the non-GPA group (1.3 per 100 person-years) (P = 0.065).

Conclusion: Routine use of GPAs for UGIB is not mandatory in patients receiving DOACs. However, GPAs could reduce the risk of UGIB in patients receiving DOACs, who are at a high risk.

Disclosure: Nothing to disclose

P1103 DEVELOPMENT OF A NEW SCORE TO PREDICT MORTALITY AND INTERVENTION IN UPPER GASTROINTESTINAL BLEEDING. THE HA(MASH) SCORE


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Introduction: There has been an increasing interest in the development of scores to establish patients' risk of death and need for intervention in an early phase after upper gastrointestinal bleeding (UGIB). However, some of them such as Glasgow-Blatchford score (GBS), are troublesome to calculate, whereas others such as MASH score need an endoscopy to be completed. Recently, AIMS65 changed the paradigm, shifting to a simple type of score, easy to use and applicable.

For these reasons, provided that the most important decision to make in the ER is whether an immediate intervention is needed, we decided to develop a score centered in this outcome, as well as in mortality.

Aims and Methods: The database was built with information of consecutive UGIB patients admitted to the “Virgen de las Nieves” University Hospital emergency room over 48 months from January 2013 to January 2017. All patients received upper endoscopy, and information regarding patients' demographic data, comorbidities, current medications, clinical presentations, hemodynamics, laboratory test results at admission, and endoscopic findings were collected. An univariate and multivariate analysis were performed, looking for individual odds ratio for every risk factor. After this analysis, we built a score weighting the relative risk of every factor, and giving to values above or below the cutoff point 1 or 2 points depending on their individual bleeding risk.

Conclusion: The HA(MASH) score can be an option for risk assessment in the Emergency Room. Although still far from perfect, it points towards simpler and more easily based scoring, and that the Glasgow-Blatchford score is somehow troublesome to calculate and the AIMS65 is not optimal predicting interventions. Previous to its external validation, de HA(MASH) score seems a very promising option.

Disclosure: Nothing to disclose

P1104 THE STATISTICAL COMPARISON OF ENDOSCOPIC PROCEDURE AND TRANSARTERIAL EMBOLIZATION FOR HEMORRHAGE CAUSED BY DUODENAL ULCER


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Introduction: Endoscopic procedure is performed for active duodenal ulcer hemorrhage. But if endoscopic hemostasis fails, transarterial embolization (TAE) is the next option. However, few studies have been performed comparing the two. We made statistical analysis for the feature between the group which only endoscopic procedure are performed (endoscopy group) for duodenal ulcer and the group which interventional radiology is additionally performed (TAE group).

Aims and Methods: From April 2005 to December 2017, 141 patients with hemorhage of benign duodenal ulcer were admitted in our hospital. The patients were divided into two group retrospectively, endoscopy group and TAE group. We made statistical analysis for laboratory data (Alb, Hb, Ptt, PT—INR) at initial diagnosis, the number of endoscopic treatment, the amount of blood transusion, comorbid disease, and 30-day mortality.

Results: Of 141 patients, 129 patients (91.5%) were success in only endoscopic procedure. 11 patients (7.8%) were underwent TAE additionally, 2 patients (1.4%) were underwent operation. 49 patients (37.3%) were male, the mean age was 62.8 year-old, range 21 to 97 years. Based on the results of t-test for laboratory data at initial diagnosis, Alb and Hb in TAE group was statistically lower than in endoscopic group (P < 0.05). In addition, the number of endoscopic examination was larger (P < 0.05). In terms of comorbid disease, hemodialysis was risk factor in TAE group. Then we performed logistic regression analysis to identify cut-off value for Alb, Hb and times of endoscopic exam. The cut-off value were Alb = 2.3, Hb = 8.3, times of...
endoscopy was twice. Sensitivity was 84.5%, 48.8%, 94.6% respectively, and specificity was 54.5%, 81.8%, 63.6% respectively.

Conclusion: This study may show the opportunity to select TAE for patients who were difficult to control duodenal ulcer hemorrhage with endoscopic procedure. Alb, Hb at initial diagnosis, number of endoscopic exam after the admission, and comorbid disease of hemodialysis might be predictable value for TAE treatment for duodenal hemorrhage.

Disclosure: Nothing to disclose

**P1105 A RETROSPECTIVE SINGLE-CENTRE REVIEW OF HEMOSPRAY® IN GI BLEEDING**

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**Introduction:** Upper GI bleeding can have a poor outcome in the absence of haemostasis. Hemospray is an inorganic powder that creates an adhesive barrier over the bleeding site and has been used as an adjunct to conventional endother-apy in high-risk non-variceal, and more recently variceal bleeds.

**Aims and Methods:** We wished to review Hemospray® use in NHS Tayside and assess clinical outcome. From the endoscopy database we identified Hemospray® use between January 2014 and October 2017. We recorded demographics, indication, co-morbidities, Blatchford score, endoscopic findings and therapy, haemostasis and 30-day mortality.

**Results:** We identified 49 applications in 46 patients (M22:F24, mean age 68.4 years, range 30–91). Indications were primary acute GI bleeding (87.8%) and NVUGIB and prevent re-bleeding. Therefore it can be used in addition to the standard treatment.

**Disclosure:** Nothing to disclose

**P1106 IS TOPICAL TRANEXAMIC ACID EFFECTIVE IN UPPER GI BLEEDING?**

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2Isfahan University of medical science, Isfahan, Iran (Islamic Republic of)
3Shahrekord University of medical science, Shahrekord, Iran (Islamic Republic of)

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**Introduction:** Non-variceal upper gastrointestinal bleeding (NVUGIB) is the most common emergency that gastroenterologists encounter. The aim of this study is evaluating effect of topical Tranexamic Acid via endoscopic procedure for control of NVUGIB.

**Aims and Methods:** In this study, 100 eligible patients with NVUGIB enrolled and divided to two equal groups: In control group the ulcer underwent epinephrine injection plus Argon Plasma Coagulation as the standard treatment. In second group, topical Tranexamic Acid solution spraying was added to standard treatment (intervention group). Estimated blood loss volume, blood transfusion volume, hemoglobin, blood pressure, heart rate, need to second endoscopy, mortality rate, need to surgery, hospitalization duration was evaluated in both groups and the differences expressed statistically.

**Conclusion:** The mean average ages of intervention and control groups were 62.8±19.6 and 63.1±17.8 yrs. respectively. Demographic features were not different between two groups. Estimated blood loss, need to transfusion, hospitalization duration and re-bleeding were significantly lower in intervention group (p-value <0.05). Eight patients (16%) in the intervention group and 17 (34%) in control group had re-bleeding and underwent re-endoscopy (p=0.038). Mortality rate, need for surgery and drug effectiveness regarding the ulcer location (duodenum or stomach) had no statistically significant differences in two groups (P-value>0.05).

**Disclosure:** Nothing to disclose

**P1107 CLINICAL COURSE AFTER HEMORRHAGE IN PATIENTS TAKING DOAC AND SIGNIFICANCE OF GASTROINTESTINAL BLEEDING**


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**Introduction:** Several direct oral anticoagulants (DOAC) have been developed to prevent cardioemophic thrombosis in patients with non-valvular atrial fibrillation. The major adverse effect of DOACs is hemorrhage, and the gastrointestinal tract is one of common sites of involvement. However, clinical course after gastrointestinal bleeding (GIB) during DOAC therapy have not been fully elucidated. This retrospective cohort study was conducted to investigate the course after hemorrhagic events during DOAC therapy. The significance of GIB was also evaluated.

**Aims and Methods:** First, all 662 patients prescribed dabigatran, rivaroxaban, apixaban, or edoxaban between April 2011 and November 2015 were listed. Their medical charts were reviewed to examine whether any hemorrhagic events developed from the day of initial prescription until the end of August 2017. Regarding 126 patients with hemorrhage, the cause of bleeding was identified to clarify the clinical significance of GIB. Additionally, the course after bleeding was investigated until the end of March 2018, if available. Finally, after excluding 30 patients with insufficient description or lack of data, 96 patients were selected as subjects.

**Results:** The hemorrhagic events occurred during DOAC therapy, GIB was identified in 38 patients (2.8%/year), majority of which were clinically relevant GIB (Bleeding Academic Research Consortium type 2 or above). Regarding 35 GIB cases with follow-up data, observational period was 157 patients-year. Of these, 24 minor bleeding occurred (17%/year) including 2 GIB, 1 intracranial hemorrhage and 1 small intestinal bleeding, and no serious bleeding was seen. On the other hand, 2 major thrombotic events developed during observation (1.3%/ year), 1 cerebral infarction and 1 acute arterial occlusion. Both patients developed GIB initially and had stopped taking anticoagulants after bleeding because of the fear for re-bleeding.

**Disclosure:** Nothing to disclose

**Abstract No: P1105**

Table 1

<table>
<thead>
<tr>
<th>Oesophageal (Variceal)</th>
<th>Oesophageal (Non Variceal)</th>
<th>Gastric (Variceal)</th>
<th>Gastric (Non Variceal)</th>
<th>Duodenal</th>
<th>Colonic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Applications of Hemospray</td>
<td>6</td>
<td>16</td>
<td>4</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Immediate Haemostasis</td>
<td>100% (6)</td>
<td>100% (16)</td>
<td>100% (4)</td>
<td>100% (7)</td>
<td>100% (14)</td>
</tr>
<tr>
<td>30 Day Haemostasis</td>
<td>83.3% (5)</td>
<td>75% (12)</td>
<td>50% (2)</td>
<td>100% (7)</td>
<td>85.7% (12)</td>
</tr>
<tr>
<td>Applications where Hemospray was used as Monotherapy</td>
<td>3/6 (50%)</td>
<td>6/16 (37.5%)</td>
<td>0/4 (0%)</td>
<td>1/7 (14.3%)</td>
<td>2/14 (14.3%)</td>
</tr>
<tr>
<td>Monotherapy 30 Day Haemostasis</td>
<td>2/3 (66%)</td>
<td>6/6 (100%)</td>
<td>–</td>
<td>1/1 (100%)</td>
<td>2/2 (100%)</td>
</tr>
</tbody>
</table>
Conclusion: GIB is common and serious adverse event during DOAC therapy. However, once GIB occurred, it seemed important for clinicians to continue anticoagulant therapy.

Disclosure: Nothing to disclose

P1108 ENDOSCOPIC EXPLORATORY VARIICES DEVASCULARIZATION FOR THE TREATMENT OF ACUTE ESOPHAGEAL VARICEL BLEEDING IN PATIENTS WITH CIRRHOSIS

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Disclosure: Nothing to disclose

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Introduction: The principal goal of band ligation is to strangulate and finally obliterate the perforating veins connecting varices to extraesophageal collaterals. But the patients still face the risk of rebleeding after endoscopic treatment. We hope to find a more effective way in preventing early rebleeding.

Aims and Methods: We aimed to evaluate the effect of EEVD (Endoscopic Exploratory Varices Devascularization) for acute esophageal variceal bleeding in patients with cirrhosis.

In the retrospective study, we compared endoscopic exploratory varices devascularization and endoscopic band ligation in 75 patients with cirrhosis (Child-Pugh score range from 7–12 points) and esophageal variceal bleeding. 46 patients underwent EEVD, and 29 did band ligation. We compared the mean time to recurrence between EEVD group and band ligation group. And the presence of the varices measured by Computed tomographic angiography (CTA) at different time points and under different conditions (before performance of EEVD; at least 24 hours after performance of EEVD into hemodynamically stable patients; 2 weeks after performance of EEVD).

Results: The number of esophageal varices in 46 patients were significantly more before performance of EEVD than at least after 24 hours. The results at least 24 hours later and after 2 weeks were similar, no newly gastroesophageal varices were observed. The number of gastric varices appears to decrease after EEVD. Mean bleeding recurrence time after EEVD was significantly longer (7.63±3.63 months) than band ligation (5.60±2.39 months, P = 0.05).

Conclusion: This technology is based on the pioneering method of Professor Li Ping, who is from Department of Gastroenterology, Beijing Ditan Hospital, Capital Medical University, Beijing, China.

Disclosure: Nothing to disclose

P1109 EFFICACY AND SAFETY OF OCTREOTIDE FOR THE TREATMENT OF SEVERE RECURRENT GASTROINTESTINAL BLEEDING IN HEREDITARY HEMORRHAGIC TELANGIECTASIA: RESULTS OF A PROSPECTIVE PHASE II MULTICENTER CLINICAL TRIAL

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Disclosure: Nothing to disclose

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Introduction: Hereditary hemorrhagic telangiectasia (HHT) is a genetic disease that leads to vascular malformations in multiple organs. Approximately 25% of the HHT patients have symptoms of gastrointestinal (GI) bleeding with iron deficiency anaemia as a consequence. Endoscopic argon plasma coagulation is the first-line therapy, but often not a long-term solution due to recurrent bleeding and the impotability to treat all GI lesions. Therefore, current treatment focuses on managing anaemia with blood transfusions, which is associated with multiple hospital visits, admissions, and a significant burden for the patients and healthcare.

Aims and Methods: The aim of this study is to investigate the efficacy and safety of octreotide as a treatment for severe gastrointestinal bleeding in patients with HHT. We included patients associated with SBA formation, which will be helpful in directing further cellular based work to elucidate the pathophysiology of SBA. Endostatin and TIMP1 are both angiogenesis inhibitors. Elevated serum levels of Endostatin have been shown to increase in patients with chronic kidney disease and peripheral vascular disease which are also associated with SBA. TIMP1 is a regulatory protein inhibiting metalloproteinases with an important role in extracellular matrix composition and healing. The identification of both Endostatin and TIMP1 as potential

Efficacy of octreotide treatment was evaluated using a commercially available human angiogenesis antibody array profiler kit (R&D systems) in a larger group of patients and controls. Samples were measured in duplicate and the median relative level and mean level of each factor was then compared between SBA patients and controls using a Mann Whitney U test, with a p value of 0.05 considered to be statistically significant.

Results: An initial assessment using the 55 antibody array assay was performed in 13 samples (7 SBA patients and 6 controls). Significantly lower levels of 4 factors were found in patients with SBA vs controls including Angiopoietin-1 (p = 0.003), Platelet derived growth factor (PDGF) AA (p = 0.029), Endostatin (p = 0.03) and TIMP1 (metalloproteinase inhibitor-1) (p < 0.04). Quantitative ELISA assessments of serum levels of PDGF-AA, Endostatin and TIMP1 in 20 SBA patients and 20 controls were then performed. As outlined in the table, SBA patients had significantly lower levels of TIMP1 (p = 0.003) and higher levels of Endostatin (p = 0.004) than controls (Table 1 shows the mean level of each factor). No differences were detected in levels of PDGF-AA.

### Table showing mean values of each factor for SBA patients and controls

<table>
<thead>
<tr>
<th>SBA</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endostatin</td>
<td>41323.51</td>
</tr>
<tr>
<td>TIMP1</td>
<td>41323.51</td>
</tr>
<tr>
<td>PDGF-AA</td>
<td>41323.51</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Controls</th>
<th>SBA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endostatin</td>
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</tr>
<tr>
<td>TIMP1</td>
<td>41323.51</td>
</tr>
<tr>
<td>PDGF-AA</td>
<td>41323.51</td>
</tr>
</tbody>
</table>

Conclusion: This assessment has revealed two previously unidentified factors that are associated with SBA formation, which will be harmful in directing further cellular based work to elucidate the pathophysiology of SBA. Endostatin and TIMP1 are both angiogenesis inhibitors. Elevated serum levels of Endostatin have been shown to increase in patients with chronic kidney disease and peripheral vascular disease which are also associated with SBA. TIMP1 is a regulatory protein inhibiting metalloproteinases with an important role in extracellular matrix composition and healing. The identification of both Endostatin and TIMP1 as potential
drivers of SBA warrants further investigation and may yield exciting advances in the diagnosis and treatment of SBA. 

Disclosure: Nothing to disclose

P1111 ENHANCED EXPRESSION OF HUMAN HERPES SIMPLEX VIRUS 1 DERIVED MICRO RNA-155 IN THE GASTRIC SPHINCTER MUSCLE USING BIOPSY SAMPLES UNDER PER-ORAL ENDOSCOPIC MYOTOMY

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Introduction: Esophageal achalasia is a rare chronic progressive disease characterized by incomplete lower esophageal sphincter (LES) relaxation. The disease occurs due to Auerbach plexus degeneration. Viruses and autoimmune disorders have been suggested as the cause of the disease; however, the exact cause remains unknown. Micro RNA (miRNA) is a single-stranded RNA that controls gene expression and plays a crucial role in many biological phenomena. In 2016, per-ororal endoscopic myotomy (POEM) for esophageal achalasia was developed and became covered by health insurance. To identify the cause of achalasia, we conducted biopsies sampling from the circular muscle layer of LES during POEM and undertook a comprehensive analysis of miRNA expression patterns.

Aims and Methods: We conducted biopsies sampling from the LES of esophageal achalasia cases during POEM. As controls, we conducted biopsies sampling from the LES of operative cases in which the esophagogastric junction was excised and had no abnormal esophagus motility. Following RNA extraction, a microarray analysis was conducted (Agilent Technology). We quantified miRNA thought to have fluctuation over 2-fold based on the microarray with SYBR Green real time PCR using small nucleic acid (LNA) primers (11 achalasia cases, 6 controls). We investigated correlations with diverse clinical factors.

Results: The expression of human herpes virus 1 (HSV-1) derived hsl1-miR-H1-3p (p<0.05) and hsl1-miR-H18 (p<0.05) was significantly prominent in achalasia patients. No clear relationships were observed with expansion type, expansion level, or disease duration. Furthermore, esophageal mucosal biopsies did not reveal the HSV-1 derived miRNA in either achalasia or control groups.

Conclusion: Considering miRNA genes constitute a latency associated transcript (LAT) and influence herpes virus pathogenicity, enhanced expression of miRNA derived from neurotropic HSV-1 in the achalasia LES implies a causal relationship.

Disclosure: Nothing to disclose

P1113 MANOMETRICS CHARACTERISTICS OF OESOPHAGEAL MOTOR ACTIVITY IN TYPE 2 DIABETICS WITH COMPLAINTS OF CONSTIPAION: COMPARISON WITH DIABETICS WITHOUT CONSTIPATION

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2Universidade Agostinho Neto, Faculdade de Medicina, Luanda, Angola 
3Hospital Fernando Fonseca, Urgência, Lisboa, Portugal 
4Hospital Center of Coimbra, Gastroenterology, Coimbra, Portugal 
5Centro Hospitalar e Universitário de Coimbra, Cirurgia, Coimbra, Portugal 
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8Service de Médico, Hospital de Covas, Coimbra, Portugal, Coimbra, Portugal

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Introduction: Some studies support that there is a significant overlap among the different functional disorders of the digestive tract.

Aims and Methods: The aim of this study was to compare oesophageal motor characteristics between type 2 diabetes with and without constipation.

Oesophageal manometry was performed in 16 diabetic individuals with complaints of constipation and 20 without constipation. Glycaemic control was similar. Waves were evaluated in the 3rd of the oesophagus (P1 = upper, P2 = middle, and P3 = distal). Results are mean±standard error.

Results: In constipated vs. non-constipated diabetics, wave distribution was as follows: peristaltic waves: 85.5±4.38% vs. 91.45±2.32%, p = 0.16; simultaneous waves: 3.30±4.1% vs. 0.93±0.28%, p = 0.015. The percent of no transmission waves of peristaltic waves between groups was significantly different: 0.12±0.01 vs. 0.37±0.15, p = 0.04. Velocity duration (cm/s) registered in constipated vs. non-constipated was as follow: P1-P2: 4.76±0.67 vs. 4.15±0.53, p<0.04; P2-P3: 7.24±0.93 vs. 4.90±0.47, p<0.017 and P1-P3, 6.71±1.20 vs. 5.01±0.21. Velocity duration (cm/s) was significantly different between groups. Wave duration (sec.) in constipated vs. non-constipated was as follow: P1-P2: 2.93±0.64 vs. 4.03±0.58, p<0.2; P2-P3: 3.42±0.67 vs. 5.07±0.51, p<0.05 and P1-P3: 2.69±0.58 vs. 4.27±0.37, p<0.01.

Conclusion: (1) Simultaneous oesophageal waves were significantly more frequent in constipated diabetics. (2) Wave duration was significantly higher within the middle and distal oesophagus of constipated diabetics. (3) Wave velocity was significantly higher within the middle and distal oesophagus of non-constipated individuals. (4) Constipated individuals have some differences in esophageal motility when compared with non-constipated individuals.

Disclosure: Nothing to disclose

References

P1114 IS THERE A ROLE OF INTERSTITIAL CELLS OF CAJAL FOR GASTRIC SLOW WAVE PATTERNS DURING GASTRIC ELECTRICAL STIMULATION

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Introduction: Gastric electrical stimulation (GES), which has been reported to have therapeutic potentials for gastroparesis. However, effective application methods of GES on stomach is not defined. The interstitial cells of Cajal (ICC) are recognized as mediators of neuromuscular transmission in the gastrointestinal tract and as pacemakers involved in the modulation of gastrointestinal motility. We aimed to investigate the efficacy of GES according to distribution of ICC in various gastric lesions of porcine models.

Aims and Methods: The study was performed in healthy fasted weaner pigs surgically implanted with gastric serosal electrodes and endoscopically applied electrodes. The experiment consisted of a 10-minute baseline, a 10-minute GES, and a 10-minute recovery. Acquisition of gastric electrical signals was performed before, during, and after electrical stimulation. A multi-channel recorder (MP150, Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study. Immunohistological labelling of interstitial cells of Cajal was performed using an anti-Cajal antibody.

Results: The number of c-kit (+) cells appeared to be 12.1±3.62 in the fundus, 6.71±1.20 in the middle, and 4.4, MP150, Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study. Immunohistological labelling of interstitial cells of Cajal was performed using an anti-Cajal antibody.

Conclusion: Intensity and distribution of interstitial Cells of cajal in gastointestinal tract might affect gastric slow wave patterns during electrical stimulation.

Disclosure: Nothing to disclose

P1115 A RAT MODEL OF FUNCTIONAL DYSPEPSIA

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2Beijing University of Chinese Medicine, Beijing, China

Contact E-Mail Address: zhaolaqing111@163.com

Introduction: Chinese medicine Jianpiliqi formula has shown strong therapeutic effects in the treatment of functional dyspepsia (FD). However, little is known about the underlying molecular basis. Recent reports have demonstrated that impaired duodenal mucosal integrity and low-grade inflammation contribute to the pathogeneses of FD.

Aims and Methods: FD was induced by stimulating rats via tail clamping that simulates FD as defined by visceral sensitivity and gastric compliance. FD rats were randomly divided into two groups, which received saline or the Jianpiliqi formula in the drinking water for 7 days.

Results: We found that Jianpiliqi formula restored duodenal epithelial integrity and suppressed low-grade inflammation. Using chamber analysis showed an increase in transepithelial electric resistance in Jianpiliqi-treated FD rats as compared to the control FD rats. Western blotting further showed that the expression of tight junction proteins occludin and claudin-1 were increased by Jianpiliqi formula-treated compared to the control FD rats. A concurrent decrease was also found in the mRNA expression of tryptase and PAR-2 that activate proinflammatory pathways leading to low-grade inflammation and high permeability.

Conclusion: The therapeutic effect of Jianpiliqi formula on FD is at least partially through the improvement of duodenal mucosal integrity and the attenuation of low-grade inflammation in the duodenum by suppressing the mast cell-mediated tryptase-PAR-2 signaling pathway. Our findings highlight the molecular basis of Jianpiliqi formula-based treatment of FD in human patients.

Disclosure: Nothing to disclose
The PGI-B.A.O. relationship showed it was always statistically significant. The simple value of PGI resulted able to M.A.O. and B.A.O. in different clinical conditions. The correlation coefficient $p = 0.0001$ and $R = 0.646, p = 0.0001$ as well as the comparison PGI-BAO ($R = 0.234, p < 0.0001$) and G17-MAO ($R = -0.247, p < 0.0001$). In 64 pts ($M/F = 30/34$) affected by CAG, the correlation M.A.O.-P.GI was statistically significant ($R = 0.357, p < 0.004$).

The PGI-B.A.O. relationship showed $R = 0.234, p < 0.115$ and G17-MAO inverse $R = -0.309, p < 0.013$. In 192 control pts ($M/F = 112/80$) with negative EGD and M.A.O.$> 5$ mEq/h and $<25$ mEq/h, the correlation between M.A.O. and PGI was confirmed ($R = 0.617, p < 0.0001$) as well as the comparison PGI-IL.A.O. ($R = 0.212, p < 0.0004$) and G17-MA.O. ($R = -0.454, p < 0.0001$).

Conclusion: PGI and G17 have been separately reported as significantly related to M.A.O. and B.A.O. in different clinical conditions. The correlation coefficient between serum markers and invasive test varied depending on the diagnosis, but it was always statistically significant. The simple value of PGI resulted able to classify the presence of a normal acid secretion. In gastric cancer screening and clinical practice measuring both serum PGI and G17 levels provides a non-invasive method to identify hypochlorhydria.

Disclosure: Nothing to disclose.

Results: Consensus (>80% agreement) was reached for 52 of 62 statements. The panel agreed on a simple definition of DS, recognizing its impact on quality of life. There was agreement on the pathophysiologic relevance of rapid passage of nutrients to the small bowel, but not on decreased gastric volume capacity in DS. Symptom recognition is crucial in DS diagnosis but the usefulness of questionnaires like Sigstads’ questionnaire for diagnosis and assessment of therapeutic response is not established. Arts’ questionnaire can discriminate early from late DS patients. The modified oral glucose tolerance test is considered useful for DS diagnosis while gastric emptying tests are not for diagnosis confirmation (low sensitivity and specificity).

Dietary intervention is the agreed first step in DS treatment, while lying down after meals and dietary supplements increasing foods viscosity were not agreed upon. Pharmacological treatment was agreed for the management of DS not responding to diet. Acorbose is effective for late DS symptoms only. Somatostatin analogues are the preferred treatment for patients with well established DS non-responding to diet and/or acorbose. Short-acting formulations are more effective than long-acting ones for symptom-control although repeated injections limit their long-term use. In refractory DS treatment, continuous enteral feeding via jejunostomy can be a valid alternative and gastric tube enteral feeding can be useful for DS after Nissen fundoplication only.

Surgical reintervention should be considered in DS non-responding to dietary and/or pharmacological interventions (best results achieved with gastric bypass reversal and gastric pouch restriction). No agreement was reached on the efficacy of partial pancreatectomy for management of refractory hypoglycemia.

Conclusion: This multidisciplinary international consensus process generated key clinical recommendations for definition, diagnosis and treatment of DS in clinical practice.

Disclosure: Nothing to disclose.

PI116 INTERNATIONAL CONSENSUS CONFERENCE ON DUMPING SYNDROME DIAGNOSIS AND MANAGEMENT

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Introduction: Dumping syndrome (DS) is a common complication of gastric/oesophageal surgery including under-diagnosed/-treated early and late symptoms. Clinical recommendations for its diagnosis and management are lacking.

Aims and Methods: This study aimed at a Delphi consensus process with international multidisciplinary experts to generate such recommendations. We defined the scope, proposed statements, and searched electronic databases by a systematic literature surveyavailable on a online access point. A Delphi consensus process (80% agreement threshold) byGRADE (Grading of Recommendations Assessment, Development and Evaluation) was used to categorize the quality of evidence and strength of recommendations.

PI117 EFFICIENCY AND SAFETY OF ENDOSCOPIC DILATION OF THE PLUMMER-VINSON RING

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Introduction: The Plummer Vincent syndrome (PVS) or Kelly Paterson is a rare entity defined by the association of higher dysphagia, iron deficiency anemia and a fibrous ring of the cervical esophagus. Although correction of sideropenia may improve these symptoms, endoscopic dilation of the oesophageal diaphragm is often necessary. The main objective of our work is to analyze the results of endoscopic treatment and to study the epidemiological, clinical and endoscopic characteristics of PVS.

Aims and Methods: We included in this study study of 77 cases of PVS collected in our unit between September 2005 and April 2018. All patients underwent surgical treatment and endoscopic dilation of the esophageal ring with Gillard Savary Bougies or hydrostatic balloon under or without scope. Other session (s) of dilation was performed in case of recurrence of dysphagia and/or oesophageal stricture under sedation with propofol.

Results: 11.373 upper gastrointestinal endoscopies were performed, including 184 in the context of PVS, over a period of 13 years (1.6%) A total of 77 patients with PVS were included, including 66 women (85.7%) and 11 men (14.3%). The average age was 39 (range: 16–78 years). All patients presented dysphagia and anemic syndrome. The anemia found in all patients was iron deficient, the mean hemoglobin level was 9.5 g/dl and ferritina 10 μg/l. High gastrointestinal endoscopy was performed in all patients; 74 cases (96%) had a single ring while 3 patients had 2 rings (3.9%). Only one patient (1.3%) had 3. All our patients underwent endoscopic dilation with an average of 1.5 dilations with Savary Gillard’s bougies in 70 cases (91%) and balloons of dilation in 4 cases (5.2%). No cases of perforation were noted after dilation. The clinical, biological and endoscopic evolution was favorable; no case of malignant degeneration was noted with a mean follow-up of 31.5 months.

Conclusion: Management of PVS is based on endoscopic dilation and minimal supplementation. Our experience confirms that endoscopic dilation is effective, well tolerated and safe.

Regular endoscopic monitoring is required despite endoscopic dilation because the PVS is a premalignant condition.

Disclosure: Nothing to disclose.

PI118 ENDOSCOPIC TREATMENT OF LARGE GASTRIC PHYTOBEZOARS WITH A SIMPLE HANDMADE BEZOARATOME

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P1119 EFFECT OF INTRACOLONIC GAS ON GASTRIC TONE AND SATIETY IN PATIENTS WITH CONSTIPATION-PREDOMINANT IRRITABLE BOWEL SYNDROME AND DYSPETIC SYMPTOMS

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Introduction: Interaction between stimuli at different segments of the intestine is critical to maintain gut homeostasis. In patients with functional gut disorders, overlap between stimuli referred to different segments of the intestinal transit is common, but the underlying mechanisms are not completely understood.

Aims and Methods: We attempted to determine the effect of increased volume of colonic contents on gastric motor responses and satiety in patients with constipation-predominant irritable bowel syndrome (IBS-C) and concomitant dyspeptic symptoms. In ten healthy subjects (4 women and 6 men, age range 20–36 years) and 11 patients with IBS-C and concomitant dyspeptic symptoms (10 female and 1 male; age range 33–67 years), gastric motor responses and satiety were studied in 2 different days: 1) during colonic gas filling with a non-absorbable gas mixture infused at 24 ml/min for 40 min (Total 960 ml), and 2) during sham infusion of 24 ml/min for 40 min. During gas filling, gastric motor activity was continuously recorded using an electronic barostat, and abdominal perception was registered from 0–6 using a graded questionnaire at 10-min intervals. At the end of colonic filling a satiety test was performed each study day by ingestion of Nutrinick 100 ml/min up to maximal tolerance.

Results: In healthy subjects, colonic gas infusion was associated to a progressive increment in gastric tone (gastric tone increment 65±32 ml greater than during sham infusion; p < 0.05), but induced no increment in perception of abdominal symptoms (mean score 1.4±0.4; NS vs sham infusion). By contrast, in patients with IBS-C colonic gas infusion was not associated to gastric contraction (gastric tone increment ±12 ±21 ml greater than during sham infusion; p > 0.05) and significantly reduced perception of abdominal symptoms (mean score 2.6±0.1; p < 0.05 vs health during gas infusion), no effect that was not observed during sham infusion (1.7±0.3; p < 0.05 vs real gas infusion; NS vs healthy controls). The nutrinick test revealed a minor decrease in the maximal volume tolerated after colonic gas infusion in healthy subjects (860 ml vs 940 ±70 ml after sham infusion), whereas in IBS-C patients the maximal volume ingested was significantly smaller when the colon was filled with gas (491 ±58 ml; p < 0.05 vs health), but remained similar to healthy controls after sham gas infusion (791 ±87 ml; p < 0.05 vs gas infusion, NS vs sham infusion in health).

Conclusion: In patients with IBS-C and concomitant dyspeptic symptoms, increments in the volume of the colonic contents produce abdominal symptoms that are associated to early satiety and a reduction in the tolerance to ingestion of nutrients. These effects suggest that dietary and pharmacological advice to treat IBS-C should consider avoidance of substances that increase the volume of colonic contents, especially in those patients with concomitant dyspeptic symptoms.

Disclosure: Nothing to disclose.

P1120 EVALUATION OF THE EFFECT OF ITRACONAZOLE, A POTENT CYT344 INHIBITOR, ON THE PHARMACOKINETICS OF A SINGLE ORAL DOSE OF TAK-906, A PERIPHERALLY-SELECTIVE D2/D3 DOPAMINE RECEPTOR ANTAGONIST

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Introduction: Gastroprotection is characterized by delayed gastric emptying in the absence of mechanical obstruction. There is an unmet need for novel treatment options for gastroparesis owing to the safety concerns of existing therapies. For example, domperidone, a peripherally-selective dopamine D2/D3 receptor antagonist, has been used for this purpose. In this phase 1 study we evaluated the pharmacokinetic properties of TAK-906, a novel peripherally-selective D2/D3 dopamine receptor antagonist, in the presence and absence of a potent CYP3A4 inhibitor, itraconazole.

Aims and Methods: This was a phase 1, single-sequence, open-label, two-period crossover trial in healthy volunteers (NCT03161405). On day 1, period 1 (3 days), eligible individuals received a single oral dose of TAK-906 25 mg. During period 2 (6 days), individuals received itraconazole 200 mg once daily on days 1–5; they also received a single oral dose of TAK-906 25 mg 1 hour after the itraconazole dose on day 4. There was a minimum washout period of 4 days between the TAK-906 dose on day 1 of period 1, and the beginning of period 2. Blood samples were collected at protocol-specified times following TAK-906 dosing during both periods to assess PK. The following safety assessments were performed throughout the study: AE and vital signs monitoring, physical examinations, and triplicate ECG measurements. The QT effects (placebo-corrected, change-from-baseline QTcF [ΔQTcF]) of TAK-906 at the geometric mean peak exposure (Cmax) in the presence and absence of itraconazole were predicted using a linear mixed-effects model. The primary objective was to evaluate the effect of itraconazole on the PK of TAK-906. The secondary objective was to assess the safety and tolerability of TAK-906 in the presence and absence of itraconazole.

Results: A total of 12 men with a median age of 33.0 years were included in the study. Compared with administration of TAK-906 alone, co-administration of TAK-906 with itraconazole increased total systemic exposure to TAK-906 (area under the concentration-time curve from zero to infinity [AUC0-∞]) by 1.28-fold (90% CI: 1.10, 1.49) and Cmax by 1.98-fold (90% CI: 1.64, 2.39; Table 1). ΔQTcF of TAK-906 alone (Cmax 9.53 ng/mL) and TAK-906 with itraconazole (18.0 ng/mL) were estimated to be 1.31 milliseconds (90% CI: 0.39, 3.01) and 1.54 milliseconds (90% CI: 0.15, 3.24), respectively. There were no AEs in period 1, and two mild AEs in period 2 considered unrelated to TAK-906 (swelling of the face prior to TAK-906 dosing and constipation after dosing). During the study, there were no deaths, and no AEs led to treatment discontinuation. No clinically significant abnormalities were observed in vital signs, ECGs (including QT interval), physical examinations, haematology and chemistry parameters or urinalysis.

Conclusion: Compared with TAK-906 alone, co-administration of itraconazole with TAK-906 increased the Cmax of TAK-906 by 1.98-fold and AUC0-∞ by 1.28-fold, indicating that TAK-906 is not a sensitive CYP3A4 substrate. The cardiovascular safety concerns associated with domperidone are unlikely to be elicited by TAK-906 under similar conditions.
Introduction: Upper esophageal sphincter (UES) abnormality has been associated with esophageal and to be predictive of inferior response to treatment in these patients. UES function following pneumatic dilatation (PD) of the lower esophageal sphincter (LES) for achalasia has not been accessed. This study’s objective is to investigate change in UES function following PD of LES for achalasia.

Aims and Methods: A Retrospective analysis of high resolution manometry (HRM) data regarding LES and UES function, before and after PD for achalasia. Continuous variables are presented as median (interquartile range-IQR).

Results: From June 2011 until December 2017, 116 patients underwent PD for achalasia, preceded by HRM in our center. Thirty-three of them had a HRM performed before and after the procedure. Median age of patients was 66.2 (IQR 18) years, 55% men. 76% had type 2 achalasia. Median LES integrated relaxation pressure (IRP) decreased by more than 65%, 3.8 mmHg (IQR 5.1) vs. 1.3 mmHg (IQR 5.0), (P = 0.013).

Conclusion: PD for achalasia was associated with a significant decrease in lower and upper esophageal sphincter IRPs. The pathophysiologic mechanism behind UES IRP decrease is its limitation in the setting of PD of LES is unclear and mandates further investigation.

Disclosure: Nothing to disclose

References:

PI112 LONG BREAKS IN PERISTALTIC INTEGRITY SEEN IN FRAGMENTED AND FAILED SWALLOWS ON ESOPHAGEAL HIGH-RESOLUTION MANOMETRY (HRM) PREDICT ABNORMAL REFUX BURDEN BETTER THAN WEAK CONTRACTION VIGOR

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Introduction: Peroral endoscopic myotomy (POEM) is an excellent endoscopic treatment for achalasia (AC). Short-term studies are ample but long-term studies are few. This study aimed to evaluate the long-term efficacy of peroral endoscopic myotomy for patients with achalasia.

Aims and Methods: A total of 115 patients (median age 45 years; interquartile range 34–57) with AC who underwent POEM at the First Affiliated Hospital of ZheJiang Chinese Medical University with a median follow-up of 36 months were enrolled in this study. Eckardt score and the lower esophageal sphincter pressure changes were analyzed, and gastroesophageal reflux was observed.

Results: During the final follow-up, the median Eckardt score reduced from 7.5 ± 1.9 preoperatively to 2.2 ± 1.3 (P < 0.001). Treatment success after 12, 24, 36, and 48 months was observed in 90.4% [confidence interval (CI) 85.5–95.0], 89.3% [CI 84.5–94.0], 87.7% [CI 82.3–93.1], and 80.8% [CI 72.7–88.9] of patients, respectively. A total of 16 (13.9%) failures occurred. Four patients were nonresponders (failure within 3 months), nine were early recurrence (between 3 months and 3 years), and three were late recurrence (after 3 years). Further, 21 (23.1%) patients had symptoms of reflux during the 2-year follow-up. Only one patient with new-onset reflux symptoms was added during the subsequent 2-year follow-up. Moreover, 71 (61.7%) patients underwent gastroscopy after POEM, and 13 (11.3%) patients were diagnosed with reflux esophagitis.

Conclusion: POEM is safe and effective for treating AC and has a better long-term effect.

Disclosure: Nothing to disclose.

References:
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Introduction: The spectrum of esophageal body hypomotility on high resolution manometry (HRM) includes fragmented, weak and failed sequences, the latter two are considered ineffective. The Chicago Classification (CC) 3.0 criteria for diagnosis of fragmented peristalsis and ineffective esophageal motility (IEM) are based on consensus 50% thresholds of fragmented and ineffective sequences respectively. Objective proportions and type of hypomotile sequences predicting abnormal esophageal reflux burden are incompletely understood.

Aims and Methods: Our aims is to evaluate thresholds of fragmented, weak and failed esophageal sequences on HRM that predict abnormal acid exposure time (AET) and mean nocturnal baseline impedance (MBI) on ambulatory pH-impedance monitoring performed off acid suppressive therapy. Clinical data, HRM and pH-impedance studies were evaluated on patients with persisting reflux symptoms were reviewed from six centers (5 in Europe and 1 in US) for this preliminary report. Incomplete studies, achalasia, esophageal outflow obstruction and prior foregut surgery were exclusions. HRM studies were analyzed according to CC 3.0, using distal contractile integral (DCI) to designate fragmented (DCI>450 mmHg cm.s with breaks>5 cm on 20 mmHg isobaric contour), weak (DCI 100–450 mmHg.cm.s) and failed (DCI < 100 mmHg.cm.s) sequences. Total AET >6% and MNBi <2292 ohms defined abnormal reflux metrics on pH-impedance testing. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated to determine likelihood of abnormal reflux metrics with varying proportions of fragmented, weak and failed sequences, using normal HRM studies (10 intact sequences with DCI>450 mmHg cm.s) for comparison.

Results: Of 351 patients (32.1±0.8 yr, 67%F), 61.5% presented with typical symptoms. AET >6% was found in 103 (29.3%), and MNBi <2292 ohms in 217 patients (61.8%). Compared to normal HRM, >50% fragmented peristalsis had an OR 2.4 (CI 1.3–4.4, p=0.002) in predicting abnormal AET, and OR 3.7 (CI 2.4–5.6, p=0.003) in predicting abnormal MNBi. Both AET and MNBi were significantly abnormal with >70% fragmented sequences compared to ≤80% AET (8.8±1.5% vs 4.5±0.6%, MNBi 1225±193 vs 2232±87 ohms, p=0.05 for each). IEM as defined by CC 3.0, predicted abnormal AET (OR 2.4, CI 1.3–4.4, p=0.009), and abnormal MNBi (OR 2.3, CI 1.3–4.2, p=0.006). When weak and failed sequences within IEM were separately analyzed, >50% weak sequences did not predict abnormal AET (OR 1.9, CI 0.8–4.2, p=0.14) but parallel >50% failed sequences resulted in numerically higher AET (5.0±1.1% vs 4.5±0.5%, p=0.21) and lower MNBi (1811±372 vs 2123±86 ohms, p=ns). The role of contraction reserve in modifying esophageal reflux burden could not be evaluated because of insufficient numbers with MRs data. >50% failed sequences uniformly predicted abnormal AET (p=0.009), but MNBi was consistently low with failed sequences (1815±151 ohms) and not discriminative (p=0.2).

Conclusion: Long breaks in esophageal peristaltic integrity seen with fragmented and failed sequences are more relevant to abnormal esophageal acid burden than weak sequences, but all hypomotility processes can contribute to low MNBi. Fragmented sequences can be graded into mild (≤70%) and severe based on abnormal reflux metrics. Failed sequences consistently predict abnormal reflux metrics, in contrast to weak sequences. Our findings suggest that further evaluation of the CC 3.0 diagnostic criteria for IEM and fragmented peristalsis is warranted in the context of reflux disease.

Disclosure: Nothing to disclose

Reference

P1125 COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE AND HIGH-RESOLUTION MANOMETRY IMPROVES DETECTION OF CLINICALLY RELEVANT ESOPHAGOGASTRIC JUNCTION OUTFLOW OBSTRUCTION

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Introduction: Combined multichannel intraluminal impedance and high-resolution manometry improves detection of clinically relevant esophagogastric junction outflow obstruction.

Aims and Methods: A total 169 patients diagnosed as having EGIJO between June 2011 and February 2018 were analyzed. All the patients received a combined manometry and high eoscapul manometry (CMHI-HRM. Sandhill system). MII was reported as having abnormal liquid bolus transit (LBT) if <80% of swallows had complete bolus transit. EGIJO was defined as a median integrated relaxation pressure of >20 mmHg and when the criteria for achalasia were not met. PPI was administered to achalasia, showing predominant passage above 60% of the non-achalasia group (n=159). The combination of dysphagia, CP, and abnormal LBT showed the best predictive power for clinically relevant EGIJO (sensitivity 90%, specificity 92.5%, positive predictive value 42.9%, negative predictive value 99.3%, positive likelihood ratio 11.9, and negative likelihood ratio 0.1). When CMHI-HRM was used, an additional 8.3% of clinically relevant EGIJO cases were identified as compared with HRM alone.

Conclusion: Clinically relevant EGIJO can be predicted using CMHI-HRM and clinical factors.

Disclosure: Nothing to disclose

P1126 A SINGLE-CENTER EXPERIENCE WITH PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA: TWO-YEAR FOLLOW-UP AND BEYOND

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Introduction: Per-Oral Endoscopic Myotomy (POEM) is nowadays a widely accepted treatment method for esophageal achalasia, not only because of its attractiveness but also because of minimal invasiveness and safety profile, although long-term outcomes are still yet to be proved. Furthermore, serious concerns regarding post-POEM reflux are more than legitimate.

Aims and Methods: The aim of our prospective single-center case series was to assess the long-term clinical outcomes of POEM in terms of efficacy, durability and complications. A total of 266 POEM procedures were performed in 254 consecutive patients with confirmed achalasia referred to our tertiary center from 12/2012 to 4/2018. Follow-up visits at 3, 12, 24, 36 and 48 months were conducted in 217, 164, 115, 66 and 44 patients. All patients underwent upper GI endoscopy, high-resolution manometry (HRM) and 24-hour pH-monitoring at 3 months after POEM; endoscopy was then repeated between 24–36 months. The main outcomes were treatment success defined as Eckardt score <3, recurrence rate, adverse events and post-POEM reflux.

Results: At 3, 12, 24, 36 and 48 months, treatment success was achieved in 97.7% (CI 96–98), 96.0% (95–97), 90.5% (89–93), 85.5% (82–89) and 81.6% (77–87) of patients. A total of 19 patients experienced treatment failure (n = 5) or recurrence (n = 14). The recurrences occurred most often in patients with type I achalasia (8 out of 43, 18.6%). At 3 months, reflux esophagitis was endoscopically confirmed in 6/71 (8.5%) of patients; 8/9 patients had LA C/D (esophagitis) and abnormal acid exposure was found on pH-metry studies was detected in 74/192 patients (38.5%). At 24–36 months, endoscopy was performed on 71 patients and reflux esophagitis was present in 21 (29.6%) of them. The proton pump inhibitors were administered on average to 37% of patients at the follow-up visits. So far there have not been any complications detected with regard to the post-POEM reflux such as Barrett’s esophagus or stenosis. The procedure-related complications were as follows: decompression of capnoperitoneum (145/254, 57.1%), subcutaneous emphysema (90/254, 35.4%), and in less than 5% of patients peristomal bleeding, mucosal injury or postprocedural fever was ever observed. Unfortunately, we experienced one fatal complication during POEM which was due to sudden cardiac death in a patient with silent pulmonary hypertension. This case of prolonged hospitalization was caused by fluidothorax/pneumothorax.

Conclusion: POEM successfully amended the spectrum of effective treatment modalities for achalasia with sustained treatment success of 91% at 2 years, which slightly decreases over time to 81.6% at 4 years after the procedure. The rate of post-POEM reflux is detected in as high as 40% of patients. Despite POEM being considered a safe method overall, severe complications may still occur.

Disclosure: Nothing to disclose

P1127 COMPARISON OF BEHAVIORAL THERAPY AND STANDARDIZED DICATION IN REDUCING SYMPTOMS OF SUPRAGASTRIC BELCHING

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Introduction: Supragastric belching (SGB) is a behavioral disorder where air is ingested into the esophagus and immediately expelled. It can appear as excessive belching and it may reduce quality of life but might not be related to anxiety or depression.

Aims and Methods: The aim of this study was to evaluate the efficacy of behavioral therapy in reducing belching, improving quality of life, and relieving depression and anxiety in a six-month follow-up compared to standardized doctors information. Patients (n = 20, age 26-79, 16 female) with SGB diagnosed in

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esophageal 24-hour impedance monitoring were randomized to receive either 5 sessions of therapy performed by a speech therapist or only standardized doctor’s information about the mechanisms of supragastric belching. The frequency and intensity of gastric belching and quality of life (QOL) were evaluated by a visual analog scale (0–10) at onset and after 6 months follow-up. RD and QOL and OQI, and BAI and HDI for anxiety and depression. After the initial 6 months follow-up also the controls had the possibility of behavioral therapy with additional evaluation after 6 months.

**Results:** The frequency and intensity of belching were significantly reduced in the therapy group (n = 7, P = 0.042, P = 0.027) but not in the controls (n = 6) at 6 months follow-up. Anxiety and depression were relieved but not significantly. QOL did not change. In all patients after therapy (n = 10, including 3 patients from control group) both the frequency (P = 0.005) and intensity (P = 0.005) of belching were significantly reduced. The study was interrupted by 2 patients and 5 patients are coming to follow-up.

**Conclusion:** Behavioral therapy seems to be effective in reducing belching in patients with SGB and to be superior to standardized doctor’s information.

**Disclosure:** Nothing to disclose.

**P1128 AGE AND MALE GENDER ARE ASSOCIATED WITH A DECLINE IN FUNCTIONAL GASTROINTESTINAL SYMPTOMS: 10-YEAR FOLLOW-UP OF THE KALIXANNA STUDY**

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**Introduction:** Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are prevalent conditions in the population. The overall prevalence in the population is stable but presentation of symptoms may fluctuate over time. Overlap of FD/IBS symptoms is common and higher than expected by change. Known factors influencing symptom fluctuation include anxiety at baseline, however to date, age and gender have not been evaluated.

**Aims and Methods:** Our aim was to explore the role of age and gender in symptom stability in a prospective population based follow-up study. Study participants were randomly selected from the national Swedish population register and surveyed in 1998 by a validated abdominal symptom questionnaire (ASQ). 1000 individuals randomly selected completed an oesophagogastroduodenoscopy in 1999–2001. All eligible from those (n = 887) were invited to a follow-up in 2010 with the ASQ. Data were analyzed by testing difference of mean age of subjects with FD and IBS versus controls at baseline and at follow-up with the T test.

**Results:** In total 703 out of 887 subjects (79.3%) completed the questionnaires. FD was reported by 110 subjects at baseline and by 92 at follow-up. FD without overlap with IBS was reported by 56 subjects at baseline and by 34 subjects at follow-up. IBS was reported by 200 subjects at baseline and by 185 subjects at follow-up. The mean age of those with FD was statistically significantly lower at follow-up but not at baseline, except in IBS without FD at baseline, showing that functional GI symptoms decline with age which is associated with male gender.

**Disclosure:** Nothing to disclose.

**P1129 DIFFERENT DYSREGULATION OF SYMPATHETIC AND PARASYMPATHETIC AUTONOMIC RESPONSE TO STRESS IN PATIENTS WITH FUNCTIONAL DYSPEPSIA**

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**Introduction:** Functional dyspepsia (FD) is a common functional gastrointestinal disorder (FGID). The pathophysiological mechanisms of FGID are complex. Accumulating evidence indicates that autonomic dysregulation contributes to FGID. The symptoms of FGID are often triggered by stress, however, the mechanisms of autonomic dysregulation in FGID, especially in response to stress are incompletely understood.

**Aims and Methods:** The aim of this study was to assess potential changes of vagal and sympathetic regulation in patients suffering from FD in response to distinct types of stressors (active mental stress vs. passive physical stress). Studied population included 10 patients diagnosed with FD and 11 age- and sex-matched healthy controls. All patients were diagnosed according to Rome IV criteria for functional gastrointestinal disorders. Blood pressure (BP) and heart rate were continuously recorded using Finometer MIDI (FMS, Netherlands) at rest and during two distinct stressors – mental arithmetic test and cold pressor test (cooling of forearm in 1–3°C water bath for 5 min). Evaluated parameters: 1) baroreflex sensitivity (BRS, calculated from spontaneous heart rate variability and BP variability) reflecting vagally-mediated heart rate regulation in response to changes of BP, 2) spectral power in low-frequency band of systolic BP variability (LF-SBP) reflecting sympathetic alpha-adrenergic stimulation of vascular smooth muscles, 3) systolic and diastolic BP, and 4) mean heart rate.

**Results:** BRS (reflecting vagal function) in patients with FD was substantially (by 50%) reduced compared to controls at rest and in response to both mental arithmetic test and to cold pressor test (p < 0.01 for all comparisons). In contrast, LF-SBP (reflecting sympathetic function) was normal at baseline, but significantly increased in FD compared to controls during both mental arithmetic test and cold pressor test (p < 0.05, p < 0.01, respectively). No differences were found in systolic and diastolic BP and heart rate.

**Conclusion:** Our data showed impaired dynamic sympatho-vagal balance in patients with functional dyspepsia at rest and in response to different types of stressors. The vagal function is reduced at baseline and not influenced by stress, while the sympathetic response is exaggerated by stress. These findings support the hypothesis of altered autonomic regulation during stress as a potential mechanism worsening the symptoms of FD. We suggest that comprehensive evaluation of stress response using noninvasive analysis of distinct autonomic effectors could help to better understand the role of autonomic dysregulation in functional gastrointestinal disorders.

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**Disclosure:** Nothing to disclose.
P1130 MAST CELL ACTIVATION SYNDROME (MCAS) IN PATIENTS WITH RAPID ONSET OF FOOD INDUCED SYMPTOMS OF DYSPEPSIA, IBS, DIARRHOEA, NAUSEA OR VOMITING: REACTS FAVOURABLY ON HISTAMINE 1 OR 2 BLOCKERS OR CROMOGLYCATE. AN OBSERVATIONAL STUDY

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Introduction: Many patients with functional dyspepsia or IBS indicate that their symptoms are being provoked by specific food or food components. This may be due to the mast cell activation syndrome. MCAS of the digestive tract is characterized by 1. Multifocal or disseminated inclusions in mucosal biopsies and 2. Stained mast cells of MC per high power field (hpf 400x).

2. Presence of symptoms attributable to pathologically increased MC activity. An additional minor criterion is symptomatic response to inhibitors of MC activation or mediator modulation. The awareness of MCAS is limited. This milder form of MC hyperreactivity must be distinguished from the more severe and systemic mast cell activation disease (MCAD) or mastocytosis where often skin and bone marrow are infiltrated with abundant MC. In regular HE stained slides MC are overlooked. Special staining with CD 117 displays the cells in characteristic brown color followed by cell count per hpf. We investigated the efficacy of histamine receptor antagonists and MC stabilizers in patients with distinct food induced MCAS.

Aims and Methods: Fifty-two patients (45 female, age 41.3 ± 23.3 years) with one or more rapid onset (<60 min), food induced symptoms of diarrhea (n = 23), functional dyspepsia (n = 15), IBS (n = 14), nausea (n = 12), abdominal pain (n = 11), bloating (n = 6), vomiting (n = 5) and cyclic vomiting syndrome (n = 5) were included. Also, of 248 patients (m = 47) with diarrhea or ulcer (n = 11), showed an increase of CD 117 stained MC (30.0 ± 13.1) per hpf. Many patients had long standing and persistent complaints with an average of 10.5 ± 18.4 years. Therapy was initiated for four weeks, first with H1 receptor antagonist and MC stabilizer (imidazoline 1–4 mg bid or fexofenadine 120–180 mg bid and subsequently H2 receptor antagonist ranitidine 150 mg bid or cromoglicate naleron 100 or 200 mg tid.

Results: Medication was tried and changed until the desired clinical response was achieved with one of the drugs. Ultimately 12 patients responded to ketotifen, 15 to fexofenadine, 2 to ranitidine and 14 to naleron. The therapeutic efficacy varied from excellent (no to minimal residual symptoms) in 17 (33%), substantial improvement (moderate to complete) in 12 (23%), modest amelioration in 10 (19%) or no effect in 10 (20%). In the control group, 226 in the FD, 261 in the IBS, and 265 patients in the overlap syndrome in comparison to FD or IBS groups are summarized.

Conclusion: This observational study shows that when rapid onset, food induced symptoms of diarrhea (n = 47), bloating disorders (n = 47), belching disorders (n = 34), and functional heartburn (n = 27) were the most frequent upper FGID in FD patients. During STW 5 treatment GIS and VAS showed significant improvement from 8.6 to 3.7 points. In all studies the tolerance of the STW 5 was good with no adverse events.

Disclosure: Nothing to disclose

Reference

P1131 OBSERVATIONAL STUDY OF FD/IBS OVERLAP SYNDROME CHARACTERISTICS AND Efficacy of TREATMENT

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Introduction: Gastrointestinal (GI) symptoms profile and prevalence or associated factors for the overlap between functional dyspepsia (FD) and irritable bowel syndrome (IBS) group still remain unclear.

Aims and Methods: The aim of study was evaluation of the clinical and demographic features of FD, IBS, and FD-IBS overlap and efficacy of STW 5 as a standard treatment.

In this observational comparative study a total of 1006 patients (254 in the control group, 226 in the FD, 261 in the IBS, and 265 patients in the overlap group, who were both FD and IBS) were included. Diagnostics were based on the Rome IV criteria for functional GI disorders. A total of 752 patients from all groups were treated with 3 x 20 drops/day of STW 5. At 4 and 8 week of treatment the symptom assessment was made. The main outcome criteria was the clinically validated Gastrointestinal Symptom Score (GIS) and Visual Analogue Scale (VAS).

Results: Patients with FD-IBS overlap had more severe symptoms (bloating, nausea, vomiting, hard or lumpy stools, defecation straining, and a feeling of incomplete bowel movement) and higher depression scores compared with non-overlap patients. The factors and symptoms, most frequently associated with overlap syndrome in comparison to FD or IBS groups are summarized.

Unmarried status, nausea, bloating, and a feeling of incomplete emptying were more frequent factors in FD-IBS overlap group vs IBS group. In contrast, young age, depression, bloating, and postprandial distress syndrome were positively associated with FD-IBS overlap group vs FD group.

Postprandial fullness (38.4%), belching (28.5%), and regurgitation (21.7%) were the most prevalent symptoms, followed by bloating (27.4%), abdominal pain (21.7%), and nausea (20.9%). At 4 and 8 week of treatment the symptom score was significantly reduced compared to baseline in all groups. STW 5 treatment showed significant reduction in the GIS score compared to baseline in all groups. The median reduction was 9.1 (IQR: 4.7–12.4) and 8.9 (IQR: 4.7–12.3) at 4 and 8 week of treatment, respectively.

Conclusion: This observational study shows that when rapid onset, food induced symptoms of diarrhea (n = 47), bloating disorders (n = 47), belching disorders (n = 34), and functional heartburn (n = 27) were the three most frequent upper FGID in FD patients. During STW 5 treatment GIS and VAS showed significant improvement from 8.6 to 3.7 points. In all studies the tolerance of the STW 5 was good with no adverse events.

Disclosure: Nothing to disclose

Reference

P1132 SUICIDAL IDEATION IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Suicide ideation, one symptom of depression, was associated with irritable bowel syndrome (IBS), but not with other functional gastrointestinal disorders (FGIDs).

Aims and Methods: The aim of the present study is to search if suicide ideation is associated with FGIDs.

1469 FGIDs patients (71% females) were included in this observational study. Patients filled the Rome III questionnaire, Beck depression inventory, and state and trait anxiety questionnaires. Data were analyzed using ANOVA with Bonferroni correction and logistic regression analysis.

Results: Suicidal ideation was reported by a minority of patients (15 %), with low intensity ("I have thoughts of killing myself, but I would not actually do it") in 190 patients (13%), Moderate intensity ("I would like to kill myself") in 11 patients (1%) and High intensity ("I would kill myself if I had the chance") in 22 patients (1%) (Table 1).

It was not associated with significant difference of sex ratio (P = 0.520) (Table 2), of age (P = 0.225) or of BMI (P = 0.300).

The prevalence of suicidal ideation is associated with increase of the three psychological scales: depression (P < 0.001; OR = 1.086; 95%CI = [1.003–1.110]), state anxiety (P = 0.006; OR = 1.040; 95%CI = [1.016–1.064]), and trait anxiety (P = 0.021; OR = 1.030; 95%CI = [1.005–1.057]).

Conclusion: This study shows a specific association between suicide ideation and some IBS subtypes, and not with other FGIDs.

Disclosure: Nothing to disclose

Reference
polymorphism was associated with increased risk of FD based on recessive (TT vs. CC; OR = 1.20, 95% CI 1.01–1.43, P = 0.04) and homozygote (TT vs. CC; OR = 1.26, 95% CI 1.02–1.55, P = 0.03) models. Furthermore, subgroup analysis identified TT and T-allele (TT+CT) genotypes both were associated with increased susceptibility to epigastric pain syndrome (EPS) compared with the CC and C-allele genotype. No association was observed in any of four allelic model genetic of SLC6A4 with FD susceptibility. However, L-allele (LL+SL) genotype of SLC6A4 was found to be significantly associated with an increased risk of EPS (OR = 1.33, 95% CI 1.04–1.70, P = 0.03) and postprandial distress symptoms (PDS; OR = 1.93, 95% CI 1.03–3.63, P = 0.04) compared to SS genotype respectively. Finally, recessive model (CC vs. TT+CT) was found to be significantly associated with an increased risk of EPS (OR = 1.33, 95% CI 1.04–1.70, P = 0.03) and postprandial distress symptoms (PDS; OR = 1.93, 95% CI 1.03–3.63, P = 0.04) compared to SS genotype respectively. In the current study, the frequencies of the CC and C-allele genotype were 0.25–0.74, and CC:0.002, and homozygote model (CC vs. TT, OR = 0.44, 95% CI 0.26–0.73, P = 0.002) and homozygote model (CC vs. TT, OR = 0.43, 95% CI 0.25–0.74, P = 0.002) demonstrated CC genotype of CCK-IR is associated with decreasing risk of FD.

Conclusion: The available evidence of our meta-analysis has shown that there are associations between GNB3, SLC6A4, and CCK-IR polymorphisms and FD susceptibility. Disclosure: None to disclose

P1134 PSYCHOLOGICAL FACTORS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS: RELATION TO DYSPEPTIC SYMPTOMS AND GASTRIC DYSMOTILITY AS MEASURED WITH ULTRASOUND

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Introduction: Altered gut-brain axis signalling may play an important pathophysiological role in functional gastrointestinal disorders (FGID). We aimed to investigate relations between psychological factors (anxiety, depression and neuroticism) and dyspeptic symptoms and gastric dysmotility in a cohort of patients with irritable bowel syndrome (IBS; n = 46), and EPQ-N (neuroticism; n = 203). Correlations were calculated by linear regression, and differences between means were evaluated by Student’s t-test.

Methods: Mean neuroticism scores for patients with FD and IBS were 3.4 and 3.7, respectively (p < 0.05). When analysing all patients with FD and/or IBS (n = 248), we found only a weak correlation between diameter of the fundus 10 minutes after soup intake and neuroticism score by linear regression (r = −0.156, p = 0.047). There were no other significant correlations between EPQ-N and upper abdominal discomfort (r = 0.171, p = 0.015), but not to postprandial symptoms. Correlation coefficient (VSI) was weak, postprandial discomfort (r = 0.308, p = 0.008), bloating (r = 0.255, p = 0.030) and upper abdominal discomfort (r = 0.239, p = 0.044) in fasting state. We found no correlations between VSI and postprandial symptoms or ultrasonographic measurements of the stomach. We found a significant correlation between HAD-D and fasting nausea in FD patients (r = 0.544, p = 0.004, n = 25). In patients with IBS, we found a correlation between change in nausea after the meal and HAD-D (r = 0.562, p = 0.045, n = 12). HAD-A was not correlated with any dyspeptic symptoms.

Conclusion: Neuroticism scores in patients with FD and IBS were lower than expected, and EPQ-N-scores were not strongly correlated to gastric dysmotility. Neuroticism scores in patients with FD and IBS were lower than expected, and EPQ-N-scores were not strongly correlated to gastric dysmotility. Disclosure: Nothing to disclose
increased rapidly. However, figures vary widely and updated population-based data for Europe are scarce.

Aims and Methods: To estimate the incidence and prevalence of EoE in both children and adult patients in a central region of Spain and analyzed the changes along the 2006–2017 period. Retrospective analysis and annual variations data for the catchment area (Hospital General de Tomelloso & Virgen de Altarragaza) were obtained from the National Institute for Statistics. Data of all patients diagnosed with EoE (evidence-based diagnosis criteria 2017) and living in these areas in the study period were retrospectively collected. Demographic, clinical, endoscopic and histological characteristics were associated with EoE diagnosis but did not predict response to PPI.

Disclosure: Nothing to disclose

Reference

P1139 MARKERS OF ESOPHAGEAL EPITHELIAL–MESENCHYAL TRANSITION ARE SIGNIFICANTLY REDUCED IN ACTIVE EOSINOPHILIC ESOPHAGITIS FOLLOWING 16 WEEKS OF TREATMENT WITH RPC4046, AN ANTI-INTERLEUKIN-13 MONOCLONAL ANTIBODY

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Introduction: HERO5 was a 16-week double-blind, placebo-controlled phase 2 multicenter trial that evaluated the efficacy and safety of RPC4046 in adults with active eosinophilic esophagitis (EoE). Fibrostenosis of the esophagus is a known complication of EoE and may be mediated in part by epithelial-mesenchymal transition (EMT). We sought to determine whether treatment with RPC4046 modulates EMT.

Aims and Methods: Esophageal biopsy sections were taken at baseline and week 16 from 69 of the 99 patients randomly assigned to weekly subcutaneous (SC) RPC4046 360 mg (n = 26), 180 mg (n = 19), or placebo (n = 24). Slides were stained by duplex immunofluorescence for e-cadherin and vimentin (Cell Signaling Technologies), counterstained nuclei with DAPI, and scanned at 20x on a Vectra® (PerkinElmer) multispectral digital microscopy system. Using Inform® software, a machine learning algorithm mapped the epithelial compartment in each slide. Nuclear, cytoplasmic, and membrane areas of each epithelial cell were defined and fluorescence intensity of each marker on a per-cell basis was recorded. For this EMT subtype, the primary endpoint was change from baseline in percentage of vimentin-positive epithelial cells and secondary endpoints were change in total e-cadherin expression per cell and change in vimentin-e-cadherin ratio per cell.

Results: The change from baseline in mean percentage of vimentin-positive cells was -4.24%, -2.75%, and -0.94% in the RPC4046 360 mg, 180 mg, and placebo groups, respectively (p < 0.05 for each active dose group vs. placebo). The change in e-cadherin expression per cell was 101.6, 102.4, and 18.3 in the 360 mg, 180 mg, and placebo groups (p < 0.05 for each active dose group vs. placebo). The change in vimentine-cadherin ratio was significantly different from zero in both dose groups (360 mg: -0.30; 180 mg: -0.18; p < 0.05 for each active dose group vs. zero). Similar effects for all markers were observed in each esophageal sampled region (proximal, mid, distal).

Conclusion: RPC4046 treatment for 16 weeks significantly improved EMT markers in esophageal tissue in patients with active EoE. A greater effect was observed with 360 mg than with 180 mg. These results, together with the overall clinical data presented separately, support the hypothesis that prevention of IL-13 binding to receptor subtypes IL-13Rα1 and IL-13Rα2 favorably impacts inflammatory and remodeling pathways and may reduce development of esophageal fibrostenotic complications that occur in EoE. Larger studies with longer term treatment are required to determine the impact of these results on the course of EoE.
Eosinophilic esophagitis (EoE) is an increasingly recognized immunemediated disease and a common cause for dysphagia and bolus obstruction.

The aim of our survey was to evaluate the therapeutic management of EoE among adult gastroenterologists in Germany. Aims and Methods: Between 11/2017 and 2/2018 a web-based questionnaire was sent to 1393 gastroenterologists (1126 in private practice (bng) and 267 hospital-based (ALGK)), containing a total of 22 questions to general, diagnostic and therapeutic aspects of EoE. Data capture and evaluation was performed using SurveyMonkey.

Results: The responder rate was 28% (bng) and 36% (ALGK). The majority of responders treat and monitor EoE patients by themselves (85%/59%). In newly diagnosed EoE patients, the initial treatment was mainly either PPI (37%/39%) or topical steroids (34%/40%). Only few initiated elimination diet (4%/6%) or 8 weeks (23%/24%), twice daily for 4 weeks (29%/45%) or 8 weeks (35%/35%) or 8 weeks (23%/43%). The devices used for endoscopic dilatation (hospital-based) were mainly bougies (61%) followed by balloons (39%). Based on their experience, most responders estimated that 25–50% of patients (47%/49%) or >50% of patients (23%/24%) need long-term treatment of EoE.

Conclusion: The results suggest a significant heterogeneity in the therapeutic management of EoE among gastroenterologists in Germany, both in private practice and in hospitals. This underlines the need of national guidance and for more educational activities.

Disclosure: Nothing to disclose

References
2. Savarino E, Tolone S, Bartolo O, et al. The GerDQ questionnaire and high resolution manometry support the hypothesis that proton pump inhibitor-responsive eosinophilic esophagitis is a GERD-related phenomenon. Aliment Pharmacol Ther 2016; 44: 522-530.

P1141 THERAPEUTIC MANAGEMENT OF EOSINOPHILIC ESOPHAGITIS: A SURVEY AMONG GASTROENTEROLOGISTS IN GERMANY

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Introduction: Eosinophilic esophagitis (EoE) is an increasingly recognized immunemediated disease and a common cause for dysphagia and bolus obstruction.

The aim of our survey was to evaluate the therapeutic management of EoE among adult gastroenterologists in Germany. Aims and Methods: Between 11/2017 and 2/2018 a web-based questionnaire was sent to 1393 gastroenterologists (1126 in private practice (bng) and 267 hospital-based (ALGK)), containing a total of 22 questions to general, diagnostic and therapeutic aspects of EoE. Data capture and evaluation was performed using SurveyMonkey.

Results: The responder rate was 28% (bng) and 36% (ALGK). The majority of responders treat and monitor EoE patients by themselves (85%/59%). In newly diagnosed EoE patients, the initial treatment was mainly either PPI (37%/39%) or topical steroids (34%/40%). Only few initiated elimination diet (4%/6%) or 8 weeks (23%/24%), twice daily for 4 weeks (29%/45%) or 8 weeks (35%/35%) or 8 weeks (23%/43%). The devices used for endoscopic dilatation (hospital-based) were mainly bougies (61%) followed by balloons (39%). Based on their experience, most responders estimated that 25–50% of patients (47%/49%) or >50% of patients (23%/24%) need long-term treatment of EoE.

Conclusion: The results suggest a significant heterogeneity in the therapeutic management of EoE among gastroenterologists in Germany, both in private practice and in hospitals. This underlines the need of national guidance and for more educational activities.

Disclosure: Nothing to disclose

References
2. Savarino E, Tolone S, Bartolo O, et al. The GerDQ questionnaire and high resolution manometry support the hypothesis that proton pump inhibitor-responsive eosinophilic esophagitis is a GERD-related phenomenon. Aliment Pharmacol Ther 2016; 44: 522-530.

P1140 COMPREHENSIVE IMPEDANCE-PH ANALYSIS OF GASTROESOPHAGEAL REFUX IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by symptoms related to esophageal dysfunction and eosinophilic inflammation. There is some overlap between EoE and GERD, with similar eosinophilic motility abnormalities [1], particularly in those EoE patients responsive to proton pump inhibitor (PPI) therapy [2]. Normal esophageal acid exposure time (EAET) has been found in two thirds of 51 EoE cases at pH-only monitoring, and EAET was not a predictor of clinical and histological response to PPI [3]. However, the limits of pH-only monitoring have long been recognized. A comprehensive reflux assessment, based on impedance-pH monitoring and including analysis of post-reflux swallow-induced peristaltic wave (PSPW) index and of mean nocturnal baseline impedance (MNBI), improves our ability to diagnose GERD [5,6], and to predict PPI response [7], and could contribute to clarify the pathogenesis of EoE.

Aims and Methods: We investigated 52 (43 males, mean age 43 years) consecutive incident EoE cases (25 eosinophilic/HPE in esophageal biopsies) with impedance-pH monitoring, always preceded by high resolution/conventional esophageal manometry. Impedance-pH parameters were compared with those found in 52 (41 males, mean age 39 years) healthy controls (HCs) and 52 (31 males, mean age 45 years) patients with hyperesisitive esophagus (HE), the latter group defined by normal endoscopy, normal EAET and positive heartburn-reflux association. Results were examined by analysis of variance and chi-square test with Bonferroni correction, significance set at P < 0.05.

Results: All EoE patients complained of dysphagia, and 24 (46%) reported heartburn. Main impedance-pH parameters are shown in the Table. EAET was comparable among the three groups. On the other hand, the number of total refluxes was significantly higher in EoE and HE than in HCs. PSPW index and MNBI were lower among the three groups of subjects, and were significantly lower in EAET than in HE in both groups of patients than in HCs.

Conclusion: Reflux parameters in EoE and HE are quite similar and significantly decreased compared with HCs, suggesting that reflux could play a role in the pathogenesis of EoE. Low values of PSPW index reflect a primary defect of esophageal chemical clearance determining mucosal damage, as shown by low MNBI values, in turn favoring penetration of food antigens and their contact with immune cells; in genetically susceptible individuals this event could be followed by interleukin 5 and 13 secretion with subsequent eosinophils recruitment and development of EoE.

Impedance-pH variables

<table>
<thead>
<tr>
<th>Source</th>
<th>EoE (n=52)</th>
<th>HE (n=52)</th>
<th>HCs (n=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAET (%)</td>
<td>1.0 (1.0)</td>
<td>1.8 (1.9)</td>
<td>1.8 (1.3)</td>
</tr>
<tr>
<td>Weak Acids</td>
<td>(n=42)</td>
<td>(n=44)</td>
<td>(n=42)</td>
</tr>
<tr>
<td>Acid refluxes</td>
<td>23 (12)</td>
<td>38 (24)</td>
<td>44 (22)</td>
</tr>
<tr>
<td>P &lt; .05 for HC vs. EoE and HE</td>
<td>16 (11)</td>
<td>30 (21)</td>
<td>30 (18)</td>
</tr>
<tr>
<td>Weak Acidic Refluxes (n, mean)</td>
<td>6 (6)</td>
<td>8 (9)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>P &lt; .05 for HC vs. EoE and HE</td>
<td>75 (16)</td>
<td>28 (16)</td>
<td>42 (17)</td>
</tr>
<tr>
<td>Weak Acidic Refluxes (n, mean)</td>
<td>3045 (843)</td>
<td>937 (552)</td>
<td>2251 (1080)</td>
</tr>
</tbody>
</table>

[Impedance-pH findings in EoE, HE and HCs.]

Disclosure: Nothing to disclose

References
Disclosure: 57 of the 86 patients identified attended gastroenterology clinic as follow-up for commencement of treatment.

It is recommended that efficacy of treatment be evaluated by repeat endoscopy.

Follow-up endoscopy findings 10 of the identified 86 patients had repeat OGD between 2009–2016. 5 were performed as follow-up following medical therapy and 5 were performed for alternate reasons listed in table 1.

<table>
<thead>
<tr>
<th>Reason for OGD</th>
<th>Histological resolution</th>
<th>Improved OGD Therapy(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up</td>
<td>Yes</td>
<td>12 weeks Swallowed fluticasone spray</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Yes</td>
<td>16 weeks PPI</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Yes</td>
<td>8 weeks PPI</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Yes</td>
<td>12 weeks PPI</td>
</tr>
<tr>
<td>Follow-up</td>
<td>No</td>
<td>12 weeks PPI</td>
</tr>
<tr>
<td>Abdo pain</td>
<td>Yes</td>
<td>3 years Swallowed fluticasone spray</td>
</tr>
<tr>
<td>Abdo pain</td>
<td>No</td>
<td>5 years PPI</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>No</td>
<td>2 years PPI, Oral steroids</td>
</tr>
<tr>
<td>Reflux</td>
<td>Yes</td>
<td>6 months PPI</td>
</tr>
<tr>
<td>Repeat</td>
<td>No</td>
<td>6 years PPI</td>
</tr>
<tr>
<td>Food bolus</td>
<td></td>
<td>Unknown</td>
</tr>
</tbody>
</table>

[Repeat OGD Findings]

In the follow-group, there was 100% histological resolution of eosinophilia, with 80% improvement in symptoms in those treated with a PPI.

Conclusion: EO is an increasingly recognized condition. European guidelines have recently been published though standardised treatment is yet to be defined. Our data shows PPIs and topical corticosteroids are the most effective therapies, in keeping with known findings. PPIs were the most popular treatment choice. It is recommended that efficacy of treatment be evaluated by repeat endoscopy.

Follow-up endoscopy indicated that 65 patients (19.46%) had esophagitis including 20.74% (N = 13) of those with predominant substernal symptoms and 18.8% (N = 58) in those with predominant substernal symptoms and 18.8% (N = 58) in those with predominant substernal symptoms. Overall, 23.95% of patients had esophagitis. Patients with eosinophilic esophagitis would be given esomeprazole 20mg bid for 8 weeks and those with normal findings for 4 weeks.

Disclosure: Nothing to disclose

References


Introduction: Eosinophilic esophagitis (EO) is a chronic, allergen-driven, immune-mediated disease that is increasingly recognized as a cause of esophageal and foregut symptoms in children and adults. The diagnosis of EO requires an invasive endoscopic evaluation with esophageal biopsies showing at least 15 eos/hpf in at least one hpf. Moreover, since symptoms are not predictive of histologic remission, current guidelines recommend to repeat the upper endoscopy in order to confirm histologic disease remission after any kind of treatment (i.e. steroids, diet). Therefore, a non-invasive tool to support the need of performing an upper endoscopy in patients with symptoms suggestive of EO is of great clinical interest. Several studies have been performed in the last years, investigating the potential role of eosinophilic esophagitis.

Aims and Methods: The aim of this prospective pilot study was to evaluate FC levels in incident cases of EO and to correlate them with clinical, endoscopic, and histological characteristics. The study cohort was composed of 86 patients under endoscopy evaluation for the assessment of EO. Eosinophils on mid/distal esophagus biopsies were examined, along with those of the baseline.

Results: Seventy patients [58M/12F; mean age 37] reporting dysphagia (94%), bolus impaction (65%) and chest pain (28%) were diagnosed with PPI-REE (N = 25) or EO (N = 38) and were subsequently recruited. Moreover, a group of 70 [56M/10F; mean age 41] subjects, sex and age matched, were also enrolled. FC levels in incident cases of active PPI-REE/EO were not significantly different from those in controls (mean 48 ± SD 34 μg/g vs 42 ± 9 μg/g; p = ns). Furthermore, among PPI-REE/EO, FC concentrations were not significantly different in relation to the level of clinical score, endoscopic severity or histological evaluation (p = ns, p = ns and p = ns, respectively).

Conclusion: This study shows that FC levels in incident cases of PPI-REE/EO patients do not differ significantly from those in controls. Our data demonstrate that FC is not a useful tool for the diagnosis and management of patients with eosinophilic esophagitis.

Disclosure: Nothing to disclose

References

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Introduction: Gastroesophageal reflex disease (GERD) could be diagnosed by the presence of heartburn as a symptom. The main tool for GERD diagnosis, and the eosinophilic symptoms are excluded to rule out functional dyspepsia. However, it is reported that the rate of pathologic eosinophilic acid reflux (PEAR) of heartburn patients is quite low in China.

Aims and Methods: The aim of this current study is to assess the epigastric symptoms for GERD diagnosis. Consecutive outpatients aged 18–65 years presented with substernal symptoms including heartburn, regurgitation, dysphagia, substernal pain and epigastric symptoms including epigastric pain, epigastric burning, early satiety and postprandial fullness were enrolled. Patients who had esophageal or gastric surgery, peptic ulcers, upper GI cancer were excluded. All patients underwent upper endoscopy, high-resolution manometry and 24-hour esophageal pH monitoring. PPI concentrations have been found in several intestinal diseases, but no data are currently available on patients with EO.

Results: A total of 334 patients were included, with predominant symptoms of heartburn (N = 80), regurgitation (N = 66), substernal pain (N = 60), dysphagia (N = 11), epigastric pain (N = 33), epigastric burning (N = 25), early satiety (N = 1) and postprandial fullness (N = 58). Overall, 23.95% of patients (N = 80) had PEAR, with 26.73% (N = 58) in those with predominant substernal symptoms and 18.8% (N = 22) in those with epigastric symptoms. The rates of PEAR were 6%, 28% and 22.41% in patients with epigastric pain, epigastric burning and postprandial fullness, respectively. And the rate of PEAR in patients with epigastric burning (28.75%, 23/80) were almost the same as those with heartburn (28.75%, 23/80). Moreover, a total of 155 patients (50.82%) had positive PPI test, including 56.34% (N = 111) of those with substernal symptoms and 40.74% (N = 44) of those with epigastric symptoms, of whom the rates were 44.8%, 54% and 33.3% in patients with epigastric pain, epigastric burning and post-prandial fullness, respectively. There was no significant difference in the positive rate of PPI test between patients with epigastric pain and those with heartburn (54.2% vs 56.2%, p > 0.05). Endoscopy indicated that 65 patients (19.46%) had eosinophilic including 20.74% (N = 43) of those with substernal symptoms and 17.1% (N = 20) with epigastric symptoms. If we combined 24h esophageal pH monitoring, PPI test and upper endoscopy, a total of 167 patients (50%) were diagnosed with GERD, 70% of whom (N = 117) had predominant substernal
symptoms and 30% (N = 50) had epigastric symptoms. Among them, 26% of patients presented with heartburn, 23% with regurgitation, 4% with dysphagia, 17% with substernal pain, 8% with epigastric pain, 9% with epigastric burning, 13% with postprandial fullness.

Conclusion: Approximately one-third of GERD patients complain of predominately epigastric symptoms. Excluding epigastric symptoms during symptom-based evaluation of GERD in primary care may miss and delay the diagnosis of real GERD. It is suggested that epigastric symptoms should not be neglected for GERD diagnosis.

Disclosure: Nothing to disclose.

P1145 NOVEL SYSTEM FOR IDENTIFICATION OF LOWER ESOPHAGEAL SPHINCTER WITH IMPEDANCE VARIATION STEP-UP METHOD: A FEASIBILITY STUDY

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Introduction: Esophageal manometry is the gold standard for lower esophageal sphincter (LES) localization and for accurate positioning of catheter based pH and multichannel intraluminal impedance pH monitoring (MII-pH). pH variation step-up method is not as accurate as esophageal manometry for LES localization, and needs patients to be OFF therapy. Gastric impedance has very low values compared to esophageal impedance and is not influenced by acid suppression.

Aims and Methods: Our aim was to evaluate feasibility of impedance variation with the step-up method for LES localization. 75 patients (31 male, mean age 48 years, range 38–57) who underwent 24-hr MII-pH monitoring were prospectively enrolled. A catheter with six impedance channel and 1 pH channel was used. Patients with known Barrett’s esophagus were excluded. High-resolution manometry (HRM) was performed before MII-pH monitoring in order to locate the upper and lower border of the LES and to evaluate esophagogastric junction (EGJ) type. A second operator, blinded to HRM finding, performed the MII-pH study: the catheter was introduced into the stomach (presence of stable impedance values <500 ohm in the second distal impedance channel located at the level of the pH sensor) and withdrawn gradually (1 cm every 15 seconds; each cm was marked with the “symptom” button) until a sharp impedance rise was seen (increase of >50% with respect to gastric baseline); in 62 patients step-up was repeated twice. Abnormal pH-MII study was defined as acid exposure time (AET) >5% and/or positive SI/SAP. A third operator blinded to both HRM and impedance results, reviewed the step-up impedance of all patients. Bland-Altman analysis with Lin concordance and correlation coefficient were used to compare MII-pH and HRM. Subgroups analysis were performed for the following parameters: ON and OFF PPI test and presence and absence of EGJ type ≥ 2.

Interobserver agreement and concordance between the step-two impedance step-up performances were evaluated using Spearman rho correlation coefficient.

Results: Descriptive data are shown in Table 1. 12/75 patients were on PPI. Median impedance rising point was on average 0.8 cm caudal (95% limits of agreement 0.2–1.4 cm) with 1 cm overlap between the two step-up impedance performances was excellent (mean 44.9 and 44.8 cm, rho 0.97). Agreement between the two step-up impedance performances was excellent (mean 44.9 and 44.8 cm, rho 0.97). Impedance variation performances were similar between patients OFF and ON PPI and between presence/absence of EGJ type ≥ 2.

Conclusion: In this ongoing study we observed a good correlation between impedance rise and manometric localization of the upper border of the LES. ON-PPI and impedance results, reviewed the step-up impedance of all patients. Bland-Altman analysis with Lin concordance and correlation coefficient were used to compare MII-pH and HRM. Subgroups analysis were performed for the following parameters: ON and OFF PPI test and presence and absence of EGJ type ≥ 2. Interobserver agreement and concordance between the two step-two impedance step-up performances were evaluated using Spearman rho correlation coefficient.

Disclosure: Nothing to disclose.

P1146 PSPW AND MNBI INCREASE THE DIAGNOSTIC YIELD OF IMPEDANCE-PH MONITORING AND ARE RELATED TO PPI RESPONSE IN GERD PATIENTS WITH ENT SYMPTOMS

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Introduction: Patients with ENT symptoms are often poor respondents to PPIs and present upper endoscopy and 24h multichannel intraluminal impedance-pH (MII-pH) within the normal range. It has been shown that mean nocturnal baseline impedance (MNBI) and post-reflux swallow-induced peristaltic wave (PSPW) indexes increase the diagnostic yield of MII-pH monitoring in GERD patients. These new variables have been assessed primarily in patients with typical GERD symptoms and few data on patients with ENT symptoms are available.

Aims and Methods: To explore whether MNBI and PSPW improve the diagnostic yield of impedance pH monitoring in GERD patients with ENT symptoms and their relationship with PPI response in these patients.

Of consecutive GERD patients presenting with ENT symptoms, 121 with absence of hiatal hernia and/or erosive esophagitis at upper endoscopy, performed within 3 months before the study, underwent MII-pH after a 3-weeks wash out from PPIs. The response to previous PPI treatment was evaluated and considered as non-satisfactory if symptom improvement was <50% on a visual analogue scale. MNBI at 3cm above the lower esophageal sphincter, PSPW, symptom association probability (SAP) and acid exposure time (AET) were calculated according to standardized criteria and considered for the data analysis.

Results: Among all 121 patients, 63 were responders and 58 non-responders to PPI. The mean reflux number was similar between responders and non-responders (39/63 (62%) responder and 24/58 (41%) non-responder patients presented positive AET and/or SAP (p <0.05). A positive PSPW and/or MNBI was observed in 41 responders (65%) and 27 non-responders (47%) (p <0.05). 13/24 non-responder patients with both negative AET and SAP presented a positive PSPW and/or MNBI. 8/34 non-responder patients with both negative AET and SAP (functional heartburn patients), presented a positive PSPW and/or MNBI. Patients with positive AET and/or SAP and patients with positive PSPW and/or MNBI presented a higher probability of PPI response. Results are summarized in Table 1.

Conclusion: The present data show that MNBI and PSPW are promising variables in patients with ENT symptoms, since increase the diagnostic yield of MII-pH. The presence of pathologic MNBI and PSPW is able to discriminate ENT patients with a satisfactory response to PPIs.

Disclosure: Nothing to disclose.

P1147 CORRELATION BETWEEN PERISTALTIC FUNCTION, ASSESSED BY HIGH RESOLUTION MANOMETRY, AND MUCOSAL INTEGRITY IN GERD PATIENTS

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Introduction: It has been shown that mean nocturnal basal impedance (MNBI) increases the diagnostic yield of 24h multichannel intraluminal impedance-pH (MII-pH) monitoring in patients with GERD. The MNBI is directly correlated with mucosal esophageal integrity and intra-luminal clearance. However, the relationship between of esophageal motility and MNBI value needs to be fully elucidated.

Aims and Methods: To explore the relationship between peristaltic vigor and MNBI in GERD patients.

Consecutive GERD patients, with recurrent typical and absence of hiatal hernia and/or erosive esophagitis at upper endoscopy underwent high resolution manometry (HRM) followed by 24h MII-pH. 87 patients with proven GERD (positive AET and/or SAP) were finally enrolled. HRM was performed with patients in a

Table

Mean reflux number (mean ± 95% confidence interval)

Responders (N. 63)

Non responders (N. 58)

Relative Risk for PPI response (95% confidence interval)

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>Non responders</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>AET+</td>
<td>13%</td>
<td>10%</td>
<td>0.8 (0.5–1.2), pns</td>
</tr>
<tr>
<td>SAP+</td>
<td>16%</td>
<td>8%</td>
<td>0.6 (0.4–1.0), pns</td>
</tr>
<tr>
<td>AET+ and/or SAP+</td>
<td>39%*</td>
<td>24%</td>
<td>1.5 (1.1–2.2), p &lt;0.05</td>
</tr>
<tr>
<td>PSPW+ and/or MNBI+</td>
<td>41% (65%)*</td>
<td>24 (47%)</td>
<td>1.6 (1.1–2.4), p &lt;0.05</td>
</tr>
<tr>
<td>AET+ and/or SAP+</td>
<td>52% (83%)*</td>
<td>37 (64%)</td>
<td>1.7 (1.0–2.8), p &lt;0.05</td>
</tr>
</tbody>
</table>

Disclosure: Nothing to disclose.
Results: Overall mean DCI value was 1426

Presence of weak or failed contraction is associated to lower MNBI values at GERD patients. Presence of large breaks does not affect the MNBI value.

Conclusion: There was no difference between MNBI at 3cm and 19cm in patients with and without presence of at least 1/10 peristaltic break. Patients with at least 1/10 weak or failed contraction presented significant lower MNBI values at 3cm compared to patients without presence of weak or failed contraction. MNBI at 19cm did not differ in these two groups of patients. Results are in Table 1.

Conclusion: MNBI at distal esophagus is directly correlated with DCl values in GERD patients. Presence of large breaks does not affect the MNBI value. Presence of weak or failed contraction is associated to lower MNBI values at distal esophagus. These results confirm the potential role of esophageal peristaltic dysfunction on epithelial integrity. Larger studies are needed.

Disclosure: Nothing to disclose

PI1148 ESOPHAGEAL HIGH-RESOLUTION MANOMETRY CAN UNRAVEL THE MECHANISMS BY WHICH DIFFERENT BARIATIC TECHNIQUES PRODUCE DIFFERENT REFUX EXPOSURE

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Introduction: Obesity is a global epidemic and consequently bariatric surgery is increasingly performed. Since there are numerous surgical techniques, the effects of these on the esophageal function are still poorly understood. Furthermore, some bariatric techniques proved to be effective as antireflux procedures, such as Roux-en-y gastric bypass (RYGB), whereas “de novo” gastroesophageal reflux disease (GERD) and dysmotilities were reported after some bariatric procedures, such as Sleeve Gastroctomy (SG).

Aims and Methods: We aimed at assessing the effect of the most commonly performed bariatric techniques on esophageal function (EFG) function, esophageal peristalsis and reflux exposure using high-resolution manometry (HRM) and impedance-pH monitoring (MII-pH).

All obese (body mass index, BMI, ≥35) patients underwent symptomatic questionnaires (GerdQ), endoscopy, HRM and MII-pH before and one year after surgery. We enrolled only obese without dysmotility or any evidence of GERD, in order to verify the real incidence of de novo GERD. Esophageal motor function and EGJ were classified according to Chicago Classification V. 3.0. EGJ contractile integral (EJI-CI) was also calculated. Intragastric pressure (IGP) and gastroesophageal pressure gradient (GEPG) were assessed. Total acid exposure time (AET %), total number of refluxes and reflux symptom association probability (RSAP) were assessed. A group of healthy-volunteers (HVs) served as control.

Results: One hundred and twelve obese subjects (9.12 years-old, mean weight 135 (97–202) Kg, mean BMI 42 (37–69) Kg/m² and 15 HVs (normal weight) were studied. Thirteen underwent endoscopic balloon placement (EBP), 12 gastric banding (GB), 26 sleeve gastroctomy (SG), 18 roux-en-y gastric bypass (RYGB), 15 mini gastric bypass (MGB), 16 biliointestinal bypass (BBIP), and 12 bilipancreatic diversion (BPD). All patients showed a significant decrease of weight and BMI one year after surgery. IGP and GEPI significantly decreased after RYG, BPD and BBIP, whereas they significantly increased after GB and SG. EGI morphology changed only after GB, with 6 patients showing Type III morphology. EGI-CI, IRP and DCI increased significantly (p < 0.001) only after GB. Hypercontractile and premature contractions waves were present in 40% of patients after GB, whereas intractility with motility (36%) waves were present after SG. “De Novo” GERD symptoms were observed in 1 SG and 2 GB. Post-operative greater AET (p < 0.05) and increased total number of reflux (p < 0.001) were present after GB and SG. RYG and MGB showed a significant decrease in AET (p < 0.05) and total number of refluxes (p < 0.001), whereas BBIP showed a non-significant reduction in AET and reflux events but similar to HVs patterns (Table 1).

Conclusion: HRM verified that different bariatric techniques produced different modification of IGP and GEPI, leading to different reflux exposure. Only GB and SG can negatively impact on esophageal function and reflux exposure, and they should be avoided in obese patients with pre-existing GERD.

Disclosure: Nothing to disclose

Abstract No: P1147

Table 1: HRM and reflux features before and after bariatric surgery

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>HRM EGI Type</th>
<th>HRM EGI pressure (mmHg)</th>
<th>HRM EGJ-CI (mmHg*cm)</th>
<th>HRM IRP</th>
<th>HRM IGP (mmHg)</th>
<th>HRM GEPI (mmHg)</th>
<th>MII-pH Ex reflux (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV</td>
<td>Type I</td>
<td>32 (28–39)</td>
<td>4 (2–6)</td>
<td>6 (5–7)</td>
<td>6 (5–7)</td>
<td>5 (3–7)</td>
<td>26 (18–40)</td>
</tr>
<tr>
<td>OBESE PRE-BIB OBESE POST-BIB</td>
<td>Type I Type I</td>
<td>19 (17–22)</td>
<td>24 (20–25)</td>
<td>4.7 (2–8)</td>
<td>15.2 (13–18)</td>
<td>11 (9–14)</td>
<td>34 (25–51)</td>
</tr>
<tr>
<td>OBESE PRE-LAGB OBESE POST-LAGB</td>
<td>Type I Type I Type III</td>
<td>24.1 (20.6–26)</td>
<td>23 (19–25)</td>
<td>5.2 (2–8)</td>
<td>14 (12–16)</td>
<td>10 (8–12)</td>
<td>30 (22–48)</td>
</tr>
<tr>
<td>OBESE PRE- SG OBESE POST-SG</td>
<td>Type I Type I Type II</td>
<td>21.3 (18.5–33)</td>
<td>24 (19–24)</td>
<td>6.5 (5.7–7.5)</td>
<td>14.5 (12–17.6)</td>
<td>10.4 (8–13.4)</td>
<td>30 (20–49)</td>
</tr>
<tr>
<td>OBESE PRE-MGBP OBESE POST-MGBP</td>
<td>Type I Type I Type II</td>
<td>22.6 (20.8–27)</td>
<td>23 (18–25)</td>
<td>6.3 (3–11.9)</td>
<td>15.5 (13–17.2)</td>
<td>10.3 (8–14.5)</td>
<td>41 (20–66)</td>
</tr>
<tr>
<td>OBESE PRE-RYGB OBESE POST-RYGB</td>
<td>Type I Type I</td>
<td>21.1 (19.8–25)</td>
<td>22 (18–23)</td>
<td>5.4 (2–9)</td>
<td>16 (14–19)</td>
<td>11.6 (9–13)</td>
<td>44 (23–68)</td>
</tr>
<tr>
<td>OBESE PRE-BPBI OBESE POST-BPBI</td>
<td>Type I Type I</td>
<td>20.1 (16–25)</td>
<td>21 (18–24)</td>
<td>5.4 (2–10)</td>
<td>15.9 (13–17.7)</td>
<td>10.4 (8–13.9)</td>
<td>30 (20–49)</td>
</tr>
<tr>
<td>OBESE PRE-DBP OBESE POST-DBP</td>
<td>Type I Type I</td>
<td>19.4 (16–23)</td>
<td>19 (17–24)</td>
<td>5.2 (2–9)</td>
<td>16.2 (14–19.3)</td>
<td>12 (10–2.1)</td>
<td>35 (20–55)</td>
</tr>
</tbody>
</table>

*P < 0.05
Disclosure: Nothing to disclose

Introduction: The modern understanding of gastroesophageal reflux disease (GERD) pathogenesis includes Th1/Th2 immune response imbalance that can be determined as phenotype of macrophages (M1 or M2). Studies using high-resolution manometry (HRM) with 22-channel water-perfused catheter have shown that esophageal motility disorders frequently occur in patients with gastroesophageal reflux disease (GERD). Aim: The aim of the present study was to investigate the role of esophageal motility disorders and immune response in diagnosis GERD phenotypes. To determine correlation between esophageal motility disorders, immune response and diagnosis of nonerosive reflux disease (NERD), erosive reflux disease (ERD) and Barrett’s esophagus (BE). METHODS: 180 patients with GERD were studied: 28 (14 men, 45.7 ± 4.2 yr) NERD, 22 (15 men, 45.0 ± 3.2 yr) ERD and 18 (13 men, 47.2 ± 2.9 yr) BE. All the patients were performed HRM with 22-channel water-perfused catheter (Solar GI MMS, The Netherlands). We analyzed distal contractile integral (DCI). Monocytes were isolated from the patients’ blood samples and cultured to macrophages in standard conditions – RPMI1640 medium, 10% FBS, 37°C, 5% CO2. Pooled analysis of macrophage and monocytes included typical M1 and M2 surface macrophage CD markers (CD25, CD80 and CD163, CD206, respectively) performed by flow cytometry (Beckman Coulter FC500). The statistical analysis was done using SPSS Statistics 17.0.

Results: In NERD patients median DCI was 991 [104;3759], in ERD – 570 [41;2462], in BE – 505 [50;1333] mm Hg *e*cm. DCI in NERD patients was significantly higher than in ERD and BE (z = 2.81, p = 0.003 and z = 3.13, p = 0.007, respectively). DCI in patients with BE tended to be lower than in patients with ERD and NERD without statistical significance. In NERD patients median expression of surface marker M1/M2 macrophage CD markers was CD25-37.2 [6.169.4], CD80-19.6 [2.8;49.3], CD163-15-7 [2.7;37.2], CD206-10.5 [0.4;21.6], in ERD was CD25-34.7 [13.1;69.4], CD80-22.8 [6.1;43.6], CD163-17.4 [6.3;37.2], CD206-12.6 [0.3;31.6]. BE was CD25-32.9 [16.3;67], CD80-21.9 [8.3;41.6], CD163-14.9 [18.34], CD206-8.9 [0.5;25.9]. We determined negative correlation between NERD and expression of CD25 marker (P = -0.402, P = 0.001) and positive correlation between BE and expression CD25 (P = 0.338, P = 0.005). In GERD patients median DCI showed significant correlation between expression CD25 and expression CD163 (r = 0.31, P = 0.041).

Conclusion: Analysis of monocyte derived macrophages phenotypes showed the prevalence of expression CD25 marker in all groups patients that characterizes M1 pro-inflammatory activated macrophages (Th1). These results suggest that type of immune response may play a major role in the pathogenesis of esophageal inflammation in GERD. We observed that NERD patients have a significantly higher DCI than ERD and BE. Patients with BE had a lower DCI than patients with ERD. This study points to a clear association between esophageal dysmotility and CDI of GERD.

Disclosure: Nothing to disclose

P1150 CARDIAC ARRHYTHMIA AND GERD IN CHILDREN

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Introduction: Gastroesophageal reflux disease (GERD) is a digestive disorder that is caused by gastric acid flowing from the stomach into the esophagus. Prevalence of GERD in children ranges from 8.5% to 20% (Amy Wu, Pharm D, Am J Health Syst Pharm. 2014;71:798-806). Among 1-year-old children the prevalence is 1.48 per 1000 person-years, it increased to a maximum at 16–17 years of 2.62 per 1000 person-years for girls and 1.75 per 1000 person-years (A. Ruigómez et al, 2009). Except typical esophageal complaints such as heartburn, acid regurgitation, dysphagia, pain behind the sternal bone, there are atypical (extraesophageal) symptoms in children with GERD (laryngitis, bronchoobstructive syndrome, sinusitis, chronic cough, heart rhythm disorders). Presence of heart rhythm disorders can be explained that inflammation of the esophageal mucosa affects local receptors that can induce afferent-erfferent reflex mechanisms of the cardiac rhythm, which can lead to secondary stimulation of the vagal nerves (M Floria, V Liviu, 2015; Cuomo R, DE Giorgi F, 2016).

Aims and Methods: The aim of investigation is to determine the frequency of heart rhythm disorders in children with GERD. 82 patients with GERD within the age of 10–17 years were investigated. The diagnosis was established according to ICD -10 (K. 21, K. 21.9). Group I included 26 patients, who had GERD with esophagitis and group II included 56 patients without esophagitis. Group III included typical GERD patients with without esophagitis was diagnosed by upper endoscopy (with using the Los Angeles Classification of Oesophagitis). Electrocardiogram (ECG) was done for each patient.

Results: Sinus tachycardia was observed in 4 children (15.4%) with GERD with esophagitis (I group) (1 person; 3.6%). 3 children (11.5%) from group I and 2 children from group II (7.3%) had sinus bradycardia. There was no statistical difference in the indices of the study groups (p > 0.05). 3 children (11.5%) from group I had short PQ interval on ECG. It was higher (p < 0.05) than in children from group II (2 persons; 3.6%).

Conclusion: Frequency of disorders of rhythm is higher (p < 0.05) in children with GERD with esophagitis (14 persons; 53%) than in children with GERD without esophagitis (8 persons; 14.2%).

Disclosure: Nothing to disclose

P1151 EFFECT OF ADVANCED DIAGNOSIS MODALITIES AND DISEASE PHENOTYPES ON PPI RESPONSE OF GASTROESOPHAGEAL REFUX DISEASE

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Introduction: In Western countries, response rates for proton pump inhibitors (PPIs) are about 60–70% and higher in heartburn than regurgitation. The differences between response rates in phenotypes have not been adequately investigated. We evaluated PPI response rates of Barrett’s oesophagus (BE), erosive esophagitis (EE), nonerosive (NERD), erosive hypersensitivity esophagus (EH) phenotypes and functional heartburn (FH), and success rates according to the different diagnostic techniques.

Aims and Methods: The aim of this trial is to investigate PPIs response rates of erosive, nonerosive (NERD), hypersensitive esophagus and functional pyrosis phenotypes that are diagnosed by only history, diagnosed by history and upper gastrointestinal endoscopy (UGE), diagnosed by history, UGE, esophageal manometry and 24 h intragastric pH-impedance. Patients were randomly chosen among the patients from the database of Ege University Reflux outpatient clinic who were on continue PPIs. Among 1233 patients, 510 patients who accepted to response phone survey were included. Exclusion criteria were medications which other than PPIs and influence the study, the upper gastrointestinal surgeries, cholecystectomy, major comorbidity, pregnancy. Subjects were evaluated with a validated questionnaire consisted of 28 questions. Pollsters were medical school students who had been educated for face to face and phone interview techniques.

Results: 54 of those patients were diagnosed with only history. 151 patients were evaluated with history and UGE. 305 patients were underwent to UGE, HRM and 24 h intragastric pH-olf (off-PPI). Last group was classified into EE (117), NERD (94), FH (16), FH (58) BE (20). Response rate under 50% for either heartburn and/or regurgitation was accepted as unresponsive (Table). Cumulative response rates for heartburn and regurgitation were 85.3% and 82.2%, respectively. When the effect of advanced diagnostic modalities on response rates for heartburn and regurgitation among phenotypes were evaluated, the highest rate was in history + UGE group (91.4%, 85.4% respectively). Conclusion: We found a higher PPIs response rate than Western populations in all GERD patients. Response rate was not different in regurgitation for history and heartburn. When it is investigated according to the groups, response rate was highest in EE and lowest in FH. Interestingly, response rates were similar between EE and NERD. It should be noted that these results were belong to a similar tertiary referral center with high criteria to treat cases. Probably due to the reason, response rates of patients who were diagnosed by using all diagnostic modalities are lower than those who were diagnosed with only history and UGE.
Aims and Methods: The first-in-man Phase 1 study of X842 in healthy volunteers comprised a Single Ascending Dose (SAD) part in which four subjects were included in each cohort. The primary objective was to determine the safety and tolerability of X842. The secondary objectives were to determine PK characteristics and PD/PD relationship of X842 and main metabolite. PD was assessed using an intragastric 24h pH-metry and sequential dose levels were tested. All available safety, tolerability, PK and PD data were reviewed prior to proceeding to the next cohort. The initial dose of X842 was 0.08 mg/kg. Standard safety assessments were applied. The Full Analysis Set (FAS) consists of all subjects who had received at least one dose of X842.

Results: X842 was safe and well tolerated. No serious or severe adverse events were reported. A clear dose-linearity was observed both for PK and for PD. Full control of 24h intragastric pH was obtained after a single dose of X842. Seventy-two minutes after administration of 2 mg/kg, the intragastric pH value presented as the mean of the 10 minutes median intervals was 4.5. The subsequent pH data showed 100% control of intragastric acidity. All means of the 10 minute median intervals for all four subjects showed pH > 4 throughout the 24 h assessment time.

Conclusion: X842 was safe, well tolerated and provided full 24h intragastric pH control. The results warrant further investigations with X842 in patients with acid-related disorders.

Disclosure: Authors are employees of Cinclus Pharma AG

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Disclosure: Minhu Chen: Speaking and Teaching: Speaker honorarium from Xi'an Jiaotong University; Astra Zeneca China, Ipsen Tianjin, Takeda China, CMS China; Shu Huan Zhang: Employee of Beijing Friendship Hospital; Capital Medical University; Chui Fung Chong: Employee of Takeda Development Center Asia PTE LTD; Nobuo Funao: Takeda Pharmaceutical Company Ltd; Ning Dai, Guijin Fei: Nothing to Disclose. The authors would like to thank all patients and their families, the study teams, all investigators, and Wen Zhou (contribution to study design and former Takeda clinical lead) for their valuable involvement in this study.

Table 1: Patient demographics and baseline characteristics (randomized set) aAt the date of informed consent.

<table>
<thead>
<tr>
<th></th>
<th>Vonoprazan (n = 143)</th>
<th>Lansoprazole (n = 133)</th>
<th>Total (n = 276)</th>
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<tr>
<td>Age1, years, mean (SD)</td>
<td>51.8 (13.7)</td>
<td>51.5 (12.5)</td>
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<td>Males, n (%)</td>
<td>105 (73.4)</td>
<td>110 (82.7)</td>
<td>215 (77.9)</td>
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<tr>
<td>Weight, kg, mean (SD)</td>
<td>69.4 (11.0)</td>
<td>71.8 (11.7)</td>
<td>70.5 (11.4)</td>
</tr>
<tr>
<td>BMI, kg/m2, mean (SD)</td>
<td>24.6 (2.9)</td>
<td>25.1 (3.3)</td>
<td>24.9 (3.1)</td>
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<tr>
<td>Never smoked, n (%)</td>
<td>93 (65.0)</td>
<td>78 (58.6)</td>
<td>171 (62.0)</td>
</tr>
<tr>
<td>No alcohol consumption, n (%)</td>
<td>91 (63.6)</td>
<td>74 (55.6)</td>
<td>165 (59.8)</td>
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<tr>
<td>No caffeine consumption, n (%)</td>
<td>131 (91.6)</td>
<td>129 (97.0)</td>
<td>260 (94.2)</td>
</tr>
<tr>
<td>Grade A/B</td>
<td>89 (62.2)</td>
<td>85 (63.9)</td>
<td>174 (63.0)</td>
</tr>
<tr>
<td>Grade C/D</td>
<td>54 (37.8)</td>
<td>46 (36.4)</td>
<td>100 (36.2)</td>
</tr>
</tbody>
</table>
P1155 THE EFFICACY OF HANGESHASHINTO IN PATIENTS WITH PPI REFRACTORY GERD - RANDOMIZED, MULTICENTER EXPLORATORY STUDY

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Introduction: The proton pump inhibitors (PPIs) are used to the upper gastrointestinal disorder, such as heartburn, and belch in the patients with gastroesophageal reflux disease (GERD). However, the proper response to PPI therapy in these symptoms. Hangeshashinto (HST), a traditional Japanese (Kampo) medicine, has been widely prescribed to relieve chemotherapy-induced diarrhea and stomatitis1) in Japan. One of the mechanisms of HST has been reported to have anti-inflammatory effect via inhibition of prostaglandin E2 production2). HST is used empirically for dyspepsia and heartburn, but has not been fully elucidated. Taken together, these reports and empirical use suggested that HST can be a promising agent for the upper gastrointestinal disorder patients. We investigated the efficacy of HST in patients with PPI refractory GERD.

Aims and Methods: We conducted the randomized, multicenter exploratory study for the efficacy in gastroesophageal reflux disease (GERD) patients refractory to PPIs. All patients were diagnosed with GERD with a frequency scale for the symptoms of gastroesophageal reflux disease (FSSG) total score ≥ 8 following treatment with PPIs for a more than 4 weeks. Patients were randomly allocated to HST (7.5mg/day with a standard-dose of rabeprazole 10mg/day (HST group) or a double-dose of rabeprazole 20mg/day (PPI double-dose group). The gastrointestinal symptoms were evaluated by FSSG and Gastrointestinal Symptom Rating Scale (GSRS). The primary endpoint was to determine the change in total score FSSG after 4 weeks treatment to estimate the difference between the two treatment groups. The secondary endpoint was the changes in GSRS, and also was assessed using the each symptom questionnaires prior to and 4 weeks following treatments. Additionally, the subpopulation analysis based on patient background factors was performed.

Results: A total of 78 patients were enrolled in this study, 70 subjects of effective patient background factors was performed. Of a total 78 patients were enrolled in this study, 70 subjects of effective patient background factors was performed. The proton pump inhibitors (PPIs) and double dose PPI. However, these results suggest that HST contributed to improve the quality of life in PPI refractory GERD patients, although detailed clinical study required to clarify clinical efficacy of the HST.

Disclosure: Nothing to disclose

References

P1156 FARNESOID-X-RECEPTOR EXPRESSION HAS A PROTECTIVE FUNCTION AND EMERGES AS A POTENTIAL TARGET TO PREVENT PROGRESSION FROM BARRETT ESOPHAGUS TO ADENOCARCINOMA

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Introduction: The major precursor condition of Esophagus Adenocarcinoma (EAC) is Barrett’s Esophagus (BE). BE is mainly attributed to inflammation due to chronic reflux of gastric and bicle acid. Risk of progression to EAC correlates with type of diet, which further accentuates the gut microbiome. In previous studies on our L2-IL-18 (IL-1B) overexpressing BE mouse model it was shown that treatment with bicle acids, especially deoxycholic acid (DCA), accelerated tumorigenesis in the mice (1).

Aims and Methods: We are aiming to clarify the effect of bicle acid exposure and the associated nuclear bicle acid receptor Farnesoid-X-Receptor (FXR) in coher- ence with diet and gut microbiome on the development of BE and EAC. Thus, we analyzed cohorts of IL-1B mice with & without FXR whole body knockout and we evaluated a high fat diet (HFD) through histology, gene expression and a characterization of the microbiome. Effects of an FXR agonist (obeticholic acid (OCA)) were analyzed on 3D organoids cells before testing on IL-1B mice fed control (CD) or high fat diet (HFD). In organoids, mice and human patients, analyses including flow cytometry, 16s-sequencing, gene expression- and bile acid analyses were performed.

Results: Gene expression analyses demonstrate that FXR, a key regulator in bile-acid-metabolic and inflammatory signaling, was upregulated in BE but down regulated in EAC. FXR in human BE cells seems to be an important player to regulate the inflammatory effects of bicle acid exposure and the differential potential of progenitor cells at the gastro- esophageal junction, suggesting a protective function that could be activated through OCA treatment. Thus, we provide evidence for a novel mechanism underlying how bicle acids accelerate esophageal carcinogenesis and how FXR activation could be used for preventive or therapeutic approaches in BE and EAC patients.

Disclosure: Nothing to disclose

Reference
Barrett’s Esophagus (BE) is a premalignant condition occurring as a result of gastroesophageal reflux disease (GERD) complications. GERD symptoms are observed in approximately 20% of the developed countries population. On the other hand, hydrogen sulfide (H2S) has been shown to prevent gastric mucosa injury induced by NSAIDs, topical irritants or stress. However, the role of H2S in the pathogenesis of BE has not been elucidated.

Aims and Methods: We investigated if the enzymatic pathway of H2S biosynthesis is involved in the development of BE and if the treatment with H2S precursor (L-cysteine) or donors (NaHS or GYY4137) prevents BE progression in vivo. An important microorganism that plays a role in the development of BE is Helicobacter pylori (H. pylori). Esophageal lesions/metaplasia index (ELMI) was assessed macroscopically and microscopically using H&E and PAS staining. Esophageal blood flow (EBF) was measured by laser flowmetry. Expression of mRNAs for proinflammatory genes (iNOS, COX-2) was determined by real-time PCR. H2S production in esophageal mucosa was assessed using methylene blue method. CTH or CBS gene knock-outs were induced using CRISPR/Cas9 technique in human-derived normal esophageal epithelial cell line (BAR-T).

Results: Chronic reflux led to esophagitis, metaplasia, fall in EBF, and upregulation of iNOS, COX-2 and decreased H2S production. NaHS and GYY4137 but not L-cysteine significantly decreased ELMI, mucin production, iNOS and COX-2 expression and increased EBF. PAG (15 or 30 mg/kg/day) or D,L-propargylglycine (PAG, 1–30 mg/kg), inhibitor of cystathionine-γ-lyase (CTH). Esophageal lesions/metaplasia index (ELMI) was assessed macroscopically and microscopically using H&E and PAS staining. Esophageal blood flow (EBF) was measured by laser flowmetry. Expression of mRNAs for proinflammatory genes (iNOS, COX-2) was decreased in esophageal metaplasia by real-time PCR. H2S production in esophageal mucosa was assessed using methylene blue method. CTH or CBS gene knock-out were induced using CRISPR/Cas9 technique in human-derived normal esophageal epithelial cell line (BAR-T).

Conclusion: We conclude that decreased H2S production in esophageal mucosa exposed to GERD could be involved in the development of BE metaplasia. CTH/CBS gene knock-out for the maintenance of H2S production may serve as a biomarker for Barrett’s esophagus. Am J Gastroenterol [Internet]. 2016; 111(1): 30–50. Available from: http://www.nature.com/doi-10.1038/ajg.2015.322.

Disclosure: Nothing to disclose

References

PI160 MUCOSA-ASSOCIATED MICROBIO DIVERSITY SIGNIFICANTLY DIFFERS IN BARRETT’S ESOPHAGUS AND PROGRESSION TO ESOPHAGEAL ADENOCARCINOMA
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Introduction: Alterations in the human gut microbiome have been linked to health and disease including metabolic syndrome, autoimmunity, and IBD. In addition, microbes and their metabolic byproducts have been linked to gut neoplasia. We hypothesized that alterations in mucosa-adjacent Barrett’s microbiota could be a risk factor for neoplasia.

Aims and Methods: We sought to detect significant differences in Barrett’s esophagus (BE) with and without neoplasia and paired squamous mucosa associated microbiota. Taxa were considered one-by-one using a generalized linear model based on the negative binomial distribution and the log link function as designed by the functions of the R Bioconductor package edgeR. We identified 53 patients who were enrolled in an IRB-approved protocol for research biopsies (Normal controls-10, Intestinal metaplasia (IM) -10, Low-grade dysplasia (LGD) -10, High-grade dysplasia (HGD) -10, Esophageal adenocarcinoma (EAC) -12). Biopsies of the Barrett’s, EAC and normal esophagus (3 cm cephalad) were obtained for mucosa-associated bacteria along with gastric secretions for 16S rRNA V4 DNA sequencing.

Disclosure: Nothing to disclose

References
Disclosure: Nothing to disclose

P1161 COMPUTER-AIDED DIAGNOSIS AND DEEP LEARNING IN THE EVALUATION OF EARLY BARRETT’S CANCER
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Introduction: The endoscopic detection and characterization of early Barrett’s cancer is challenging especially for endoscopists with limited Barrett experience. The evaluation of Barrett’s esophagus with the help of computer-aided diagnosis (CAD) may be a valuable adjunctive tool for endoscopists managing patients with Barrett’s esophagus. As of date, there is only limited experience in the literature on computer aided diagnosis of early Barrett’s cancer.

Aims and Methods: A CAD system was trained using deep learning and then tested for sensitivity and specificity using 33 endoscopic images of histologically confirmed early Barrett’s cancer and 41 images of Barrett’s mucosa without dysplasia. All endoscopic images were collected prospectively at the Klinikum Augsburg and included near-focus white light and narrow band Images. Early Barrett’s cancer was limited to the mucosa or superficial submucosa (sm1/C2).

Conclusion: CAD can be trained to classify Barrett’s cancer using a deep learning approach with excellent diagnostic performance. A much larger pool of images is needed to improve the ability of the CAD system. However, if developed further, CAD using deep learning could become a useful adjunctive tool for endoscopists in the evaluation of Barrett’s esophagus.

Disclosure: Nothing to disclose

Reference

P1162 THE IMPACT OF THE POLICY-PRACTICE GAP ON COST-EFFECTIVENESS OF BARRETT’S OESOPHAGEAL NEOPLASIA MANAGEMENT
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Introduction: Oesophageal adenocarcinoma (OAC) incidence has increased dramatically over the last four decades. Barrett’s oesophagus (BO) is the most important risk factor to develop OAC. Clinical guidelines recommend surveillance and, if there is an indication, endoscopic eradication therapy (EET) of BO patients. However, an important policy-practice gap exists between recommended and observed intervals for BO surveillance.

Aims and Methods: We aimed to determine how current practice of surveillance of BO affects on the cost-effectiveness of the surveillance programme, compared to the recommended policy in the Dutch guideline. We used the Microsimulation Screening Analysis (MIASCAN) model to simulate a 60-year-old Dutch BO cohort and evaluated 4 different surveillance strategies. In the first strategy, surveillance was simulated according to the Dutch guideline: non-dysplastic BO (NBDO) patients underwent surveillance every 3–5 years, low-grade dysplasia (LGD) patients every 6 months to 1 year, and patients with T1a, HGD, or persistent long-segment LGD received EET. The other three strategies simulated a more intensive surveillance strategy for either NBDO (every 2-3.5 years), LGD patients (every 3-6 months), or both in accordance with intervals observed in practice. For each strategy, we computed number of

Results:

Costs: We analyzed the cost-utility of paired mucosa-associated microbes changing in bacteria in samples representing progression of disease from intestinal metaplasia to LGD to HGD to adenocarcinoma. We found significant increases in phyla Synergistetes, OP9, and Chlamydiae and significant decreases in the archaea Crenarchaeota (p < 0.05, FDR corrected). At the genus level, Pyrodictobacter, Pseudoxysites, Synergistetes, and Paenibacillus were the microbes most significantly increased and Sphingobacter, Protoniobivri, and Spingobacterium among those most significantly decreased. Overall the significant changes either up or down are in genera that represent < 10% of the entire bacterial community.

Conclusion: There are significant changes in specific bacterial genera, both increased and decreased, in esophageal biopsy samples representing the presumed progression of Barrett’s mucosa toward neoplasia. Further study will be needed to elucidate the ability of the effectiveness of the ability of these microbes that could contribute to protection from or induction of dysplasia.

Disclosure: Nothing to disclose

Reference

P1164 THE LONG-TERM OUTCOME OF ENDOSCOPIC THERAPY IN ULTRA-SHORT BARRETT’S ESOPHAGUS WITH HIGH-GRADE DYSPLASIA AND EARLY ESOPHAGEAL CARCINOMA
T. Greener, Y. Iwaya, Y. Shimamura, J.D. Mosko, G. Kandel, C. Teshima, P.P. Korian, G.R. May, N.E. Marcon
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Introduction: According to current guidelines, endoscopically visible columnar metaplasia <1 cm does not qualify as Barrett’s esophagus (BE). However, Barrett’s neoplasia (high-grade dysplasia (HGD) and early esophageal adenocarcinoma (EEA)) is still encountered in many of these patients.

Aims and Methods: Our aim was to evaluate the long-term outcomes and safety of endoscopic eradication of neoplasia in patients with HGD in ultra-short (US) BE. Data on patients with histology proven HGD, EEA undergoing endoscopic eradication was collected prospectively. Consecutive endoscopic resection (EMR) combined with radio-frequency ablation (RFA) were performed until endoscopic and histologic eradication of dysplasia and metaplasia was achieved.

Results: Between 2004 and 2017, 511 patients underwent endoscopic eradication for HGD/EEA, of which 83(16%) patients had an US (≤1cm) segment of BE. Eighteen patients were found to have high-risk histological features and were referred for surgical consultation. In the remaining 65 patients, 71% had EEA and 29% had HGD. Complete eradication of neoplasia and intestinal metaplasia (IM) was achieved in 92%(40/65) and 74% (48/65) of patients, respectively. After a median follow-up of 9.9 months following the first negative endoscopy control, neoplasia recurred in 10% and IM in 6%. Esophageal dilation was required in 38.5% (median 3 dilations) at a median follow-up of 23 months.

Conclusion: Routine biopsies and surveillance is not recommended in BE less than 1cm in length. However, a significant proportion of our patients were found to have neoplastic BE within an US segment. In these patients, endoscopic therapy consisting of EMR and RFA was found to be highly effective and safe.

Disclosure: Nothing to disclose
P1165 HYBRID ARGON PLASMA COAGULATION IS SAFE AND EFFECTIVE FOR THE ABLATION OF DYSPLASTIC BARRETT’S ESOPHAGUS: INTERIM ANALYSIS OF A PROSPECTIVE STUDY
E.P. Skacel1, J.E. Baars2, T. Tsoutsman3, M.J. Manlapig Rubio1, P. Bhate1, J. Kench1, A. Majumdar1, A. Kaffes1, A. Nakagawa1, E.P. Skacel1, 2, J.E. Baars2, T. Tsoutsman3, M.J. Manlapig Rubio1, P. Bhate1, J. Kench1, A. Majumdar1, A. Kaffes1, A. Nakagawa1
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Introduction: Endoscopic therapy is recommended for removal of dysplastic Barrett’s oesophagus (BO) to prevent progression to oesophageal adenocarcinoma. Hybrid Argon Plasma Coagulation (HAPC) is an upcoming ablative technique. Limited data and equipment are available. HAPC can be performed using a standard electrosurgical unit that is available in most hospitals. It is therefore more widely available with reduced equipment cost compared to Radio Frequency Ablation.

Aims and Methods: The primary aim of this feasibility study is to assess efficacy of HAPC for ablation of dysplastic BO. The secondary aim was to assess adverse event rates.

This was a prospective single-arm study including patients with histologically confirmed low-grade dysplasia, high-grade dysplasia or T1a adenocarcinoma. Patients with a BO segment >1cm, previous oesophageal ablative therapy and presence of endoscopically visible abnormalities at initial treatment were excluded. Submucosal injection of a sodium chloride 0.9% fluid cushion followed by APC treatment using a flexible HAPC probe and ERBE waterjet™ was performed. HAPC therapy was performed at 8-week intervals until complete endoscopic removal of BO had been achieved upon inspection with high-resolution WLI and virtual (v) chromoendoscopy. Biopsies were taken after eradication of BO. If BO was detected additional HAPC sessions were performed, to a maximum of 5 sessions. After each session adverse events were assessed by phone call at 24 hours and during follow-up visit in clinic 2 weeks post treatment. Patients underwent follow-up endoscopy after treatment at 3, 6, 12, 18, 24, 30, 42, 48, 54 and 60 months.

Results: In total 8 patients [75% male, mean age 66 ± 6 ± 6 years] were enrolled. Currently, 3 patients have achieved histologically complete eradication after a mean of 2.5 HAPC sessions (2-4 treatment cycles). The patients tolerated HAPC treatment well and BO was successfully eradicated using HAPC. None of the patients required the maximum number of 5 sessions at this stage. Five patients are currently being treated with HAPC sessions and are awaiting complete eradication. Median procedure time of all procedures was 12 minutes (IQR: 10.5–18.5 minutes). No treatment-related complications or post-procedural adverse events have been reported to date.

Conclusion: Our interim analysis shows that HAPC is effective and safe for the ablation of dysplastic BO. The aim of this feasibility study was to assess efficacy of HAPC for ablation of dysplastic BO.

Disclosure: Nothing to disclose

P1166 WIDE-FIELD ENDOSCOPIC SUBMUCOSAL DISSECTION FOR THE TREATMENT OF BARRETT’S ESOPHAGUS NEOPLASIA (WF-ESD)
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Introduction: The role of ESD on Barrett’s esophagus (BE) neoplasia has been confirmed in the field. WF-ESD, a method similar to conventional EMR and ESD, but with wider field of application, is currently being treated with HAPC sessions and are awaiting complete eradication, to a maximum of 5 sessions. After each session adverse events were assessed by phone call at 24 hours and during follow-up visit in clinic 2 weeks post treatment. Patients underwent follow-up endoscopy after treatment at 3, 6, 12, 18, 24, 30, 42, 48, 54 and 60 months.

Results: In total 8 patients [75% male, mean age 66 ± 6± 6 years] were enrolled. Currently, 3 patients have achieved histologically complete eradication after a mean of 2.5 HAPC sessions (2-4 treatment cycles). The patients tolerated HAPC treatment well and BO was successfully eradicated using HAPC. None of the patients required the maximum number of 5 sessions at this stage. Five patients are currently being treated with HAPC sessions and are awaiting complete eradication. Median procedure time of all procedures was 12 minutes (IQR: 10.5–18.5 minutes). No treatment-related complications or post-procedural adverse events have been reported to date.

Conclusion: Our interim analysis shows that HAPC is effective and safe for the ablation of dysplastic BO. The aim of this feasibility study was to assess efficacy of HAPC for ablation of dysplastic BO.

Disclosure: Nothing to disclose

References

P1167 CLINICOPATHOLOGICAL FEATURES OF GASTRIC ADENOCARCINOMA OF THE FUNDIC GLAND TYPE ACCORDING TO COLOR AND MORPHOLOGICAL CLASSIFICATION
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Introduction: Gastric adenocarcinoma of fundic gland type (GAFG) is newly added as a special type category in Japanese classification of gastric carcinoma, the 15th Edition (1). GAFG is an uncommon variant of gastric adenocarcinoma which has a distinct clinicopathological, immunohistochemical, and endoscopic features (2-4). GAFG is defined by positive immunohistochemical staining for MUC5A and/or H-K-C (Type 1 and/or part-143

Aim and Methods: The primary aim of this feasibility study is to assess efficacy of HAPC for ablation of dysplastic BO. The secondary aim was to assess adverse event rates.

This was a prospective single-arm study including patients with histologically confirmed low-grade dysplasia, high-grade dysplasia or T1a adenocarcinoma. Patients with a BO segment >1cm, previous oesophageal ablative therapy and presence of endoscopically visible abnormalities at initial treatment were excluded. Submucosal injection of a sodium chloride 0.9% fluid cushion followed by APC treatment using a flexible HAPC probe and ERBE waterjet™ was performed. HAPC therapy was performed at 8-week intervals until complete endoscopic removal of BO had been achieved upon inspection with high-resolution WLI and virtual (v) chromoendoscopy. Biopsies were taken after eradication of BO. If BO was detected additional HAPC sessions were performed, to a maximum of 5 sessions. After each session adverse events were assessed by phone call at 24 hours and during follow-up visit in clinic 2 weeks post treatment. Patients underwent follow-up endoscopy after treatment at 3, 6, 12, 18, 24, 30, 42, 48, 54 and 60 months.

Results: In total 8 patients [75% male, mean age 66 ± 6 ± 6 years] were enrolled. Currently, 3 patients have achieved histologically complete eradication after a mean of 2.5 HAPC sessions (2-4 treatment cycles). The patients tolerated HAPC treatment well and BO was successfully eradicated using HAPC. None of the patients required the maximum number of 5 sessions at this stage. Five patients are currently being treated with HAPC sessions and are awaiting complete eradication. Median procedure time of all procedures was 12 minutes (IQR: 10.5–18.5 minutes). No treatment-related complications or post-procedural adverse events have been reported to date.

Conclusion: Our interim analysis shows that HAPC is effective and safe for the ablation of dysplastic BO. The aim of this feasibility study was to assess efficacy of HAPC for ablation of dysplastic BO.

Disclosure: Nothing to disclose

References
P1168 GASTRIC CANCER MORTALITY BY AGE, GENDER, AND BODY MASS INDEX

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Aims and Methods: Patients with gastric cancer diagnosed from 2005 to 2013 in a single tertiary center were enrolled and followed up until December 2017. To evaluate gender-specific gastric cancer mortality by age and BMI, they were categorized into five age groups: 50–59, 60–69, 70–79, and ≥80yr. BMI groups by Asian-Pacific guideline: <18.5, 18.5–23, 23–25, 25–30, and ≥30 kg/m². Cox regression analysis using hazard ratios (HRs) and 95% confidence intervals (CIs) was performed to assess gender-specific mortality by age and BMI. Results: A total of 9,081 gastric cancer patients (4,887 men and 4,194 women) underwent ESD (n=10,165, 17.6%), gastrectomy with or without chemotherapy (n=4,458, 75.4%), or palliative chemotherapy only (n=420, 7.0%). In adjusted analysis, mortality was higher in advanced stage (HR: 3.39, 95% CI: 3.16–3.67) and increased by aging (HR: 1.69, 95% CI: 1.57–1.82). Mortality was higher in low BMI (HR: 0.78, 95% CI: 0.72–0.84) and male sex (HR: 1.59, 95% CI: 1.36–1.85). Conclusion: Gastric cancer mortality increased by aging and was higher in low BMI and male sex.

Disclosure: Nothing to disclose

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P1169 ENDOSCOPIC PREDICTION OF TUMOR INVASION DEPTH IN EARLY GASTRIC SIGNET RING CELL CARCINOMA

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Aims and Methods: The medical records of patients from 7 tertiary hospitals (Daejeon and Chungcheong province), who underwent surgery or endoscopic resection from January 2011 to December 2016, were reviewed to examine endoscopic findings and clinical data. The patients were divided into two groups (derivation group and validation group), in order to develop an endoscopic prediction model for submucosal (SM) invasion through this study. Results: In total, 331 patients (129 patients, derivation group; 202 patients, validation group) were classified: the group of patients whose pathologic results, two groups were classified: the group of patients whose pathologic results were not suitable for ESD (ESD qualified group, n=205) and the group of patients whose pathologic results were not suitable for ESD (ESD disqualified group, n=26). The preoperative clinical characteristics were compared between two groups. Results: Forty-four percent of the patients (205/466) who underwent gastrectomy for cT1b gastric cancer was qualified for the ESD, their size of endoscopic lesion tended to be smaller than 2cm (1cm < size ≤ 2cm, odd ratio[OR]=0.499, 95% confidence interval[CI]=0.313-0.796, P=0.003; size ≤ 1cm, OR=0.267, 95% CI=0.144-0.495, P=0.000) and located to the distal part of stomach (middle third, OR=0.531, 95% CI=0.279-1.010, P=0.034; lower third, OR=0.362, 95% CI=0.196-0.673, P=0.000). In addition, ESD qualified group showed significantly higher proportion of well-differentiated adenocarcinoma (OR=0.565, 95% CI=0.379-0.843, P=0.005) in endoscopic biopsy. [Table 1]

P1170 CLINICAL SUBMUCOSAL INVASIVE GASTRIC CANCER: IS SURGERY THE ONLY OPTION?

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Aims and Methods: The aim of this study is to analyze surgical outcomes of cT1b gastric cancer and to determine the favoring factors for endoscopic submucosal dissection (ESD).

Conclusion: From January 2010 to December 2014, we retrospectively reviewed 466 patients who underwent curative gastrectomy for cT1b gastric cancer with differentiated type histology and 3cm or less in diameter. According to final surgical pathologic results, two groups were classified: the group of patients whose pathologic results were qualified for ESD (ESD qualified group, n=205) and the group of patients whose pathologic results were not suitable for ESD (ESD disqualified group, n=260). The preoperative clinical characteristics were compared between two groups.

Results: Forty-four percent of the patients (205/466) who underwent gastrectomy for cT1b gastric cancer was qualified for the ESD, their size of endoscopic lesion tended to be smaller than 2cm (1cm < size ≤ 2cm, odd ratio[OR]=0.499, 95% confidence interval[CI]=0.313-0.796, P=0.003; size ≤ 1cm, OR=0.267, 95% CI=0.144-0.495, P=0.000) and located to the distal part of stomach (middle third, OR=0.531, 95% CI=0.279-1.010, P=0.034; lower third, OR=0.362, 95% CI=0.196-0.673, P=0.000). In addition, ESD qualified group showed significantly higher proportion of well-differentiated adenocarcinoma (OR=0.565, 95% CI=0.379-0.843, P=0.005) in endoscopic biopsy. [Table 1]

Disclosure: Nothing to disclose

P1171 THE CLINICAL CHARACTERISTICS AND THERAPEUTIC OUTCOMES OF NON AMPULLARY DUODENAL NEUROENDOCRINE TUMOR (NADNET): MULTICENTER, RETROSPECTIVE STUDY

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Aims and Methods: The aim of this study was to evaluate the treatment outcomes of non ampullary DNETs which were resected endoscopically or surgically. We searched medical records of patients diagnosed as non ampullary DNET from 2004 to 2017 in seven university hospitals. We analyzed clinical characteristics and compared therapeutic outcomes according to endoscopic lesion size and treatment methods retrospectively.

Results: We enrolled 50 non ampullary DNET patients who received endoscopic treatment and 11 patients who received surgical treatment. In endoscopically treated patients, the mean lesion size was 8.2mm and surgical treatment group was 13.9mm. En bloc resection, endoscopic complete resection and pathologic complete resection (CR) rate was 88%, 92% and 50% respectively in endoscopic treatment group. Endoscopic treatment group was divided into 3 groups (1–5mm, 6–10mm, ≥11mm). The pathologic CR rate was significantly low in the lesion size ≥11mm (P < 0.05). The lymphovascular invasion was significantly high
Disclosure: In endoscopic treatment group, the group of lesion size 1.34–2.77; location, RR 0.57, 95% CI 0.34–0.97). Meanwhile, for cUL (−) group and 29.6% (61/206) in cUL (+) group. In both groups, the most expected that LCI facilitate the endoscopic recognition of early gastric cancer and adenoma by emphasizing its color difference as well as surface unevenness on the mucosal surface.

Aims and Methods: The aim of this study was to evaluate the usefulness of LCI for recognition of early gastric cancer and adenoma compared to conventional white light imaging mode (WLI), WLI with indigo carmine contrast (IC) and blue laser imaging bright mode (BLI-brt). We used LASEREO system with EG-L590ZW or EG-L600ZW endoscopy (FUJIFILM Co., Tokyo, Japan). We retrospectively analyzed 84 lesions in 76 patients who were examined by all four imaging (WLI, IC, BLI-brt and LCI) before endoscopic submucosal dissection at the University Hospital from June 2014 to March 2018. Both subjective and objective evaluation methods were adopted to quantify the recognition of early gastric cancer and adenoma. Subjective evaluation was performed by three endoscopists. Each lesion was assigned the recognition score (RS) from 0 (excellent visibility) to 0 (no visibility). Objective evaluation was performed with the L*α*β* color-space-based color difference scores (CDS) between inside and outside of the lesion (40 × 40 pixels), which was calculated by using CIE76 formula (defined by commission internationale de l’éclairage, Vienna, Austria).

Results: The overall mean RS of LCI was significantly higher (p = 0.001) than that of WLI/IC/BLI-brt (2.41 ± 0.71 vs. 1.77 ± 0.74/2.16 ± 0.86/1.33 ± 0.81). The overall mean CDS of LCI was significantly higher (p < 0.001) than that of WLI/IC/BLI-brt (23.94 ± 9.53 vs. 14.38 ± 7.53/15.54 ± 6.81/14.73 ± 7.94). Subgroup analysis based on tumor type revealed that both RS and CDS of LCI for type 0-IIb or 0-IIc lesions (44 lesions) were significantly higher (p < 0.05) than those of WLI/IC/BLI-brt. On the other hand, regarding type 0-Ia or 0-IIa adenomas (67 lesions), both RS and CDS of LCI, as well as IC, were significantly higher (p < 0.05) than those of WLI, however no significant difference was seen between LCI and IC.

Conclusion: The LCI mode was significantly useful for recognition of flat- or depressed-type early gastric cancer compared to WLI, IC, and BLI-brt.

Disclosure: Nothing to disclose.

P1174 PROGNOSTIC VALUE OF NEUTROPHEL-TO- LYMPHOCYTE AND CR-REACTIVE PROTEIN-TO-ALBUMIN RATIOS IN GASTRIC ADENOCARCINOMA

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Introduction: The natural history of different neoplasms is influenced by Inflammation, immunity and nutritional status. Asian studies have proven neutrophil-to-lymphocyte and C-reactive protein (CRP)-to-albumin ratios to be related with mortality in patients with gastric adenocarcinoma. This study aimed to investigate this relationship in Western patients.

Aims and Methods: Patients with gastric adenocarcinoma submitted to R0 resection surgery from January/2013 to December/2017 were included. The study consisted of: registration of neutrophil, lymphocyte, CRP and albumin values within 3 months before surgery; calculation of neutrophil-to-lymphocyte and CRP-to-albumin ratios; evaluation of their relationship with gender, age, tumor size, T, N, M, stage (TNM), presence of lymphatic, vascular and peritoneal invasion; evaluation of the relationship between these ratios and mortality.

Results: One hundred and twenty-seven patients with leukocyte formula (age 67.6 ± 12.4 years old, 52% male) were included, of whom 70 had preoperative CRP and albumin evaluation (age 70.5 ± 11.9 years old, 58.6% male). The average follow-up time was greater than 44 months.

The neutrophil-to-lymphocyte ratio and the number of neutrophils were unrelated to tumor characteristics and did not predict mortality (AUC = 0.562, p = 0.327 and AUC = 0.470, p = 0.653, respectively). The number of lymphocytes correlated with tumor size (p = 0.005). Based on the ROC curve analysis, it was established 1667 lymphocytes as a cutoff value, with shorter survival times in patients below this cutoff (p = 0.003).

CRP and CRP-to-albumin ratio correlated with tumor size (p = 0.042 and p = 0.046, respectively), with shorter survival times when CRP > 10.2 mg/L or CRP/albumin > 0.028 (p = 0.002 and p = 0.003, respectively). Albumin values were unrelated to the studied variables and had no value predicting mortality (AUC = 0.606, p = 0.162).

Conclusion: In this study, the number of lymphocytes and CRP were related to tumor size and survival in patients with gastric adenocarcinoma. There was no additional benefit in using neutrophil-to-lymphocyte and CRP-to-albumin ratios.

Disclosure: Nothing to disclose.

P1173 USEFULNESS OF LINKED COLOR IMAGING FOR RECOGNITION OF EARLY GASTRIC CANCER AND ADENOMA – COMPARISON WITH WHITE LIGHT/INDIGO CARMINEL BLUE LASER IMAGING

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Introduction: Linked Color Imaging (LCI) is a novel color enhancement feature available by using LASEREO endoscopy systems (FUJIFILM Co., Tokyo, Japan), which can enhances the slight difference in mucosal color. Recently we reported that color enhancement of the diffuse redness in gastric mucosa by LCI mode was significantly useful for the diagnosis of active H. pylori infection. We expected that LCI facilitate the endoscopic recognition of early gastric cancer and adenoma by enhancing its color difference between normal and atypical mucosal color. Furthermore, light source of LCI consist of normal white light and short-wavelength narrowband light, which is used to obtain more detailed mucosal surface and microvesSEL patterns. Therefore, we expected LCI to facilitate the endoscopic recognition of early gastric cancer and adenoma by emphasizing its color as well as surface unevenness on the mucosal surface.
Autoimmune atrophic gastritis (AAG) is an autoimmune condition that affects patients of all ages causing atrophy of the corpus-fundus mucosa of the stomach, with subsequent vitamin B12 and iron deficiency. AAG may be associated with a number of autoimmune disorders, namely type 1 diabetes mellitus, thyroiditis, and Hashimoto’s thyroiditis, and Addison’s disease. It has been hypothesised that the presence of concomitant autoimmune disorders may be associated with the development of type neuroendocrine tumours (NET).

**Aims and Methods:** The aim of the study was to assess the prevalence of autoimmune disorders in relation to the development of NETs in patients with AAG diagnosed in two Italian tertiary referral centres for gastrointestinal disorders (Pavia and Aviano). Over the last twenty years, both centres consecutively enrolled and followed-up all patients diagnosed with AAG (corpus/fundus atrophy with antrum sparing and positivity to anti-parietal cells antibody, according to the Sydney-Houston classification). We therefore analysed the association of autoimmune disorders with the presence of NETs.

**Results:** Patients suffering from AAG (mean age 63 ± 16 years; F:M ratio 2:3:1) have been evaluated in the two centres. At least one concomitant autoimmune disorder was present in 244/448 patients (54.4%; mean age 60.3 ± 15 years; F:M ratio 2.4:1), whereas at least two autoimmune disorders were present in 132/448 (29.5%; mean age 63.2 ± 14 years; F:M ratio 1.9:1:1). The most common autoimmune disorders were as follow: 175/448 (39.1%) Hashimoto’s thyroiditis, 45/448 (10.0%) connective tissue disorder, 32/448 (7.1%) type I diabetes mellitus, 24/448 (5.3%) vitiligo, 17/448 (3.8%) Grave’s disease, 13/448 (2.0%) primary biliary cirrhosis and or primary sclerosing cholangitis, 11/448 (2.5%) coeliac disease, 10/448 (2.2%) rheumatoid arthritis. Moreover, 64/448 (14.2%) patients were also diagnosed with a neuroendocrine tumour, 39/448 (8.7%) of which at least two autoimmune disorders (Group 1) were present in 244/448 patients (54.4%; mean age 62.4 ± 15 years, F:M ratio 2.4:1), whereas at least two autoimmune disorders were present in 132/448 (29.5%; mean age 63.2 ± 14 years; F:M ratio 1.9:1:1). The most common autoimmune disorders were as follow: 175/448 (39.1%) Hashimoto’s thyroiditis, 45/448 (10.0%) connective tissue disorder, 32/448 (7.1%) type I diabetes mellitus, 24/448 (5.3%) vitiligo, 17/448 (3.8%) Grave’s disease, 13/448 (2.0%) primary biliary cirrhosis and or primary sclerosing cholangitis, 11/448 (2.5%) coeliac disease, 10/448 (2.2%) rheumatoid arthritis. Moreover, 64/448 (14.2%) patients were also diagnosed with a neuroendocrine tumour, 39/448 (8.7%) of which at the time of diagnosis. The overall prevalence of NETs did not differ between patients with or without autoimmune comorbidities (p = 0.685), nor it was increased in patients with two or more concomitant autoimmune diseases (p = 0.584).

**Conclusion:** Over half of patients with AAG present at least one concomitant autoimmune condition namely thyreopaties, connective tissue disorders, type I diabetes mellitus, vitiligo, and rheumatic disorders. The presence of autoimmune comorbidities does not increase the risk of developing NETs. The not negligible proportion of NETs in our AAG cohort warrants a proper endoscopic follow-up.

**Disclosure:** Nothing to disclose.

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**P1176 THE ROLE OF BIOPSY IN DETERMINING TREATMENT STRATEGY IN EARLY GASTRIC CANCER**

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**Introduction:** Biopsy-based histologic diagnosis is a critical factor for determining treatment strategy in early gastric cancer (EGC). There were some studies about histological discrepancies between initial forcep biopsy and endoscopic resection (ER) pathology. However, there was no study to investigate the role of biopsy diagnosis in determining treatment including ER and surgery in EGC.

**Aims and Methods:** The aim was to compare between histologic diagnosis from biopsy sample and final diagnosis from ER and surgical specimen. In addition, we tried to find predictive factors related to discrepancy. 1,043 patients with a biopsy diagnosis of gastric adenocarcinoma were treated by ER or surgery. To compare the histological discrepancy rate, we checked the histologic diagnosis from the biopsy sample and the final diagnosis from the ER and surgical specimen. Clinicopathologic characteristics were also analyzed.

**Results:** Of 44% of EGC patients were treated by ER, and 56% of EGc patients were treated by surgery. Among patients who received ER, subjects with histologic discrepancies (Group 1) was 10.3%. Subjects with differentiated EGC (D-EGC) based on biopsy and undifferentiated EGC (UD-EGC) on ER pathology was 9.2%. Among them, curative resection (CR) was 33.3%, and non-curative resection (non-CR) was 66.6%. Subjects with UD-EGC on biopsy and D-EGC on ER pathology was 16% of Group 1, and all of them were diagnosed with CR. In surgery group, subjects with histologic discrepancy were 11.0%. Among histologic discrepancy group (Group 2), subjects with D-EGC on biopsy, and UD-EGC on pathology was 22.1%. All of them were included in beyond expanded indication (EI) for ER. Subjects with UD-EGC on biopsy and D-EGC on pathology was 17.4% of Group 2. Among them, patients who were diagnosed with absolute indication (AI) of ER was 13.3%, EI was 40%, and beyond EI of ER was 46.7% according to final pathology. In patients with D-EGC on biopsy and UD-EGC on final pathology (ER and surgery), age, size, tumor location in the upper-third segment of the stomach, and submucosal 2 invasion were significant predictive factors. Patients with this group were more likely to have elevated gross appearance, but did not reach statistical significance. In patients with UD-EGC on biopsy and D-EGC on final pathology (ER and surgery), elevated gross appearance of tumor was significant predictive factor.

**Conclusion:** In retrospective view, unfavorable treatment decisions were made in some discrepancy to histologic diagnosis. Among patients who could be treated by ER, but had surgery. In contrary, there were patients whose initial treatment regimen should be surgery not ER. To determine the treatment strategy for EGC more properly, not only biopsy but also endoscopic characteristics should be considered especially for lesions with predictive factors.

**Disclosure:** Nothing to disclose.
Results: 123,395 UGE were performed during the study period, and 1374 GC were diagnosed (1.11%). 1289 patients with GC were finally included in the analysis. Mean age was 74.1 years (SD: 11.2) and 62% were males. Global MGC rate was 4.73% (61/1289, CI 95%: 3.7%-5.7%). Without significant differences across centers (p=0.23). Median time between negative UGE and MGC diagnosis was 13.1 months (range: 3-35.2). The median number of negative UGEs in MGC group was 1 (range: 1-3). Gastritis (51%), intestinal metaplasia (41%), gastric atrophy (31%) and gastric ulcers (29.5%) were the most common findings at negative UGE. These ulcers were benign at histology and were not endoscopically monitored. Compared to confirmed malignant ulcers in Non-MGC group (n = 610), ulcers at negative UGE were smaller (median: 10 vs 31 mm, p=0.02) and less frequently biopsied (median: 1 vs 3.5, p<0.001). At multivariate analysis, negative UGE was independently associated with younger age (OR: 0.96, p=0.001), PPI therapy (OR: 5.72, p<0.001), previous Billroth II surgery (OR: 5.2, p=0.002) and absence of alarm symptoms (OR 0.21, 47.5% vs 78.5%, p<0.001) (Table 1). The gastric body (52.4%) and intestinal-type (55.6%) were the most common location and histological subtype of MGC, respectively, without differences with Non-MGC. Compared to Non-MGC, MGC were smaller (31 vs 41 mm, p=0.04), more frequently flat-depressed (49.2% vs 29%, p=0.003) and diagnosed at an earlier stage (Stage I-II: 47.4% vs 28.3%, p=0.023). Overall 2-year survival rate was similar for MGC (34%) and Non-MGC (35.3%) (log-rank p=0.59).

Conclusion: MGC is frequent and associated with poor 2-year survival. Our study found independent factors associated with MGC and negative UGE that may be helpful for clinical practice. High-quality UGE may help to reduce MGC incidence.

Disclosure: Nothing to disclose

P1179 PRETREATMENT PREDICTIVE VALUE OF BLOOD NEUTROPHIL/LYMPHOCYTE RATIO IN 50 GASTRIC CANCER RESECTABILITY
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Introduction: New parameters complementary to clinical TNM classification are needed to orient preoperatively about the possibility of a R0 gastric resection. Blood neutrophil/lymphocyte ratio (N/L) reflects the systemic antitumoral inflammatory response in patients and it has been related with post-operative survival in Asiatic studies. Nevertheless, there are few data concerning pretreatment predictive value of these N/L ratio and radical tumor resection

Aims and Methods: We aimed to analyse the potential predictive value of an elevated blood neutrophil/lymphocyte ratio (N/L) in relation to R0 tumoral resectability. Observational retrospective study of 257 consecutive gastric cancers, without haematological diseases or neoadjuvant treatment. The optimal cut-off of N/L was: <5 (ROC curves). Frequency of R0 resection was compared between the group of “normal” N/L ratio: <5 vs “high” N/L ratio ≥5. Multivariate analysis (logistic regression, determining odds ratio (OR) and 95% confidence interval (CI95%)).

Results: A radical R0 resection was performed in 139 gastric carcinomas (54.1%). A “high” N/L ratio was performed according to N/L ratio, with the following adjustment variables: preoperative ASA (1-4), tumoral differentiation grade (well, moderate, poor, undifferentiated) and presurgical TNM stage. Results: A radical R0 resection was performed in 139 gastric carcinomas (54.1%). A “high” N/L ratio was performed according to N/L ratio, with the following adjustment variables: preoperative ASA (1-4), tumoral differentiation grade (well, moderate, poor, undifferentiated) and presurgical TNM stage.

Conclusion: 1.- The presence of a “normal” N/L ratio <5 at the diagnosis of a gastric carcinoma is significantly related with a higher frequency of R0 tumoral resection.
2.- In our series, this higher proportion of R0 resection is independent of pre-surgical ASA, tumoral differentiation grade and presurgical TNM.

Disclosure: Nothing to disclose

P1180 YOUNG AGE AND RISK OF LYMPH NODE METASTASIS IN DIFFERENTIATED TYPE-EARLY GASTRIC CANCER
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Introduction: Young patients with gastric cancer reportedly have a worse prognosis than older patients owing to delayed diagnosis and more aggressive tumor behavior. However, it is unclear whether this applies to early gastric cancer (EGC), for which endoscopic resection is indicated. We aimed to investigate the association between age and lymph node metastasis (LNM).

Aims and Methods: We identified 4,055 patients diagnosed with EGC of differentiated histology who underwent surgery. The association between age and LNM was examined using logistic regression for each T stage separately with adjustments for multiple covariates. We compared LNM rates for each of the Japanese Endoscopic Resection Guidelines criteria in younger (<40 years) and older patients (≥40 years).

Results: The median number of lymph nodes examined was the same for T1a and T1b stages (n=34). The median number of lymph nodes examined was not significantly different within T1a stage (P-value = 0.093), but within T1b stage, the number of lymph nodes examined was significantly different (P-value = 0.019), with the highest number between 50 and 59 years (median = 37), and the lowest number in the 20 to 49 and over 70 age brackets (median = 34). LNM rate and age were not significantly associated within each stage (P-values = 0.269, 0.783 for T1a and T1b, respectively). Among patients fulfilling endoscopic resection criteria, the LNM rate in younger patients was lower than in older patients.

Conclusion: In differentiated-type EGC, young age at diagnosis was not associated with LNM rate. Therefore, endoscopic resection criteria for early gastric cancer can be applied to younger patients.

Disclosure: Nothing to disclose

P1181 PPI AND GASTRIC CANCER IN FUNCTIONAL DYSPEPSIA-BRIDGING THE GAP BETWEEN SCIENTIFIC EVIDENCE AND CLINICAL PRACTICE
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Introduction: PPIs are commonly prescribed for a long period of time. Therefore, the long-term safety issue was raised. There are some adverse events including: bone fractures, enteric infections, community-acquired pneumonia and nutritional deficiencies. As PPIs inhibit acid production atrophic gastritis could be worse, a precursor of gastric adenocarcinoma. Two recent wide health database reports reported a higher risk for gastric cancer (GC) among PPIs long term user (HR 2.44, SIR 3.38) which increased with the duration of PPIs use (1,2). PPIs were proved to be more effective than placebo for the improvement of symptoms and quality of life in Functional Dyspepsia (FD), Epigastric Stress type.

Aims and Methods: We aimed to bridge the gap between evidence and decision making by formulating a decision analysis model focusing on patients with FD

Abstract No: P1178

Table 1: Baseline characteristics. Initial negative endoscopy in MGC patients vs Diagnostic endoscopy in Non-MGC patients

<table>
<thead>
<tr>
<th>Age (years, (mean))</th>
<th>Initial negative endoscopy in MGC patients (n=61)</th>
<th>Diagnostic endoscopy in Non-MGC patients (n=1228)</th>
<th>Univariate (P values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>60.6%</td>
<td>61.6%</td>
<td>0.88</td>
</tr>
<tr>
<td>PPI therapy</td>
<td>78.7%</td>
<td>46.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>H. pylori infection</td>
<td>73.7%</td>
<td>62.3%</td>
<td>0.082</td>
</tr>
<tr>
<td>Family history of gastric cancer</td>
<td>3.9%</td>
<td>7.6%</td>
<td>0.42</td>
</tr>
<tr>
<td>Elective endoscopy</td>
<td>87.3%</td>
<td>86.6%</td>
<td>1</td>
</tr>
<tr>
<td>High-definition</td>
<td>36.1%</td>
<td>40.7%</td>
<td>0.47</td>
</tr>
<tr>
<td>Sedation</td>
<td>26.2%</td>
<td>33%</td>
<td>0.27</td>
</tr>
<tr>
<td>Endoscopist experience (&lt; 5 years)</td>
<td>24.6%</td>
<td>21%</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Conclusion: 1.- The presence of a “normal” N/L ratio <5 at the diagnosis of a gastric carcinoma is significantly related with a higher frequency of R0 tumoral resection.
2.- In our series, this higher proportion of R0 resection is independent of pre-surgical ASA, tumoral differentiation grade and presurgical TNM.

Disclosure: Nothing to disclose

P1181 PPI AND GASTRIC CANCER IN FUNCTIONAL DYSPEPSIA-BRIDGING THE GAP BETWEEN SCIENTIFIC EVIDENCE AND CLINICAL PRACTICE
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Introduction: PPIs are commonly prescribed for a long period of time. Therefore, the long-term safety issue was raised. There are some adverse events including: bone fractures, enteric infections, community-acquired pneumonia and nutritional deficiencies. As PPIs inhibit acid production atrophic gastritis could be worse, a precursor of gastric adenocarcinoma. Two recent wide health database reports reported a higher risk for gastric cancer (GC) among PPIs long term user (HR 2.44, SIR 3.38) which increased with the duration of PPIs use (1,2). PPIs were proved to be more effective than placebo for the improvement of symptoms and quality of life in Functional Dyspepsia (FD), Epigastric Stress type.

Aims and Methods: We aimed to bridge the gap between evidence and decision making by formulating a decision analysis model focusing on patients with FD
P1183 SARCOPENIA AS AN INDEPENDENT PROGNOSTIC FACTOR FOR SURVIVAL AND PERIOPERATIVE COMPLICATIONS IN PATIENTS WITH GASTRIC CANCER
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Introduction: Patients with cancer often show signs of malnutrition, which might influence morbidity and mortality while undergoing chemotherapy or surgical treatment. The tolerability of perioperative chemotherapy in patients with gastric cancer is often limited.

Aims and Methods: To evaluate the influence of sarcopenia in patients with locally advanced, not metastasized, gastric or gastro-esophageal junction (GEJ) cancer undergoing curative treatment (perioperative chemotherapy and surgery) on morbidity and mortality in order to identify patients in need for nutritional intervention.

Methods: Retrospective study, conducted in two hospitals (Universitätsklinikum Frankfurt and Krankenhaus Nordwest) as part of the University Cancer Center Frankfurt (UKT). A large proportion of the patients were treated in the FLOT trial (NCT01216644). Patients charts were reviewed for the following items: age, sex, tumor type, TNM stage, treatment, Clavien-Dindo-Score, BMI, survival data. Two consecutive CT scans were retrospectively analyzed to determine the degree of sarcopenia. Additionally, the mean total muscle area (TMA) was measured at L3 and set in relation to body height, resulting in the skeletal muscle index. SMI. SMI = TMA [cm²]/[height [m]]. Sarcopenia was defined as follows: male patients: BMI < 25: SMI < 43 cm²/m²; BMI ≥ 25: SMI < 53 cm²/m²; female patients: SMI < 41 cm²/m² (regardless of the BMI). Survival was calculated using the Kaplan-Meier method, multivariate analysis was performed using the Cox regression.

Results: 60 patients (72.3%) were male and 23 (27.7%) female. 45 patients (38.8%) had GEJ type 1–3 and 38 (45.8%) gastric tumors, respectively. Sarcopenic patients were significantly older than non-sarcopenic patients (mean age 65.1 years vs. 59.5 years, p = 0.041), terminated the chemotherapy significantly earlier (50% vs. 22.6%, p = 0.037) and showed higher Clavien-Dindo scores, indicating more severe perioperative complications (score ≥3 43.3 vs. 17.0%, p = 0.009). Sarcopenic patients had a significantly shorter survival than non-sarcopenic patients (139.6 [95% CI, 101.3–177.9] vs. 206.7 [95% CI, 179.3–233.8] weeks, p = 0.004). Cox regression analysis did not reveal factors influencing survival other than sarcopenia.

Conclusion: Sarcopenia is present in a large proportion of patients with locally advanced gastric or GEJ cancer and is an independent prognostic factor for survival. Besides, it significantly influences tolerability of chemotherapy and surgical complications.

Disclosure: TG acts as consultant, served on the speakers bureaus and/or received travel grants from Lilly, MSD, BMS, Celgene, Shire, Bayer and Servier. SEAB has an advisory role with Merck, Roche, Celgene, Lilly, Nordic Pharma, Bristol-Myers Squibb and MSD Sharp & Dohme; is a speaker for Roche, Celgene, Lilly, Nordic Pharma, AIO GmbH, MCI, promedics, and Forum für Medizinische Fortbildung; He is CEO/Founder of IKF Klinische Krebsforschung GmbH and has received research grants from Sanofi, Merck, Roche, Celgene, Vifor, Medac, Hospira, Lilly, German Cancer Aid (Krebshilfe), German Research Foundation and the Federal Ministry of Education of Research. All other authors declare no conflict of interests.

P1184 HOXC10 DIRECTLY REGULATED BY MIR129-5P CAN MODULATE WNT SIGNALING PATHWAY IN GASTRIC CANCER: CCND1 IS A CRUCIAL TARGET GENE

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Introduction: HOX genes are highly conserved at the genomic level and have been well-described as important players in regulating numerous processes including differentiation, receptor signaling, motility, apoptosis, angiogenesis, and metastasis. HOX10 is a member of the HOX gene family and has been found to function as oncogenes in the progression of many cancers, thus it might be useful as a marker for cancer diagnosis or prognosis. We have previously found that HOXC10 is up-regulated in gastric cancer and functions as a candidate tumor promoter, whose high expression indicates poor survival outcome. However, the potential regulatory network of HOXC10 remains less understood.

Disclosure: Nothing to disclose
The WNT signaling pathway is well known for its role in controlling cellular proliferation, differentiation, and apoptosis. In cancer, β-catenin associates with TCF/LEF transcription factors to drive expression of WNT target genes, such as CCND1/CD44, c-MYC and MMP7.

Small, noncoding microRNAs (miRNAs) are important posttranscriptional regulators of gene expression and are involved in the regulation of miRNAs target gene expression. MiR-129 family members were reported to be down-regulated in gastric cancer cells and play important roles in regulating cell proliferation in gastric cancer.

Aims and Methods: The aim of this study is to determine the potential regulatory network of HOXC10 in gastric cancer. As HOXC10 is an important transcription factor, ChIP-chip assay was performed firstly. Bioinformatic analyses, such as Gene Ontology (GO), Koyo Encyclopedia of Genes and Genomes (KEGG) were performed for each mechanism affected by the target genes of HOXC10. Additionally, the potential miRNAs targeting HOXC10 were investigated through miRNA, pita, RNAhybrid, and targetSCAN. Reverse transcription polymerase chain reaction (RT-PCR) and western blotting were utilized to measure mRNA and protein expression, respectively.

Results: According to ChIP-chip assay, we found a variety of genes involved in the development of gastric cancer. Through KEGG analyses, these target genes may be involved in many cancer-related signaling pathways. We focused on the Wnt-related signaling genes and found down-regulation of HOXC10 significantly influenced mRNA expression including CCND1, CD44, CCND2, MMP7, CREBBP, especially the downregulation of CCND1. Meanwhile, HOXC10 also modulated the phosphorylation of β-catenin but not its total protein levels, which can also influence the expression of CCND1. Positive correlations were found between CCND1 and HOXC10 (r = 0.13, P < 0.01) based on TCGA database. Besides, combined with miRanda, pita, RNAhybrid and targetSCAN, seven miRNAs were reported to target HOXC10. We verified that miR-129-5P can significantly decrease mRNA expression of HOXC10, thereby down-regulating CCND1 expression in two ways. Conclusion: HOXC10 may be an important direct target of miR-129-5P and play a critical role in gastric cancer by regulating various pathways, particularly the Wnt signaling pathway. CCND1 is found to be a crucial target of HOXC10. Disclosure: Nothing to disclose

P1185 OVEREXPRESSION OF CD44V9 IN GASTRIC CANCER CELLS CONFER RESISTANCE TO TRASTUZUMAB BY INDUCING ANTIOXIDANT ENZYMES

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Introduction: Cancer stem cells play a role in tumour recurrence, cell proliferation, invasion, and resistance to therapy. CD44 variant 9 (CD44v9), one of the variant isoforms of CD44, is a specific cell surface marker of cancer stem cells. CD44v9 increases expression of the antioxidant glutathione (GSH) via stabilising variant isoforms of CD44, is a specific cell surface marker of cancer stem cells. CD44v9 increases expression of the antioxidant glutathione (GSH) via stabilising xCT, a glutamate-cysteine transporter, which provides resistance against reactive oxygen species (ROS). Trastuzumab, a recombinant monoclonal antibody against HER2, has been shown to selectively exert anti-tumour effects in advanced gastric tumours that overexpress HER2. However, trastuzumab-resistant gastric cancer cells associated and being the main precancerous lesion.

Aims and Methods: NCI-N87, a high HER2-expressing gastric cancer cell line, was used for this study. The pCMV expressing plasmid encoding human CD44v9 and standard CD44 was transfected into NCI-N87 cells (NCI-N87-CD44v9 and NCI-N87-CD44s). Cells were incubated for 48 h with different concentrations of trastuzumab and cell viability was evaluated by the MTS assay. Intracellular GSH levels were measured by a luminescence-based assay. Intracellular ROS levels were detected using an oxidant-sensitive fluorescent probe (DCFH-DA) while mitochondrial ROS was assessed by staining with MitoSOX followed by confocal microscopy. Protein expression was determined by western blotting.

Results: Trastuzumab (10, 50 and 200 μg/mL) caused death of NCI-N87 cells (19.73%, 27.3%, and 37.8% cell death, respectively) and NCI-N87-CD44s cells (16.2%, 20.3%, and 27.8% cell death, respectively). However, efficacy of trastuzumab was significantly reduced in NCI-N87-CD44v9 cells (13%, 16%, and 17.1% cell death at 10, 50, and 200 μg/mL of trastuzumab, respectively). Trastuzumab increased intracellular ROS levels in NCI-N87 cells and NCI-N87-CD44s, but not in NCI-N87-CD44v9. Trastuzumab also increased mitochondrial ROS regardless of the extracellular GSH levels were significantly higher in NCI-N87-CD44v9 than in NCI-N87 (2.99-fold: p < 0.01) and NCI-N87-CD44s (1.38-fold; p < 0.01). The expression of MnSOD, a mitochondrial ROS scavenging enzyme, was significantly higher in NCI-N87-CD44v9 than in NCI-N87 (2.78-fold; p < 0.04). In addition, MnSOD mRNA-treated NCI-N87-CD44v9 reacquired sensitivity to trastuzumab (p < 0.01).

Conclusion: CD44v9 positive gastric cancer cells attained trastuzumab resistance via attenuation of ROS accumulation, which was caused by an increase in the antioxidants GSH and MnSOD. Targeting cellular antioxidant enzymes could enhance the efficacy of trastuzumab against CD44v9 positive gastric cancer cells.

Disclosure: Nothing to disclose

P1186 PLASMACYTIC AND MUCOUS CELL EXPRESSION OF MICRORNAS ALONG THE GASTRIC CARCINOGENESIS CASCADE

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Introduction: Gastric carcinogenesis comprises the sequential progression from chronic gastritis, atrophic or intestinal metaplasia, dysplasia, these changes appear to happen diffusely in the gastric mucosa, which may have implications in these patients' surveillance.

Aims and Methods: We aimed to characterize plasma and tissue expressions of different miRNAs for different stages of gastric carcinogenesis.

Single-centre cross-sectional study in patients who underwent upper gastrointestinal endoscopy (n = 42), who were classified in 3 groups: 14 with normal mucosa (control group); 13 with extensive atrophic/metaplastic gastritis and 15 early gastric neoplasia. In each patient, peripheral blood samples and endoscopic biopsy samples from the antrum, corpus and superficial lesion (if present) were collected. Seven miRNAs (miR-21, miR-146a, miR-181b, miR-370, miR-375e and miR-400) and an endogenous control (RNU6-1B) were extracted and quantified in these samples through relative quantification by real time-PCR.

Results: We found a significant decrease in the mucosal expression of miR-146a e miR-370 between the control and metaplasia groups (86% reduction, p = 0.018 and 92% reduction, p = 0.003, respectively) and between normal gastric mucosa and superficial lesions (71% reduction, p = 0.02 and 66% reduction, p = 0.027, respectively). MiRNA-181 showed a tissue expression 44 times greater in the superficial lesion group versus control group (p = 0.001) and there were no significant differences between control and gastric metaplasia. In patients with neoplasia, there were no significant differences in miRNA expression between lesion samples and normal antrum and corpus mucosa. We found no statistically significant differences in the plasmatic miRNA expression of the seven miRNAs between the different groups and no association with their tissue expression.

Conclusion: We found significant changes in tissue expression of several miRNAs across the different stages of gastric carcinogenesis, suggesting a tumor suppressor role for miRNAs such as miR-146a and miR-370 and oncogenic potential for miR-375e in gastric carcinogenesis pathways. In patients with early neoplasia, these changes appear to happen diffusely in the gastric mucosa, which may have implications in these patients' surveillance.

Disclosure: Nothing to disclose

P1187 POLYMORPHISM -511C/T (RS16944) OF THE IL1B GENE AND LOW LEVEL OF PGI REPEATEDLY INCREASE GASTRIC CANCER RISK: SIBERIAN PROSPECTIVE CASE-CONTROL STUDY

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Introduction: Data on the association of IL1B gene polymorphism with gastric cancer (GC) risk are quite contradictory. Low serum level of peptidogen I (PGI) and PGI/PGII ratio is detected in atrophic gastritis (AG), including Helicobacter pylori (H. pylori) associated and being the main precancerous lesion.

Aims and Methods: We aimed to study the influence of polymorphism -511C/T (rs16944) gene IL1B and low levels of peptidogenins on the GC risk in a prospective case-control study (8 years of prospection).

Results: In a single-factor analysis, low PGI and PGI/PGII ratio were associated and being the main precancerous lesion.

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Disclosure: Nothing to disclose
level (B = −0.033, p < 0.001, OR = 0.967, 95% CI 0.95–0.98) and PGI PGH ratio (B = 0.011, p = 0.057, OR = 0.985, 95% CI 0.73–1.37) were significant in the model. Carriers of the T/T genotype of the IL1B had an increased GC risk as compared to carriers of the C/C genotype (B = 2.39; p = 0.047; OR = 10.9; 95% CI 1.03–116.04). In persons with family history of cancers the GC risk was also increased (B = 0.048; OR = 3.475; 95% CI 1.009–11.97).

Conclusion: The obtained data suggest that the T/T genotype IL1B gene, the low level of PGI and the PGI/PGH ratio are associated with an increased GC risk in Korean population.

Disclosure: Nothing to disclose.

## P1188 GENETIC EVENTS AND CLONAL DIFFERENCES IN MULTIPLE OCCURRENCE OF GASTRIC CANCER

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Introduction: Recent molecular analysis by international large-scale collaborative studies of TCGA (The Cancer Genome Atlas) and ICGC (International Cancer Genome Consortium), elucidated the genetic background of gastric cancers into four subgroups e.g., Epstein-Barr Virus (EBV) positive, microsatellite instability high (MSI), chromosomal instability (CIN) and genomically stable (GS) gastric cancers. However, the information of genetic analysis of clinically available samples are still limited. In particular, recurrent occurrence of early gastric cancers was observed even after endoscopic submucosal dissection (ESD), but their molecular events were not elucidated.

Aims and Methods: To explore molecular events in multiple early gastric cancers, tumor tissues from patients who developed synchronous (simultaneous or within one year) and metachronous (one year after initial neoplasm) multiple early gastric cancers were investigated. We performed next generation sequencing on the 83 tumor samples from 31 patients by using “gastric cancer panel” which we created in house comprising 351,050 base pairs of 58 significantly mutated genes (SMG) (Nature 2014; 513: 202–209). Of these 31 patients, 15 patients had synchronous recurrence, 11 metachronous, and 5 both synchronous and metachronous. Average number of recurrence was 3 (maximum 6 times). In addition, we performed immunohistochemical staining of proteins produced by DNA mismatch repair (MLH1, MSH2, PMS2, and MSH6) and microsatellite instability assay (MSI).

Results: We found total of 467 somatic mutations of 58 SMGs in 83 samples (cut-off level of allelic fraction-AF above 5%). We also performed immunohistochemical staining of repair genes and microsatellite instability assay. We then classified 83 tumor tissue samples from 31 patients into 4 groups proposed by TCGA and ICGC international collaborative study group. Our analysis revealed that multiple gastric cancers belonged to the three categories. (1) All recurrences in 2 patients are microsatellite instability high (MSH-H only) (23/31, 65%, (2) one tumor is microsatellite stable (MSS)/genetically CIN, but the recurrence is MSI-H (6/31, 19%), (3) all tumors are MSS and genetically CIN (23/31, 75%). Of particular interest is that in one case with exceptionally frequent recurrence (6 times), microsatellite and immunohistochemical analysis revealed all these six tumors showed microsatellite instability high (MSI-H) and the methylation of the promoter region of MLH1.

Conclusion: The multiple gastric tumors belonged to these three categories; all microsatellite instability-high (MSI-H) (23/31, 65%), microsatellite/CIN and MSI-H (6/31, 19%), all MSS and CIN (23/31, 75%). It could be concluded as with multiple occurrence, principal genotypes may vary and modality of treatment should be modified according to the molecular types if the tumor advanced.

Disclosure: Nothing to disclose.

## P1189 RISK OF OVERALL MORTALITY AFTER HELICOBACTER PYLORI TREATMENT IN PATIENTS WITH HYPERTENSION

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4Luoto Hospital, Medicine, Shenzhen, China
5First People’s Hospital of Shenzhen, Medicine, Shenzhen, China
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Introduction: The eradication rates of Helicobacter pylori (H.pylori) eradication failure. Shenzhen, Guangdong province, is one of the rapidly-growing cities in China with a large migrant population. Risk factors for H pylori resistance in relationship to the migratory environment of China have not been well-investigated.

Aims and Methods: Since September 2016, we recruited patients who tested 14C-Urea breath test-positive after first-line H.pylori eradication from 5 hospitals located throughout Shenzhen in Southern China. Participants completed a questionnaire profiling potential risk factors of H pylori eradication failure, including geographical origin, educational status, source of drinking water, residential family size, and medication/smoking/alcohol history. All participants underwent an upper gastrointestinal endoscopy with three antral and two corpus biopsies obtained for Helicobacter culture and antibiotic susceptibility (Zhangjiaka Investigation Center, Hangzhou, China) for 6 antibiotics: amoxicillin, clarithromycin, metronidazole, tetracycline and furazolidone. Potential risk factors for antibiotic resistance were analyzed.

Results: In this interim analysis we enrolled 746 patients (52.4% male), with a mean age of 43.1 ± 12.5 years. 711 (95.3%) and 473 (63.4%) were born outside Shenzhen and Guangdong province respectively. Among 557 patients (74.7%) with a positive H.pylori culture, the antibiotic resistance for amoxicillin, clarithromycin, levofloxacin, metronidazole, tetracycline and furazolidone were 1.3%, 34.1%, 42.4%, 92.5%, 0% and 0% respectively. 313 patients (56.2%) were resistant to multiple antibiotics. Multivariate testing found a geographical origin from non-coastal cities to be independently associated with clarithromycin resistance (OR = 0.006, OR 2.52; 95% CI 1.160–7.874), while patients’ geographical origin provincial gross domestic product per capita of < 20,000 USD showed borderline association (p = 0.070, OR 2.144, 95% CI 0.925–4.973). These two factors did have association with metronidazole or levofloxacin resistance (p > 0.05). Other significant factors include increasing age for resistance to clarithromycin (p = 0.007, OR 1.019, 95% CI 1.005–1.033), metronidazole (p = 0.002, OR 1.047, 95% CI 1.017–1.079) and levofloxacin (p = 0.001, OR 1.025, 95% CI 1.011–1.039) and prior antibiotic use for resistance to metronidazole (p = 0.024, A1524 United European Gastroenterology Journal 6(85)

Disclosure: Nothing to disclose.

Tuesday, October 23, 2018 09:00–17:00

H. pylori II – Hall X1

Disclosure: Nothing to disclose.

## P1190 MIGRATORY AND SOCIAL PARAMETERS INFLUENCING AMOXICILLIN/H. pylori RESISTANCE IN SOUTHERN CHINA: A MUNICIPALITY-WIDE MULTICENTER PREVALENCE STUDY

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The aim of this study is to investigate the trend of the prevalence and grades of AG and IM according to sex in Korean population. From March 2003 to February 2018, we prospectively enrolled 2002 subjects without H. pylori infection regardless of sex that suggests sex or gender-specific characters such as eating habits including salty or spicy foods are related with the development of AG and IM.

Conclusion: Significantly decreased prevalence and grades of AG and IM at corpus only in female in spite of decreased H. pylori infection regardless of sex suggests that sex or gender-specific characters such as eating habits including salty or spicy foods are related with the development of AG and IM.

Disclosure: Nothing to disclose

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### Table 1: Grades and prevalence of atrophic gastritis and intestinal metaplasia in the antrum and the corpus from 2003 to 2018

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2002</td>
<td>2002</td>
<td>2002</td>
<td></td>
</tr>
<tr>
<td>AG grade</td>
<td>0.58(0.706)</td>
<td>0.40(0.650)</td>
<td>0.54(0.800)</td>
<td>0.004</td>
</tr>
<tr>
<td>Antrum</td>
<td>46.8%(130/278)</td>
<td>32.7%(127/388)</td>
<td>36.9%(263/712)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total IM</td>
<td>0.51(0.837)</td>
<td>0.37(0.677)</td>
<td>0.47(0.795)</td>
<td>0.001</td>
</tr>
<tr>
<td>Antrum IM</td>
<td>31.4%(95/303)</td>
<td>26.0%(134/515)</td>
<td>30.7%(363/1184)</td>
<td>0.119</td>
</tr>
<tr>
<td>Total AG</td>
<td>0.42(0.738)</td>
<td>0.28(0.632)</td>
<td>0.29(0.672)</td>
<td>0.018</td>
</tr>
<tr>
<td>Antrum</td>
<td>28.1%(77/274)</td>
<td>20.2%(83/410)</td>
<td>18.3%(149/815)</td>
<td>0.002</td>
</tr>
<tr>
<td>Total IM</td>
<td>0.38(0.730)</td>
<td>0.23(0.565)</td>
<td>0.23(0.569)</td>
<td>0.001</td>
</tr>
<tr>
<td>Antrum IM</td>
<td>24.4%(74/303)</td>
<td>16.1%(83/515)</td>
<td>15.2%(180/1184)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male AG</td>
<td>0.58(0.774)</td>
<td>0.35(0.634)</td>
<td>0.57(0.800)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male IM</td>
<td>0.58(0.913)</td>
<td>0.39(0.699)</td>
<td>0.55(0.856)</td>
<td>0.034</td>
</tr>
<tr>
<td>Male Antrum</td>
<td>57.6%(49/85)</td>
<td>27.6%(45/163)</td>
<td>39.5%(121/306)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male Antrum IM</td>
<td>34.4%(32/93)</td>
<td>26.7%(58/217)</td>
<td>34.8%(167/480)</td>
<td>0.100</td>
</tr>
<tr>
<td>Female AG</td>
<td>0.46(0.801)</td>
<td>0.29(0.664)</td>
<td>0.38(0.772)</td>
<td>0.220</td>
</tr>
<tr>
<td>Female IM</td>
<td>0.50(0.862)</td>
<td>0.40(0.660)</td>
<td>0.50(0.800)</td>
<td>0.284</td>
</tr>
<tr>
<td>Female Antrum</td>
<td>42.0%(81/193)</td>
<td>36.4%(82/225)</td>
<td>35.0%(142/406)</td>
<td>0.248</td>
</tr>
<tr>
<td>Female Antrum IM</td>
<td>32.1%(29/93)</td>
<td>16.6%(36/217)</td>
<td>21.7%(104/480)</td>
<td>0.016</td>
</tr>
<tr>
<td>Female AG</td>
<td>0.48(0.802)</td>
<td>0.36(0.662)</td>
<td>0.41(0.746)</td>
<td>0.189</td>
</tr>
<tr>
<td>Female IM</td>
<td>0.30(0.621)</td>
<td>0.25(0.576)</td>
<td>0.27(0.786)</td>
<td>0.528</td>
</tr>
<tr>
<td>Female Antrum</td>
<td>27.7%(53/191)</td>
<td>21.0%(50/238)</td>
<td>15.6%(76/478)</td>
<td>0.001</td>
</tr>
<tr>
<td>Female Antrum IM</td>
<td>32.0(0.685)</td>
<td>0.21(0.543)</td>
<td>0.14(0.458)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female AG</td>
<td>0.40(0.710)</td>
<td>0.28(0.608)</td>
<td>0.23(0.590)</td>
<td>0.009</td>
</tr>
<tr>
<td>Female IM</td>
<td>0.32(0.685)</td>
<td>0.15(0.479)</td>
<td>0.10(0.379)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female Antrum</td>
<td>21.4%(45/210)</td>
<td>15.8%(47/298)</td>
<td>10.8%(76/704)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Results: Biochemical evaluation of anti-Hp antibodies was performed in 697 patients. The highest value of Helicobacter pylori (Hp) infection was found in 139 (22.8%); 118/527 (22.4%) of TH patients, 3/25 (12.0%) of CD patients, 5/13 (38.5%) of RA patients, 7/21 (33.3%) of PA patients. In patients with two or more coexisting autoimmune diseases, Hp infection was observed in 2.7 subjects with HT and CD, 2.4 patients with HT and PA, 1.3 subjects with HT and RA, and in 1/4 subjects with HT and VI. No cases of Hp infection were found in the 4 patients affected with SS.

Conclusion: The overall prevalence of Hp infection in the population of patients with autoimmune diseases was 22.8%, which is significantly lower than the medium value reported for the Italian general population and is partly due to the lower mean age of patients with autoimmune diseases. This data seems to confirm previous reports of a lower prevalence of Hp infection in patients with autoimmune diseases compared to the general population of the same age.

Disclosure: Nothing to disclose.

Results: 1154 doctors from 14 different regions of Russian Federation were examined. High prevalence of Hp (59%) among physicians was found. The lowest prevalence of infection was found in Saratov (35.8%), the highest incidence of infection was recorded in Krasnodar (76.2%). The prevalence of Hp in the group of doctors under the age of 30 y. o. was 45.2%, in the group of 31-60 y. o. – 65.2%, respectively. 20% of specialists refused to take part in the testing, 50% of doctors noted that they would not take antibiotics if an infection was detected. Treatment for eradication Hp among 619 of Hp-positive physicians was received only in 114 (18.9%) doctors and therapy achieved success in 104 (9%)

Conclusion: The first observation epidemiological study on Hp infection among Russian physicians showed differences in infection rates in various regions of Russia with an average of 59%. The low awareness of physicians about their Hp status was a lack of interest in the appropriateness of self-diagnosis and eradication of Hp was revealed.

Disclosure: Nothing to disclose.
P1196 OPTIMIZATION OF 13C UREA BREATH TEST THRESHOLD LEVELS FOR THE DETECTION OF HELICOBACTER PYLORI INFECTION IN A NATIONAL REFERRAL LABORATORY
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Introduction: Threshold values for C13-urea breath test (C13-UBT) positivity may be affected by sociodemographic factors, host factors such as C13 excretion kinetics, bacterial factors and laboratory factors including urea dose. Manufacturer-recommended cutoffs for C13-UBT assays may not be applicable in all settings. Optimizing C13-UBT cut-offs may have profound public health ramifications.

Aims and Methods: We aimed to determine the optimal threshold for C13-UBT positivity in our population. Consecutive test samples collected at our central laboratory (from patients undergoing a first-time C13-UBT between 1st January 2010 and 31st December 2015 were included. The difference between values at 30 min and at baseline (T30-T0) was expressed as delta over baseline (DOB). Cluster analysis was performed on the C13-UBT test results to determine the optimal cut-off point with minimal interclass variance.

Results: 234,831 patients (87,291 (37.2%) male, age 39.9 ± 19.9) underwent a first-time C13-UBT, including 124,701 (53.1%) negative and 110,130 (46.9%) positive results. Male subjects: the manufacturer-recommended cutoff of 3.5 DOB. Cluster analysis determined an optimized cutoff of 2.74 DOB, representing an additional 2180 (0.93%) positive subjects who had been previously categorized as negative according to the manufacturer-specified cutoff of 3.5 DOB. Mean positive and negative DOB values were 19.54 ± 14.95 and 0.66 ± 0.51, respectively. The cut-offs for male and female subjects were 2.23 and 3.05 DOB, respectively. Threshold values for <45 year-olds, 45-60 year-olds and >60 year olds were 2.67, 2.55 and 2.93 DOB, respectively. Of the 2180 (0.93%) patients with DOB 2.23-3.05 and >3.05 subsequently completed the study. The eradication rate was 64.0% according to intention-to-treat analysis and 68.4% by per-protocol analysis.

Conclusion: Major referral laboratories should optimize threshold values for C13-UBT cut-offs. The cut-offs for male and female subjects were 2.23 and 3.05 DOB, respectively. Optimizing C13-UBT cut-offs may have profound public health ramifications.

Disclosure: Nothing to disclose

References

P1198 A MOLECULAR DIAGNOSTIC TEST USING REVERSE BLOT HYBRIDIZATION ASSAY FOR IDENTIFICATION OF GENOMIC MUTATION RESPONSIBILITY FOR ANTIBIOTICS RESISTANCE OF HELICOBACTER PYLORI
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Introduction: The rapid identification of antibiotics-resistance of H. pylori is important to eradicate H. pylori infection. The aim of this study was to examine a newly designed reverse blot hybridization assay (REBA) for identification of antibiotics-resistance of H. pylori strains.

Aims and Methods: REBA for identification of genomic mutations responsible for antibiotic-resistance of H. pylori was developed: clarithromycin resistance (23S rRNA A2143G, A2142G and A2142C), fluoroquinolone resistance (gyrA Codon 87 C261G/A, and Codon 91 A272G and G271A-T), tetracycline resistance (16s rRNA AGA nt, 965-967 TTC). DNA extracted from H. pylori strains and other bacterial species. Polymerase chain reaction and REBA was performed.

Results: The diagnostic accuracy, a test using twelve samples of H. pylori strains and clones were performed, and findings of PCR-REBA were consistent with those of prepared samples. In cross-reactivity testing using 26 other bacterial species, no cross reactivity was observed among bacterial species. For validation of findings of PCR-REBA, data of direct DNA sequencing of seven samples of H. pylori strains were performed. Findings of PCR-REBA were consistent with those of direct DNA sequencing data.

Conclusion: REBA showed a good performance of rapid and accurate identification of antibiotic-resistance of H. pylori. It may become an effective diagnostic test for tailored eradication treatment of H. pylori.

Disclosure: Nothing to disclose

References
2. K. Heeman, J. Kim, H.-Y. Wang, H. Lee. Personal communication

P1197 CLARITHROMYCIN RESISTANCE AND FEMALE GENDER AFFECT HELICOBACTER PYLORI ERADICATION FAILURE IN CHRONIC GASTRITIS
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Introduction: Helicobacter pylori infection affects 54.4% of population in Korea. The eradication rate of the first-line triple therapy (a proton pump inhibitor, clarithromycin and amoxicillin) for H. pylori infection has gradually decreased in Korea. The eradication failure is influenced by host-related, bacterial, and environmental factors. It has been reported that the clarithromycin (CAM) resistance of H. pylori infection affects 54.4% of population in Korea.

Aims and Methods: We aimed to evaluate whether clinical parameters, clarithromycin resistance and female gender affect H. pylori eradication failure. A total of 203 patients with H. pylori-positive chronic gastritis were consecutively enrolled. All the participants received a diagnosis of H. pylori infection by a rapid urease test or detection of H. pylori genomic DNA from gastric mucosal tissues. They received clarithromycin-based triple therapy for 7 days. A clarithromycin resistance test was performed by detection of A2142G and A2143G point mutations in H. pylori 23S rRNA using a dual-priming oligonucleotide PCR. The CAM resistance was examined for polymorphism G681A of exon 5 and G636A of exon 4 by PCR with restriction fragment length polymorphism. The patients were classified into three groups by genotypes from gastric mucosal tissues. H. pylori eradication failure in patients with chronic gastritis.

Results: Of 203 patients, 190 completed the study. The eradication rate was 64.0% according to intention-to-treat analysis and 68.4% by per-protocol analysis. CAM resistance was identified in 73 patients (37.5%), and their eradication rate was 50.7%. Clarithromycin resistance (odds ratio 19.13, 95% confidence interval 7.99-45.09) and female gender (odds ratio 1.73, 95% confidence interval 1.51-1.95) were significantly associated with eradication failure. The other clinical parameters such as age, cigarette smoking, alcohol intake, the body-mass index, hypertension, and diabetes were not significantly associated with eradication failure.

Conclusion: Clarithromycin resistance and female gender are factors affecting H. pylori eradication failure in patients with chronic gastritis.

Disclosure: Nothing to disclose

References

P1199 EVALUATION OF THE RIDAGENE HELICOBACTER PYLORI REAL-TIME PCR ASSAY COMPARED TO CULTURE FOR THE DETECTION OF CLARITHROMYCIN RESISTANCE IN AN IRISH CENTRE
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Introduction: Helicobacter pylori antimicrobial susceptibility testing is important for determining the prevalence of antibiotic resistance in a given population, in order to recommend the most appropriate treatment regimens. Furthermore, it provides the opportunity to tailor an individual patient’s therapy. As traditional culture-based approaches are time-consuming, recently developed molecular methods provide a more rapid alternative for the detection of H. pylori and its resistance to antibiotics.

Aims and Methods: Our aim was to evaluate the Ridagene H. pylori real-time PCR assay compared to culture-based methods for the detection of clarithromycin resistance in Irish H. pylori infection. Following ethical approval and receipt of informed consent, gastric biopsy samples of patients diagnosed with H. pylori infection by the rapid urease test (RUT) were processed for culture and clarithromycin susceptibility testing using Enterotubes (Biomerieux, France). DNA was isolated from biopsies using the QIAamp DNA Mini Kit (Qiagen, UK) and analysed for the 3 most common clarithromycin-mediated point mutations (A2146C, A2142G and A2142C) using the Ridagene H. pylori real-time PCR assay (R-Biopharm AG, Germany).

Results: Of 51 RUT- and culture-positive patients (mean age 47.4 ± 14.2 years; 46.6% female) we analysed. The Ridagene assay detected H. pylori DNA in 96.9% (N = 49/51) of samples. Using biopsies that were both culture- and H. pylori DNA-positive, the rate of clarithromycin resistance detected by culture-based methods was significantly higher than that of the Ridagene assay (51.2% (N = 65/127) vs 38.6% (N = 49/127), respectively; X2 = 4.1; P = 0.04). Results were concordant from both methods in 80.3% (N = 102/127) of cases. The sensitivity and specificity of the Ridagene assay
compared to culture for the detection of clarithromycin resistance were 67.7% (95% CI: 64.5–70.8%) and 91.9% (95% CI: 82.2–97.5%), respectively. The positive predictive value was 89.8% (95% CI: 78.9–95.4%) and the negative predictive value was 73.1% (95% CI: 65.5–79.5%).

Conclusion: Although the Ridgeway assay is rapid and easy to use, the low sensitivity compared to culture for the detection of clarithromycin resistance in our cohort limits its use to cases where culture-based methods are unsuccessful. Further studies are required to characterise the full range of clarithromycin-resistance-mediating mutations present in our patients.

Disclosure: Nothing to disclose

P1200 THE USEFULNESS OF LINKED COLOR IMAGING AND THE POTENTIAL OF AUTOMATIC DIAGNOSIS SYSTEM FOR DIAGNOSIS OF H. PYLORI INFECTION

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Introduction: Linked Color Imaging (LCI) is a novel image-enhanced endoscopy to enhance the slight difference in mucosal color. The lighting in LCI mode enhances hemoglobin related information. Using the latest LASEREO system (VP-7000&LL-7000) and latest endoscopy (EG-L600ZW7, EG-L600WR7) (FUJIFILM Co., Tokyo, Japan), we expected LCI to enhance the difference in presence of patients and support the diagnosis of active Hp infection. However, the endoscopic diagnosis of Hp infection does not have objective indicators; it depends on physician’s experience. Therefore, it is necessary to establish universal methods for the endoscopic diagnosis of Hp infection, such as artificial diagnostic aid.

Aims and Methods: The aims of this study are (1) to evaluate the diagnosability of our artificial intelligence (AI) system for Hp infection and (2) to evaluate the usefulness of LCI for diagnosis of Hp infection compared to the conventional endoscopy with white-light image (WLI).

In our new AI system, LCI images were classified into two types based on the slight difference of the red color, high hue images (red-purple) and low hue images (red-orange). Then, the presence or absence of Hp infection was learned by machine learning for each type of LCI image. The trained classifiers gave us the diagnosis of Hp infection automatically. We retrospectively analyzed 133 patients with Hp positive (55 patients) or negative (78 patients) were examined with WLI and LCI at Asahi University Hospital from December 2016 to January 2018. The diagnostic accuracy of Hp infection was determined by more than two different examinations: histologic examination, serum antibody test, stool antigen test, 13C Urea breath test. The absence of Hp infection was determined by the 13C area breath test at least 2 months after Hp eradication therapy. For this study, we used 3 endoscopic images per patient, which were taken from lesser curvature or greater curvature of middle to lower of gastric body. Three LCI images were read into AI system, and randomly arranged 3 LCI and 3 WLI images were made a judgment of Hp-positive/negative by 3 endoscopists, A: an expert involved in the development of LCI, B: a gastroenterology specialist, C: a senior resident.

Results: The levels of accuracy/sensitivity/specificity of diagnosis of Hp infection by AI system with LCI were 82.9%/74.5%/85.5%, respectively. On the other hand, A with WLI and LCI were 76.5%/82.9%/88.0%, and 88.0%/85.9%/89.7%, respectively. Those of diagnosis by B with WLI and LCI were 75.9%/58.2%/88.5%, and 87.2%/78.2%/93.6%, respectively, and diagnosis by C with WLI and LCI were 74.4%/69.1%/78.2%, and 85.7%/85.5%/85.9%, respectively. The accuracy and sensitivity of diagnosis with LCI was significantly higher than those of WLI by all three endoscopists (p = 0.018–0.048). There was no significant difference between diagnosis of physicians and AI system. The kappa value of variability among 3 physicians for LCI (kappa value: between A&B = 0.86, A&C = 0.71, B&C = 0.72) was higher than that for WLI (kappa value: between A&B = 0.58, A&C = 0.57, B&C = 0.65). There were 7 cases (5%) that were wrongly diagnosed by all physicians and one case (1%) by AI system.

Conclusion: LCI had significantly higher accuracy and sensitivity of diagnosis of Hp infection compared to conventional WLI. We recommend LCI mode for screening of Hp infection in routine endoscopy as costless and convenient. The usefulness of the open AI system for Hp infection diagnosis was confirmed. Learning more images, our new proposed AI system will be able to support an inexperienced physician.

Disclosure: Nothing to disclose

P1201 SPANISH PRIMARY CARE SURVEY ON THE MANAGEMENT OF H. PYLORI INFECTION: PERCEPTIONS, ACCESS TO INFORMATION AND CONTINUOUS MEDICAL EDUCATION

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Introduction: The preferences and decisions of Primary Care physicians in the management of H. pylori, or their access to different health technologies (i.e. diagnostic methods), courses and information have not been widely taken into consideration, even though Primary Care physicians currently manage this infection in most of the cases.

Aims and Methods: To evaluate these perceptions, access to continuous medical education and information of Spanish Primary Care physicians. A multidisciplinary committee formed by H. pylori experts from the Spanish Association of Gastroenterology (AEG) and the three societies of Primary Care in Spain (SEMICYUC, SEMERGEN and SEMG) designed an online survey registering 140 variables regarding demographics, type of practice, continuous education received, preferences on management and access to health technology. Survey was submitted via email to the members of the three societies. Responses were anonymously codified. Truncated responses were included up to last question answered. Responses were weighed by province, gender, age and type of practice. Categorical variables were represented as percentage and 95% confidence interval (CI), numerical variables as mean and standard deviation (for normal distribution) or median and inter-quartile range (IQR) (if not normal). Survey was performed using the AEG-REDCap platform.

Results: A total of 1,581 responses were received between December 2017 and March 2018. After removing blank and duplicate responses 1,425 were valid for analysis (representing 5% of all Primary Care doctors in Spain). Of them, 46% (95%CI = 64·68%) were women and the average age was 48 years (SD ± 11). 59% were from urban context, 20% from semi-urban and 21% from rural. 93% provided public practice. No respondent bias was identified in the known variables. 80% of physicians had completed at least one Maastricht consensus, and 21% had read Maastricht V. 87% of doctors had read at least one national or international guideline or consensus on H. pylori or dyspepsia. 34% had attended a continuous education course related to H. pylori, the majority of them in the last four years (median 2, IQR = 1–4 years). Course access was region dependent, ranging from 18% in Andalucía to 65% in Madrid. Only 16% of doctors responded they knew local H. pylori prevalence, 63% did not know and 21% knew that there was no data or it was outdated. Local prevalence reported by those who “knew” was higher than the prevalence expected by those who “did not know” (43% vs. 32%). Information on resistance to clarithromycin rates showed similar patterns: only 31% responded knowing them, and 21% reported there was no data or outdated, and expected resistance was lower (16%) than reported (23%).

Conclusion: Although Spanish Primary Care physicians seem relatively updated through literature, continuous medical education updates are region dependent and should be extended nationally. Lack of knowledge on, and underestimation of, prevalence and resistance rates are due both to lack of educational updates as well as lack of scientific studies in the literature.

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, MSD, Merck, Abbott, Sanofi, and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayolco. Dr. Ricote Belinchon has received retribution for formative actions from Allergan, Almirall and Heel.

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Introduction: Stool antigen tests have become a widely acceptable method for detection of H. pylori. This non-invasive method provides an alternative to the more invasive techniques of biopsy. Gastric disease attributed to H. pylori is chronic gastritis and peptic ulcer disease. The recent Maastricht V. Consensus Report indicates that serology tests performance may be variable (kappa value: between A&B = 0.44, A&C = 0.50, B&C = 0.55), due to different rates of resistance-mediating mutations present in our patients.

Further studies are required to characterise the full range of clarithromycin-resistance-mediating mutations present in our patients.

Disclosure: Nothing to disclose

P1202 EVALUATION OF CURIAN HPSA FLUOROMETRIC ASSAY: A NOVEL, RAPID IMMUNOASSAY FOR THE DETECTION OF HELICOBACTER PYLORI ANTIGENS IN HUMAN STOOL

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Introduction: Helicobacter pylori antibodies in human stool specimens. The test uses monoclonal anti-Helicobacter pylori antibodies for both capture and detection. For clear interpretation, the Curian Analyzer (reader) is used to report results.

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**P1203 EFFICACY OF VONOPRAZAN-BASED THERAPY COMPARED TO PROTON PUMP INHIBITOR (PPI) IN H. PYLORI ERADICATION THERAPY**

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**Introduction:** PPI-based therapy is one of the most popular H. pylori eradication therapies. However, first-line PPI-based therapy is decreasing in Japan, because H. pylori acquired resistance to antibiotics. It is known that most antibiotics are not effective under strong acid secretion. So in order to improve the eradication rate, gastric acid secretion must be reduced more rapidly and strongly.

Vonoprazan is newly developed potassium competitive acid blocker (P-CAB) and more effective in reducing gastric acid secretion than PPI. Therefore, the selection of a PPI-based therapy should receive eradication treatment. Therefore, the selection of a PPI-based therapy in human stool specimens.

**Disclosure:** Nothing to disclose

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**P1204 EFFICACIES OF DIFFERENT PROTON PUMP INHIBITOR-BASED 14-DAY BISMUTH-CONTAINING QUADRUPELM REGIMENS FOR THE INITIAL ERADICATION OF HELICOBACTER PYLORI IN THE SOUTHEAST COASTAL REGION OF CHINA: AN OPEN-LABEL, RANDOMIZED CLINICAL TRIAL**

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**Introduction:** Helicobacter pylori (H. pylori) is reported to be associated with a range of gastrointestinal diseases such as gastritis, peptic ulcer, gastric cancer, and mucosa-associated lymphoid tissue lymphoma. Although the prevalence of H. pylori infection has decreased on a global scale, it remains a serious concern in China with a prevalence of 66% among rural populations and 47% among urban populations. The Kyoto global consensus report on China with a prevalence of 66% among rural populations and 47% among urban populations.

In the southeast coastal region of China, the eradication rate of H. pylori was 5.0% (8/159).

**Conclusion:** Vonoprazan-based regimen was superior to conventional PPI (Rabeprazole and Lansoprazole) in eradication rate of H. pylori. In addition, it was a safe regimen on the issue of adverse events.

**Disclosure:** Nothing to disclose

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**P1205 APPARENT INTRACELLULAR HELICOBACTER PYLORI DETECTION BY IMMUNOHISTOCHEMISTRY AS INDEPENDENT RISK FACTOR FOR FAILURE OF FIRST-LINE ERADICATION THERAPY**

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**Introduction:** Helicobacter (H.) pylori is considered as an extracellularly living bacterium; however, the microorganism can also be found in cells of parietal and chief cells. Using immunohistochemical staining we have been able to observe that the detection of apparent intracellular Helicobacter pylori (aiHp) has been associated with reduced eradication rates after antimicrobial therapy.

**Aims and Methods:** Considering antimicrobial resistance, we aimed to investigate the impact of aiHp detection on the success rate of the first-line eradication therapy.

**Results:** Overall eradication rate was 78.8% by eHp versus 46.2% by aiHp. In patients with aiHp occurrence were naïve to treatment and have received antimicrobial therapy consisting of amoxicillin and furazolidone in the southeast coastal region of China were 0.1%. Furthermore, as a component of BQ regimens, proton pump inhibitor (PPI) plays an important role in the eradication of H. pylori.

**Disclosure:** Nothing to disclose
to some antibiotic combinations, the data from the present study show that culture and antibiotic susceptibility testing were not systematically performed. Resistance data was available in 677 treatment-naive patients. Although resistance.

Resistance affected nearly all prescribed combinations (data shown in table). In patients previously treated with clarithromycin, the ITT efficacy in first-line therapy was 92% (95% CI 89–95%, 14 studies, I² = 63%). The incidence of AEs was 46% (95% CI 39–52%, 14 studies, I² = 75%). The incidence of AEs was 46% (95% CI 39–52%, 14 studies, I² = 75%), and mostly mild.

Conclusion: Treatment with Single-Capsule Bismuth Quadruple Therapy for 10 days represents a highly effective option (≥ 90%) in first and second-line, regardless of the type and dose of PPI, even in patients with clarithromycin or metronidazole resistant strains or in those who were previously treated with clarithromycin.

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayoly.

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Introduction: Single-capsule bismuth quadruple therapy (scBQT) plus a proton pump inhibitor (PPI) has been proposed as first alternative and rescue therapy for the eradication of Helicobacter pylori.

Aims and Methods: To perform a meta-analysis evaluating the efficacy and safety of scBQT as any line of treatment. Studies were selected up to January 2018. Efficacy was estimated using the inverse variance method, and safety through the incidence rate of adverse events (AEs).

Results: In total, 20 studies (2,085 patients) were included in the analysis. Intention-to-treat (ITT) efficacy was 92% (95% CI = 89–95%, 14 studies, I² = 63%). The incidence of AEs was 46% (95% CI = 36–56%, 16 studies, I² = 90%), and mostly mild.

Conclusion: Treatment with Single-Capsule Bismuth Quadruple Therapy for 10 days represents a highly effective option (≥ 90%) in first and second-line, regardless of the type and dose of PPI, even in patients with clarithromycin or metronidazole resistant strains or in those who were previously treated with clarithromycin.

Disclosure: Dr. Gisbert has served as a speaker, a consultant and advisory member for or has received research funding from Almirall, Nycomed, AstraZeneca, Casen Recordati, Mayoly and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions. Dr. Nyssen has no conflict of interests.
Results: So far, 21,302 patients from 27 European countries have been evaluated. Of 1,231, 1,230 have been treated with single capsule bismuth quadruple therapy, of which 1,231 have finished follow-up. Of them, 1,148 have been prescribed the following the technical sheet (10 days, 3 capsules q.d.) Average age was 52 years, 66% were women, and 18% had peptic ulcer. Results are shown in the Table. The majority of cases (70.4%) were naive to H. pylori treatment. PPI type or dose did not influence eradication rate. 33% of cases suffered from adverse events (severe in 3%, and only 1% withdrew treatment due to adverse events). Only two serious adverse events were reported: hospitalization due to diarrhea and an allergic reaction treated with anti-histamine drugs, both solved without complications.

Table 1

<table>
<thead>
<tr>
<th>First-line (naive)</th>
<th>Second-line</th>
<th>Third-line</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ITT PP</td>
<td>Compliance</td>
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<td>N %</td>
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<tr>
<td>610</td>
<td>666 92</td>
<td>602 633 96</td>
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<tr>
<td>243</td>
<td>273 89</td>
<td>240 720 96</td>
</tr>
<tr>
<td>124</td>
<td>151 82</td>
<td>120 842 95</td>
</tr>
</tbody>
</table>

ITT: intention-to-treat; PP: per-protocol.

Conclusion: Treatment with single capsule bismuth quadruple therapy achieves H. pylori eradication in approximately 90% of patients by intention-to-treat in clinical practice, both in first- and second-line, with a favorable safety profile. Disclosure: Dr. Giëbert has served as a speaker, a consultant and advisory member for BMS, and has received research funding from AstraZeneca, Cassen Recordati, Mayol and Allergan. Dr. McNicholl has received retribution from Allergan and MSD for formative actions and is an advisor of Mayol.

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Introduction: With the increasing antibiotic resistance to Helicobacter pylori (H. pylori) worldwide, traditional triple therapies have become increasingly ineffective, with some studies reporting eradication rates as low as 50%. High antibiotic resistance is one of the most important reasons. Selecting optimal therapies for antibiotic-resistant H. pylori infection has become an important global public health task. Compared to high rates of resistance observed with clarithromycin, metronidazole, and levofloxacin, H. pylori to furazolidone remains low in China. Although a number of studies with limited sample size demonstrate high efficacy of furazolidone, amoxicillin-based quadruple therapy (FABQT) for treatment of H. pylori, data on the impact of adverse events are not well described. Predictors of failed H. pylori eradication other than the choice of regimen or poor medication adherence are largely unknown. Therefore, we performed a retrospective study of patients who received FABQT for treatment of H. pylori at our center.

Aims and Methods: The aim of the study is to evaluate the outcome of furazolidone-based quadruple therapy for treatment of H. pylori and identify predictors of failed eradication. Patients with H. pylori infection treated with furazolidone, amoxicillin, bismuth, and proton pump inhibitor therapy (from January 2015 to December 2015 in Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China) and received 3 weeks or less of therapy were included. H. pylori eradication was defined as absence of infection according to endoscopy and medical adherence were evaluated. Intention-to-treat (ITT) and per-protocol (PP) analyses were used to assess the H. pylori eradication rates. Categorical variables were compared using the ch^2 test or Fisher's exact student t-test. Univariate and multivariate analysis were performed to identify predictors of failed H. pylori eradication.

Results: Of the 992 patients treated and retested for H. pylori, the overall eradication rates were 95% (95%CI 94–96%) by intention-to-treat (ITT) and 95% (95%CI 94–97%) by per protocol (PP) analyses. H. pylori eradication rates as primary therapy were 95% (95% CI 94–97%) and 96% (95% CI 94–97%) by intention-to-treat and per protocol analyses, respectively. As rescue therapy were 91% (95% CI 87–96%) and 91% (95% CI 86–96%) per ITT and PP analyses, respectively. Among the 859 patients who completed the study protocol, 144 (17%) reported treatment-related adverse events including 24 (3%) leading to premature discontinuation of therapy. In the multivariate analysis, poor medication adherence (AOR = 6.7, 95%CI 2.8-15.8), > 2 previous H. pylori treatments (AOR = 7.4, 95%CI 2.2-24.9), alcohol consumption during therapy (AOR = 4.4, 95%CI 1.5-12.3), and possibly smoking during therapy (AOR = 1.9, 95%CI 0.9-4.3) were associated with failed H. pylori eradication.

Age, gender, education level, PPI type, bismuth dose, therapy duration, and the indication for treatment were not associated with failed H. pylori eradication.
Conclusion: Furazolidone-ampicillin quadruple therapy in high clarithromycin-resistant areas and H. pylori demonstrated high eradication rates as primary and rescue therapy with a favorable safety profile. Patient education targeting complete abstinence from alcohol and improved medication adherence may further optimize H. pylori eradication.

Disclosure: Nothing to disclose

P1210 CONCOMITANT VERSUS SEQUENTIAL THERAPY FOR THE TREATMENT OF HELICOBACTER PYLORI INFECTION: A TUNISIAN RANDOMIZED PROSPECTIVE STUDY

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Introduction: The objective of this study is to compare, in Tunisia, a region with 15% mean local resistance to clarithromycin, the efficacy rates of the concomitant versus the sequential H. pylori eradication therapy.

Aims and Methods: Our prospective randomized study included 152 patients with newly diagnosed H. pylori infection, randomized to receive a 10-day concomitant or sequential therapy. Treatment outcome was assessed by histopathological examination at least 6 weeks after therapy. Only patients per protocol (PP) (n = 106) were analyzed for eradication rates. Secondary end points included patient compliance and safety.

Results: The concomitant therapy group achieved statistically significant higher eradication rates when compared with the sequential treatment group in the PP analysis (49.1% versus 32.7%, p = 0.001), after adjusting for age, gender, the presence or not of ulcer and/or non-ulcer dyspepsia. Both groups displayed moderate compliance (71.4%, 95% CI 70.0%-100% vs. 75.4%, 95% CI 98%-100% with concomitant). Regarding treatment safety, major adverse events that led to the discontinuation of both regimens were few, with no statistical difference between the two groups (36.8% for the concomitant therapy group and 36.6% for the sequential therapy group). However, diarrhea, dizziness, headache and anaorexia were related with concomitant therapy with statistical significance (p = 0.03, 0.002, 0.000, 0.002, respectively).

Conclusion: Concomitant therapy led to statistically significant higher eradication rates when compared to sequential therapy with moderate compliance and an acceptable safety profile. The 10-day quadruple concomitant scheme should be adopted for first-line H. pylori eradication in Tunisia.

Disclosure: Nothing to disclose

P1211 SINGLE-CAPSULE BISMUTH-BASED QUADRUPLE THERAPY AS SECOND-LINE OR SALVAGE TREATMENT FOR HELICOBACTER PYLORI INFECTION: A NEW WINDOW OF OPPORTUNITY IN A SOUTH-EUROPEAN COUNTRY?

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Introduction: Helicobacter pylori (H. pylori) infection is highly prevalent in Portugal, with very low eradication rates. A new capsule-based quadruple treatment became recently available. This study aims to determine whether this quadruple regimen is useful as a second-line or salvage therapy.

Aims and Methods: This was a multicentric, retrospective study, with most patients included in a prospective database but without any direct intervention of the investigation team before or during treatment. All consecutive patients that were treated with bismuth-based quadruple therapy as second-line or salvage treatment between July-2017 and February-2018 were enrolled. Their medical records, review and clinical and laboratory parameters, as well as data on treatment efficacy and adverse events were retrieved. Patients were also contacted by telephone after treatment in order to confirm compliance (considered as adequate when at least 90% of prescribed medication was taken), adverse events and global satisfaction with this specific therapy.

Results: A total of 73 subjects were included (female – 74%; mean age – 56.3 ± 13.6 years). Patients had previously completed a mean of 2 eradication schemes (1 to 5): triple clarithromycin-based – 45.2%; sequential – 28.3%; concomitant – 17.8%; fluoroquinolone-based – 16.4%; rifabutine-based – 2.7%. The proton pump inhibitor of choice was esomeprazole (32.9%), followed by omeprazole (31.5%). Compliance was achieved in 87.7% and the overall eradication rate was 87.7% (95% confidence interval: 78.9–93.9). Treatment-related adverse effects were experienced by 22 patients (30.1%), being mild in 8, moderate in 6 and severe in 8. In the main drawbacks of the treatment in the patient’s perspective were its’ high price (26%) and the adverse effects (17.8%). Failure to eradicate H. pylori was correlated with the following: previous rifabutine-base scheme (28.6% vs. 0%) and higher number of previous treatment regimens (2.6 ± 1.2 vs. 1.7 ± 0.7).

Conclusion: In this South-European country a single capsule bismuth-based quadruple therapy is an excellent alternative in patients who have failed previous eradication schemes, with acceptable compliance and side effects.

Disclosure: Nothing to disclose

P1212 HIGH-DOSE CLARITHROMYCIN WITH P-CAB PLUS AMOXICILLIN TRIPLE THERAPY REGIMEN IS MOST RECOMMENDED ON 1ST HPYLORI ERADICATION REGIMEN: A MULTICENTER CORPECTIVE CASE STUDY

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Introduction: It has been believed that drug resistance is the most important cause that lead to failure to eradicate Helicobacter pylori (Hp). In Japan, Hp 1st eradication therapy, most of reports said that the success rate of eradication therapy about 70% regardless of CLR dose (400 or 800 mg/day) in Japan. Recently the ratio of CLR resistance in Japan comes up to over 30 %, we need to overcome CLR resistance on Hp eradication. On the other hand, recently it is considered that the stability of continuous gastric acid suppression is more important factor rather than CLR resistance. At the point of gastric acid suppression, we have been used so high acid suppressive drug P-CAB (Potassium-Competitive Acid Blocker) rather than conventional PPIs. Since Feb. 2015, we have used P-CAB instead of previous PPIs in AMX and CLR based Hp eradication therapy to improve success rate of eradication.

Aims and Methods: The aim of this study is to elucidate the importance of CLR dose on success rate of P-CAB-VPZ-based triple therapy regimens. AMX plus P-CAB was used in a multicenter center (8 hospitals), prospective case study from Jan. 2012 to Jan. 2018. A total of 3,471 patients (Hp positive) were enrolled. Mean age of the patients was 52.1 years old. Fisher’s exact test was used in all statistical analyses. Regimen of VAC (400 or 800) was VPZ (40 mg/day) b.i.d., AMX (1,500 mg/day) b.i.d. plus CLR (400 or 800 mg/day) b.i.d. for 7 days. The judgement of success or failure on the eradication therapy had been done with urea breath test on 3 months after eradication therapy to avoid false negative results. We compared which is better CLR 400 or 800 mg/day on P-CAB-based triple therapy regimen and checked their adverse events.

Results: The average success rate of VAC regimens was 91.0 % (3,032/ 3,332 = 91.0%, PPS). Success rate of VAC 800 showed significantly high (1,303/1,371 = 95.7%, PPS) rather than VAC 400 (1,762/2,001 = 88.1%, PPS) (p < 0.001). It was noteworthy that the average success rate of VAC 800 regimens (238/251 = 94.8 %) were significantly high rather than the average success rate of VAC 400 regimens (207/249 = 83.1%) (p < 0.001) on CLR resistance group. These results suggest that using high dose CLR with VPZ (P-CAB) plus AMX regimen is better on Hp eradication triple therapy regimen to overcome CLR resistance. Although its mechanism is unclear, the rapid and potent gastric acid-inhibitory effect of VPZ would provide a good environment for effective antibacterial action. VPZ has been available for Hp eradication since 2015, and the efficacy of first-line eradication therapy in Japan has dramatically improved.

Conclusion: High-dose CLR with P-CAB plus AMX triple therapy regimen is much better on Hp eradication therapy even if CLR resistance. We have been able to expect significantly high success rate (more than 97 %) as Hp 1st eradication therapy. This regimen is most recommended on 1st eradication regimen.

Disclosure: Nothing to disclose

P1213 THE HELICOBACTER ERADICATION ASPIRIN TRIAL (HEAT): RECRUITMENT AND DEMOGRAPHICS OF THE RANDOMISED PATIENT POPULATION

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Disclosure: Nothing to disclose
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Introduction: The Helicobacter Eradication Aspirin Trial (HEAT) is a multicentre, double blind, randomised controlled trial investigating whether Helicobacter pylori eradication reduces the incidence of hospitalisation for peptic ulcer bleeding (1). Participants are subjects aged over 60, taking low dose aspirin for at least 1 year at recruitment; all participants were recruited from primary care. H. pylori positive participants were randomised to receive one week active trial treatment (lansoprazole 30mg, clarithromycin 500mg and metronidazole 400mg twice daily) or placebo. Recruitment to the trial started in 2012 and closed in 2017; follow-up is endpoint driven and is ongoing.

Aims and Methods: Participants are followed up using a bespoke web-based trial management system that communicates directly with HEAT Toolkit software downloaded at participating GP practices, which issues MIQUEST (2) queries screening for follow-up. The primary endpoint of the study is the rate of hospitalisation due to definite or probable peptic ulcer bleeding. The study will end when 87 adjudicated events have occurred. Events are tracked by accumulating information from MIQUEST searches of GP databases via the HEAT toolkit, patient contact, review of national secondary care admission and mortality data.

Results: HEAT is being conducted in practices across the whole of the UK with 188,428 invitation letters sent from 1,260 practices. A total of 37,247 positive response were received, representing a 20% response rate. Of those, 30,025 patients were consented to the study of whom 5,356 H. pylori positive patients were randomised. The percent of H. pylori positive patients varied from 13% to 39% throughout the country. Multiple deprivation scores applied to the data indicated an increase in response with less deprivation, but a decrease in the number of randomised patients. The mean age at randomisation for all participants was 73.6 ± 7.0 (SD) years, and 47% of participants are male. Only 7.2% of participants are smokers although 52.9% are ex-smokers. A total of 15% of the randomised patients have withdrawn from the trial, and 100 patients have died so far.

Conclusion: The trial methodology has shown that recruitment of large numbers of participants in primary care is achievable, with the assistance of the NIH Clinical Research Network, and could be applied to other outcomes studies at relatively low cost.

Discourse: Nothing to disclose

References

Tuesday, October 23, 2018
09:00-17:00

P1214 IMBALANCE OF TREG/TH17 IN RAT NSAID-INDUCED INTESTINAL INJURY
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Introduction: Non-steroidal anti-inflammatory drugs (NSAIDs) are some of the most commonly prescribed drugs in the world. However, recently its gastrointestinal (GI) adverse effect is more and more concerns of the public and scientific community, especially extensive injury has attracted people's attention. The pathogenesis of it is not yet clear, therefore there is no effective treatment measures. Treg/Th17 have been described as two distinct subsets from Th1 and Th2 character. Although Treg/Th17 have the opposite effects on autoimmunity, Treg/Th17 balance is essential for maintaining GI health. Proinflammatory and Th17 cells and CD25+Foxp3+ T cells both significantly increased in the experimental groups (P<0.05). However the ratio of CD4+/CD8+Treg/Th17-1 cells decreased significantly in the experimental group (P<0.05). 3. The specific transcription factor RORγt of Th17 and Foxp3 of Treg. The expression of RORγt-mRNA significantly increased (P<0.01), and the Foxp3-mRNA expression level also increased, although it was not statistically significant (P>0.05), while the ratio of Foxp3/RORγt decreased (P>0.05). 4. The IL-6 and IL-17A levels in the experimental group increased significantly (P<0.05), while the IL-10 expression was significantly decreased (P<0.05), although the TGF-β1 expression was decreased, it was not statistically significant (P>0.05). 5. Pearson correlation analysis: The injury scores has a significant negative correlation with Treg/Th17, Foxp3/RORγt, IL-10, TGF-β1 (P < 0.05), and has a significant positive correlation with IL-6, IL-17A (P < 0.05).

Conclusion: There is an imbalance of Treg/Th17 in NSAID induced intestine injury, immune imbalance may be involved in the pathogenesis of NSAID induced intestinal injury.

Disclosure: Nothing to disclose

P1215 TERMINAL ILEITIS: WHEN IS IT NOT CROHN'S DISEASE?
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Introduction: Terminal ileitis (TIS) is defined as inflammation of the terminal ileum (TI) signified by ulcers, erosions, oedematous/erythematous mucosa. It can be idiopathic or secondary to crohn’s disease (CD), infections and medications. The aim of this study was to assess the outcome of patients with idiopathic terminal ileitis (ITI).

Aims and Methods: Patients with TIS and no history of CD (ITI group) were compared to patients with terminal ileum Crohn’s disease (TICD). Patients with a recent history of gastroenteritis, NSAIDs and antibiotics receptor blockers use were excluded.

Results: 23 patients with TIS (mean age 39 years; 57% females) were compared to 27 patients with TICD (mean age 39 years; 59% females). The number of small bowel capsules examinations (SBCE) in the ITI group included: abdominal pain (52%), bloating, nausea, vomiting (48%), diarrhoea (39%), persistent iron deficiency anaemia (22%), weight loss (4%), rectal bleeding (4%), low b12 and calcium (4%). All patients in the CD group had a SBCE to assess disease activity.

In patients with TIS, 17% had evidence of minor findings on colonoscopy including erosions/apathous ulcers with histology showing non-specific inflammation in 7% (n = 4 50%). In tandem, all patients with ITI (5) who underwent small bowel (SB) MRI had a normal investigation compared to the TICD group in whom MRI SB was abnormal in 75%.

Similarly the mean faecal calprotectin (FC) (160 ± 99 ug g⁻¹ p = 0.071) and CRP (13 vs 7 mg L⁻¹ p = 0.098) were higher in the TICD group compared to the ITI group, although these did not reach statistical significance.

The mean number of ulcers on (SBCE) in TI were significantly less in the ITI group (3) than those with TICD (5) (p < 0.005). There was luminal narrowing in 2 patients (7%; p = 0.493) and mucosal oedema in 10 patients with TICD (37%; p = 0.001) with CD. Whereas patients with ITI had more apathous/ small ulcers, patients with TICD had more circumferential, deep, large, linear ulcerations.

Follow-up data with an average of 9 month was available for 78% (18) of the ITI group, 80% of those who underwent a repeat SBCE showed an improvement in the findings which corresponded to an improvement in CRP (3 previously 7mg L⁻¹ to 3mg L⁻¹ (p < 0.018). At follow-up 39% improved clinically without treatment whilst 33% were treated as IB. One patient who was treated with budesonide, improved.

Conclusion: Patients with ITI demonstrated a lower CRP, FC, and a normal MRI. SBCE findings for the ITI group were milder compared to TICD group and they were more likely to improve over time without treatment. Milder findings on SBCE can further reassure physicians to treat patients with a small number of ulcers in TI conservatively.

Disclosure: Nothing to disclose
P1216  **H. PYLORI INFECTION MAY INDUCE SMALL INTESTINAL MUCOSAL BREAKS:**

**Aims and Methods:** This study was a retrospective study at the Nippon Medical School Hospital from January 2008 through March 2016. Patients aged 20-85 years were selected from a general pool of subjects who underwent capsule endoscopy for current or past obscure gastrointestinal bleeding. The background included age, gender, history, treatment with NSAIDs and/or acid suppressant (PPI, or histamine H2-receptor antagonist), final diagnosis, and whether *H. pylori* infection had a positive result by at least one diagnostic method: the serum antibody to *H. pylori*, 13C-Urea breath test, or *H. pylori* antigenic agent of the stool within before and after 30 days capsule endoscopy examination. Patients diagnosed with inflammatory disease, malignancy, or other conditions were excluded. All subjects' videos were re-evaluated by two skilled reviewers to count small intestinal mucosal breaks. Eligible analyzable patient variables were compared between patients infected with *H. pylori* and uninfected patients.

**Results:** Ninety-two patients (30 infected *H. pylori*/62 uninfected) were eligible for the study. By multivariate analysis of variables regarding the number of small intestinal mucosal breaks, patients treated with NSAIDs had more small-intestinal mucosal breaks than patients untreated NSAIDs (38%/8.21 vs. 18%/13.71P = 0.009, and the possible association was detected between patients infected *H. pylori* and infected patients 67%/14.21 vs. 37%/26.71; (P = 0.056). In comparing between patients infected *H. pylori* and uninfected patients, the rate of patients with small intestinal mucosal breaks was greater in patients infected *H. pylori* (7%/13.40 vs. 1%/7.62; P = 0.01). After excluding the patients treated with NSAIDs, the number of small intestinal mucosal breaks was also statistically greater in patients infected *H. pylori* than in uninfected patients (1.16 ± 1.51 vs. 0.38 ± 0.62; P = 0.001).

**Conclusion:** There is a high possibility that *H. pylori* infection induces small intestinal mucosal injury.

**Disclosure:** Nothing to disclose

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References:


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P1217  **EVIDENCE FOR IMMUNE FUNCTION IN ACTUAL DISPEPSIA AND THE IRRITABLE BOWEL SYNDROME: A SYSTEMATIC REVIEW**

**Introduction:** **Functional dyspepsia (FD) and the irritable bowel syndrome (IBS) are functional gastrointestinal disorders (FGIDs), for which there are no explicit pathological changes identified on routine endoscopy. There is evidence in the literature of a dysregulated gastrointestinal immune response potentially driving the onset and continuation of symptoms such as early satiety, bloating, abdominal pain and nausea in FD and IBS, however the mechanisms by which this occurs has not been fully characterised.**

**Aims and Methods:** We systematically reviewed the FD and IBS literature in order to collate the evidence for immune activation in common FGIDs. Our review focused on answering the research question: “Do IBS and FD have clinically definable immune profiles?” We aspired to elucidate the cell types and associated molecules that may be implicated in the subtle inflammatory phenotype observed in these conditions. A search of seven literature databases was conducted using the following keywords and phrases: ‘immun*’, ‘functional gastrointestinal disorder’, FGID, ‘functional dyspepsia’, ‘non-ulcer dyspepsia’, ‘idiopathic dyspepsia’, ‘irritable bowel syndrome’, and IBS. References were then screened for suitability based on defined inclusion and exclusion criteria. Data presented relating to immune effectors such as cytokines and cellular populations were collated for analysis.

**Results:** The 51 papers determined to meet stringent selection criteria for this review provided evidence of specific alterations in the systemic and local immune systems in both FD and IBS. In addition to duodenal eosinophilia (FD) and increased colonic mast cells (IBS), variations in circulating IL-6 and IL-10 cytokine activity, along with increases in circulating α4β7 gut-homing T cell numbers and faecal IL-17 have been observed in both conditions. There seems to be no change in the proportion of either circulating or local CD3+ lymphocyte numbers in either condition. Patients with FD have higher peripheral proportions of both activated (CD45RO+) and naive (CD45RA+) T lymphocytes, however there is debate in the literature regarding the proportions of small intestinal mast cells in this condition suggesting disease heterogeneity. There was evidence for a peripheral B cell activation in IBS patients, with studies reporting increased expression of activation markers (CD80*, CD69*) and higher IgG expression, suggestive of antigen presentation and reaction. Further to this, increased numbers of activated T lymphocytes (CD45RO+*) were reported in the colon of IBS patients.

**Conclusion:** Evidence from the literature suggests that underlying immune activity in FD and IBS is likely related to subtle alterations in the activation status of the cellular populations at both the systemic and local level, rather than an influx of newly recruited cells. Heterogeneity among subgroups of patients with either FD or IBS complicate studies in the field. It is evident that well-characterised patient cohorts including sufficient participant numbers will be required to elucidate the interplay of immune mechanisms that drive the development of FGIDs.

**Disclosure:** Nothing to disclose

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References:


P1219 BREATH TESTS FOR SMALL INTESTINAL BACTERIAL OVERGROWTH DIAGNOSIS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Small intestinal bacterial overgrowth (SIBO) is a syndrome characterized by increased colonization of the small bowel by colonic bacteria. Despite jejunal culture remains the diagnostic mainstay, in clinical practice the diagnosis is achieved by glucose breath test (GBT) or lactulose breath test (LTB). Therefore we performed a meta-analysis to estimate pooled sensitivity and specificity of breath tests for SIBO diagnosis.

Aims and Methods: We searched in main databases (PubMed, Scopus, ScienceDirect, EMBASE) articles using the following keywords: (Small intestinal OR bacterial overgrowth) AND (breath test OR diagnosis OR lactulose OR glucose). Only studies in which breath tests were compared to culture of jejunal aspirate were selected. Data were entered the MetaDisc 1.4 software to calculate pooled sensitivity, specificity, positive and negative likelihood ratio (LR) and summary of area under the curve (SROC), as well as their 95% confidence intervals (CI).

Results: Twelve studies, enrolling 630 patients overall were selected. GBT showed a pooled sensitivity of 58.3% (95% CI 51.4–64.9%), a specificity of 83.5% (95% CI 79.1–87.2%), a positive LR of 2.7 (95% CI 1.6–4.7), a negative LR of 0.5 (95% CI 0.4–0.8) and a SROC of 0.76. LTB had a sensitivity of 70.6% (95% CI 61.6–78.4%), a positive LR of 1.3 (95% CI 0.7–2.2), a negative LR of 0.8 (95% CI 0.6–1.1) and a SROC of 0.56.

Conclusion: Breath tests do not show excellent performances in comparison to the gold standard. However, keeping into account that SIBO is a benign disease that in most cases requires a simple antibiotic therapy, they can be considered as a surrogate test to replace the invasive one. In this context, GBT has a better sensitivity and specificity than LTB and, therefore, should be preferred.

Disclosure: Nothing to disclose

References

P1220 THE CHANGING AND CHALLENGING FACE OF PROTON PUMP INHIBITOR-RELATED SMALL INTESTINAL BACTERIAL OVERGROWTH

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Introduction: In the last decade the relationship between proton pump inhibitors (PPI) and small intestinal bacterial overgrowth (SIBO) has covered an extensive, controversial interest in the literature, with meta-analysis confirming this association (1,2).

Aims and Methods: To update, in our experience, this phenomenon from a temporal point of view, comparing two periods: 2005–2010 vs 2012–2017. This dichotomy was chosen based on an increased interest on this issue in the literature from 2010 on.

Methods: From November 2012 to November 2017, 970 consecutive out-patients eligible for the study. 458 were eligible for Hydrogen Breath test for SIBO diagnosis (GHBT) (388 on PPI, 70 pts off PPI for at least 5 years: 50 IBS, 20 ST, 12 PCD patients). The use patterns from 2010 on.

Results: Mean age and gender distribution in the group A, B and C were comparable (46±18 SD, 39±20 ± 21 yrs; M: 55%, 57%, 59%). The use patterns of PPI in the 2 period were: *LcT MT 2005–10 79%, Not evaluated 21%

2012–17 25% 35% 40%. * P < 0.001

SIBO in group A e B was as follows: LcT MT ST IBS C

Group A 50% 19% 17% 18% 5%

Group B 68% 22% 14% 20% 5%

Conclusion: 1) LcT treatment has decreased significantly from 79% to 25%, leaving room to a MT (35%) and ST (40%) patterns of therapy.

2) Although the frequency of SIBO in LcT in group A remains high (50%), it involves only 25% of pts on PPI, practically “saving” those on MT and on ST modalities.

3) Informed medical culture, increased awareness of potential side-effects and financial restraints from Health Institutions may be the reasons for such changes.

Disclosure: Nothing to disclose

P1222 SCREENING FOR COELIAC DISEASE

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Introduction: Coeliac disease (CD) is a lifelong autoimmune disease affecting about 1% of the population, although many are undiagnosed. Coeliac disease is caused by an abnormal immune response, in genetically susceptible individuals, against gluten proteins from wheat, rye and barley. We screened for coeliac disease in a previous cross-sectional population-based study (1). In the current study we screened for coeliac disease antibodies in seven additional population-based studies from our biobank.

Aims and Methods: The aim was to determine coeliac disease prevalence, as reflected by coeliac disease antibody positivity, in the eight Danish studies included in the biobank at Center for Clinical Research and Disease Prevention and evaluate a possible change over time. The studies are listed in the table below. In total, we screened serum samples from 16.779 participants collected between 1976 and 2012 for tissue transglutaminase (TTG) IgA/IgG and deamidated gliadin peptide (DGP) IgG.

Results: The results of the screening are listed in the table below, both for the coeliac disease antibody positivity (IgA/IgG-TTG<7 U/ml and/or IgG-DGP<10 U/ml) and the additional cut-off of only TTG>10 U/ml.

Conclusion: The coeliac disease antibody positivity was around 1% in all the 8 studies. We found no marked changes of the prevalence over time.

Disclosure: Conflict of interest: The study was supported by the Tryg Foundation (7-11-0213), Dansk Coliak Forening (the Danish Celiac Disease Patient Organization) - The Nordic Insulin and Diabetes Foundation (NNH16001646), Independent Research Fund Denmark and Thermo Fisher Scientific, Allerod, Denmark. Thermo Fisher Scientific, performed the coeliac disease screening.

Reference
P1223 SERONEGATIVE COELIAC DISEASE: CLINICAL FEATURES AND PREVALENCE AMONG COELIAC PATIENTS

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Introduction: Seronegative coeliac disease (SCD) is characterized by villous atrophy (VA) in the absence of a gluten-free diet (GFD) but without both/either IgA/IgG endomysial (EMA) and IgA/IgG tissue-transglutaminase (tTG) antibodies [1]. The quality of data on the epidemiology of SCD is limited due to the rarity of the condition and the confusion pertaining to the nomenclature. Prevalence of SCD is increased in areas in which seropositive coeliac patients is believed to be common. We think that we should distinguish true SCD in which reasons for seronegativity include early disease, late disease (with possible refractory CD), dermatitis herpetiformis and first degree familiarity for CD. Masked SCD is a second group of patients which display seronegativity at diagnosis because immunosuppressants or a GFD had already been started prior to antibody testing. Finally, a third group is that of patients with total IgA deficiency (serum IgA ≤ 2 standard deviations below normal age-adjusted means) in whom the finding of positive IgG EMA/tTG should support the diagnosis of conventional seropositive CD and not that of SCD [1].

Aims and Methods: To define prevalence and clinical features of patients affected by true SCD, masked SCD and CD+IgA deficiency among all the coeliac patients directly diagnosed in two referral centers for CD (Sheffield, UK and Pavia, Italy) from 01/2010 to 12/2017. IgA positive EMA/tTG and a VA while on a gluten-containing diet allowed the diagnosis of conventional seropositive CD.

Results: 692 coeliac patients (229M, mean age at diagnosis 42 ± 17 years, 154 classical) were directly diagnosed in 7 years. 24 patients (4M, 47 ± 17 years, 17 classical) had negative IgA and/or IgG EMA/tTG at diagnosis (prevalence 3.47%). In this group true SCD was diagnosed in 17 of them (prev 17/692 = 2.45%, 2M, 50 ± 17 years, 12 classical). 5 had masked SCD (prev 5/692 = 0.72%, 1M, 40 ± 19 years, 3 classical, 4 on a GFD and 1 on steroids and azathioprine at time of diagnosis) and showed positive serology after discontinuation of immunosuppressants or a GFD. Finally, 2 patients (4M, 47 ± 17 years, 17 classical) aged at diagnosis was higher in true SCD than in the group of seropositive CD (p = 0.50) and masked SCD (p = 0.70), but not statistically significant.

Conclusion: We proposed a redefinition of the diagnostic categories of SCD. Our partial data show that true SCD is rare among coeliac patients, being this result in accordance with the high sensitivity of EMA/tTG. SCD is characterized by peculiar clinical features allowing the distinction from seropositive SCD. With the recruitment of a larger sample size we think we will be able to see if prevalence of this condition has changed over the years.

Disclosure: Nothing to disclose

References:

P1224 ADULT COELIAC DISEASE REMISSION ASSESSMENT: DOES A D1 BIOPSY INCREASE THE DETECTION OF VILLOUS ATROPHY?

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Introduction: The diagnosis of Coeliac disease (CD) requires the presence of villous atrophy (VA) in biopsies. The duodenal bulb (D1) has been shown to be a sensitive site for detecting villous atrophy (VA) in newly diagnosed CD. However there is a scarcity of data from those with established CD.

Aims and Methods: In patients with established CD, we aim to determine whether D1 biopsies improved the identification of VA compared to biopsies from the second part of the duodenum (D2) alone. 251 patients with established CD were prospectively recruited from the endoscopy department at the Royal Hallamshire Hospital between 2013 and 2017. All patients were undergoing repeat gastroscopy to assess dietary adherence, with one biopsy taken from D1 and four from D2. Biopsies were classified according to Marsh criteria. We assessed concordance of histology between the D1 and D2 sites, and 95% confidence intervals were calculated for all results using a binominal distribution.

Results: 251 patients were recruited (70.5% female, age range 17–81 years, median age 53 years) having been on a gluten-free diet for a median duration of 6 years. Concordant results: 35.1% (n = 85, 95% CI = 29.16–40.96) had normal duodenal biopsies in both D1 and D2; 32.5% (n = 81, 95% CI = 26.49–38.35) had VA in D1 and D2; 18.5% (n = 46, 95% CI = 13.54–23.11) had raised intra-epithelial lymphocytes (IELs) only in both D1 and D2. Disaccordant results: 4.4% (n = 11, 95% CI = 1.85–6.91) had VA in D1 but not D2; 2.4% (n = 6, 95% CI = 0.50–4.30) had raised IELs in D1 but normal histology in D2. 2.8% (n = 7, 95% CI = 0.75–4.83) had VA in D2 but normal histology in D1; 4.8% (n = 12, 95% CI = 2.14–7.42) had IELs in D2 but normal histology in D1.

Conclusion: VA was confined to the duodenal bulb in 4.4% of patients with established CD. Thus a D1 biopsy in addition to distal duodenal biopsies increases the likelihood of detecting VA, although the significance of isolated VA in the bulb in patients on a gluten-free diet is yet to be determined.

Disclosure: Nothing to disclose

References:
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P1225 EFFECTS OF BLINDED ACUTE AND SUB-ACUTE GLUTEN CHALLENGE ON EXTRA-INTESINAL AND GASTROINTESTINAL SYMPTOMS IN NON-COELIAC GLUTEN SENSITIVITY VERSUS HEALTHY CONTROLS

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Introduction: Non-coeliac gluten sensitivity (NCGS) is characterised by gastrointestinal (GI; e.g. bloating) and extra-intestinal (e.g. fatigue) symptoms that subjectively disappear after dietary exclusion of gluten, in the absence of coeliac disease. Previous research has shown that a 3-day exposure to gluten increases depression scores in self-reported NCGS patients, however acute effects of gluten were not investigated (Peters et al., 2014).

Aims and Methods: We aimed to investigate the effect of single-blind acute and sub-acute administration of 16g gluten on psychological and GI symptoms in healthy volunteers (HV) and NCGS patients.

Sixteen grams of gluten or whey protein (placebo) were mixed in 250mL of low fat, unsweetened yoghurt, which was consumed as an acute challenge. GI symptoms (bloating, cramps) were assessed using visual analogue scales (VAS;
100nm) every 15′ until 180′ after administration. At the same time points, extra-intestinal symptoms (fatigue, tension, depression) were assessed usingVAS derived from the Profile of Mood States Questionnaire. Participants then consumed two gluten-free or gluten containing (8g) muffins at different time points per day for the following 5 days, as a sub-acute challenge. GI symptoms (oral values obtained) and extra-intestinal symptoms (VAS) were scored for the end of each day. After a washout period of 2 weeks, participants crossed over to the alternative dietary arm. Responses over time (compared to pre-administration for the acute challenge and compared to the mean of the 2 days before the intervention) for the sub-acute challenge) were analysed using (generalized) linear mixed models.

Results: Twenty HV (3 men, 29.7±2.6 years) and 10 NCGS patients (4 men, 32.9±3.1 years) completed the study. After acute administration of gluten compared to placebo, fatigue scores increased in NCGS patients (p=0.015), but normally in HV (p=0.74). Similarly, NCGS patients had higher tension scores after gluten compared to placebo (p=0.043), contrary to HV (p=0.31). Acute challenge of gluten did not alter depression scores compared to placebo (p=0.41). After 5 days of sub-acute administration, no significant differences in fatigue or scores were observed between healthy controls and NCGS patients (p=0.70) nor between conditions (p=0.48), but tension and depression scores were higher in both groups after gluten compared to placebo (p=0.003 and 0.076, respectively).

Immediately following the acute challenge, NCGS patients showed increased fatigue (p<0.0001) and pain (p=0.019) compared to HV, regardless of whether gluten or placebo was ingested. This continued during the sub-acute challenge where GI symptoms increased in the NCGS patients compared to healthy controls (abdominal pain: p=0.038; bloating: p=0.015), regardless of gluten versus placebo intake.

Conclusion: These findings provide new insights into NCGS, which might be characterized by acute gluten-induced increases in extra-intestinal symptoms such as fatigue, rather than GI symptoms. During a sub-acute challenge, using dietary factors involved in symptom generation in NCGS is warranted.

Disclosure: Nothing to disclose

P1226 IS SEROLOGIC PREDICTIVE OF PERSISTING VILLOUS ATROPHY IN PATIENTS WITH ESTABLISHED COELIAC DISEASE?
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Introduction: Monitoring of mucosal remission is essential in Coeliac Disease (CD) to assess adherence in patients with persisting symptoms and to prevent complications. However, duodenal biopsies are invasive, expensive and poorly tolerated by many patients. Paediatric ESPGHAN guidelines support a diagnosis of CD when immunoglobulin-A anti-tissue transglutaminase (IgA tTG) antibody titres are greater than 10 times the ULN and EMA antibodies for predicting VA was 93.2% (95% CI 93–100%). A biopsy avoidance strategy may be implemented into adult gastroenterological practice.

Aims and Methods: The aim of this study was to assess whether an IgA tTG value of greater than 10 times the ULN could produce a 100% positive predictive value (PPV) for the detection of VA. We performed a prospective analysis of CD patients diagnosed in an university hospital. Symptoms of CD, VA on biopsy, IgA-endomysial (IgA-EMA) antibodies, IgT and Human Leucocyte Antigen (HLA) genotype were used for analysis. We then compared the tTG antibody level against small bowel histology.

Results: 443 CD patients (66.8% female, median age 41 years, range 15–84 years) were diagnosed between 2008 and 2016. 56.9% (n=252, 95% CI=52.12–61.53) had a tTG value of greater than 10 times the ULN, and 100% of these patients had VA on biopsy. 292 fulfilled ESPGHAN guidelines for features of malabsorption and of these, 157, weight loss =45 and anaemia =190. Of these symptomatic patients, 70.4% (n=179, 95% CI=64.86–76.08) had a tTG value 10×ULN. The proportion reaching the 10×tTG threshold was 55.4% (n=87, 95% CI=47.64–63.19) for diarrhoea, 60.0% (n=27, 95% CI=45.69–74.31) for weight loss, and 74.2% (n=141, 95% CI=67.99–80.43) for anaemia. Of the 151 patients who did not experience malabsorptive features, 49.0% met the 10×ULN tTG (n=74, 95% CI=41.03–56.98). The sensitivity of tTG antibodies and EMA antibodies for predicting VA was 93.2% (95% CI=90.89–95.57) and 90.7%, respectively (95% CI=88.05–93.44). Combined tTG and EMA was 98.6% (95% CI=97.67–99.72). All patients had compatible HLA typing, thereby failing to add any further diagnostic value.

Conclusion: An IgA tTG level of greater than 10 times the ULN had a PPV of 100% for predicting VA. Using this threshold, 56.9% of patients would have been correctly diagnosed with CD and avoided duodenal biopsy. Symptoms and HLA typing did not add any supportive information. This study provides evidence that a biopsy avoidance strategy may be implemented into adult gastroenterological practice.

Disclosure: Nothing to disclose

P1227 BIOPSY AVAIDANCE STRATEGY IN ADULT COELIAC DISEASE
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Introduction: Currently, the diagnosis of adult Coeliac disease (CD) requires the presence of villous atrophy (VA) on duodenal biopsy. However, biopsies are expensive, invasive and poorly tolerated by many patients. Paediatric ESPGHAN guidelines support a diagnosis of CD when immunoglobulin-A anti-tissue transglutaminase (IgA tTG) antibody titres are greater than 10 times the upper limit of normal (ULN) and combined with supportive criteria. This study examines whether serological testing alone could be sufficient for diagnosis in adult patients, thus avoiding the need for gastroscopy and duodenal biopsies.

Aims and Methods: The aim of this study was to assess whether an IgA tTG value of greater than 10 times the ULN could produce a 100% positive predictive value (PPV) for the detection of VA. We performed a prospective analysis of CD patients diagnosed in an university hospital. Symptoms of CD, VA on biopsy, IgA-endomysial (IgA-EMA) antibodies, IgT and Human Leucocyte Antigen (HLA) genotype were used for analysis. We then compared the tTG antibody level against small bowel histology.

Results: 443 CD patients (66.8% female, median age 41 years, range 15–84 years) were diagnosed between 2008 and 2016. 56.9% (n=252, 95% CI=52.12–61.53) had a tTG value of greater than 10 times the ULN, and 100% of these patients had VA on biopsy. 292 fulfilled ESPGHAN guidelines for features of malabsorption. Of these, 157, weight loss =45 and anaemia =190. Of these symptomatic patients, 70.4% (n=179, 95% CI=64.86–76.08) had a tTG value 10×ULN. The proportion reaching the 10×tTG threshold was 55.4% (n=87, 95% CI=47.64–63.19) for diarrhoea, 60.0% (n=27, 95% CI=45.69–74.31) for weight loss, and 74.2% (n=141, 95% CI=67.99–80.43) for anaemia. Of the 151 patients who did not experience malabsorptive features, 49.0% met the 10×ULN tTG (n=74, 95% CI=41.03–56.98). The sensitivity of tTG antibodies and EMA antibodies for predicting VA was 93.2% (95% CI=90.89–95.57) and 90.7%, respectively (95% CI=88.05–93.44). Combined tTG and EMA was 98.6% (95% CI=97.67–99.72). All patients had compatible HLA typing, thereby failing to add any further diagnostic value.

Conclusion: An IgA tTG level of greater than 10 times the ULN had a PPV of 100% for predicting VA. Using this threshold, 56.9% of patients would have been correctly diagnosed with CD and avoided duodenal biopsy. Symptoms and HLA typing did not add any supportive information. This study provides evidence that a biopsy avoidance strategy may be implemented into adult gastroenterological practice.

Disclosure: Nothing to disclose

(continued)
P1228 HUMAN LEUCOCYTE ANTIGENS COELIAC HAPLOTYPES: FROM GENETIC FACTORS TO IMMUNOLOGIC APPROPRIATE FOR WEIGHT LOSS: THE FIRST HUMAN CASE REPORT

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Introduction: Celiac disease (CD) is an autoimmune enteropathy caused by gluten intolerance and is associated with the number of copies of DQB1*02. Mean age at diagnosis was significantly higher among patients in the low-risk group compared to those in the high-risk group (46.83 ± 7.93 versus 37.72 ± 12.39, P = 0.004). Disease severity (at least 10-pound weight loss and diarrhea) was found to be associated with high risk haplotypes, and the number of DQB1*02 copies.

Aims and Methods: A total of 75 patients established CD, tested for IgT antibodies at diagnosis, were typed for HLA- DQA1, and -DQB1 genes, and divided according to the number of DQB1*02 alleles: group 1, homzygous; group 2, heterozygous; group 3, no gene.

Results: We report that the mean of IgT antibody indexes was not significantly different in group 1 patients than in group 2 (118.90 ± 93.98 versus 142.45 ± 100.24, P = 0.529), or group 3 patients (90.74 ± 91.87 versus 142.45 ± 100.24, P = 0.221). Nonetheless, patients in group 1 showed more severe histological lesions (Marsh 3a,b) compared to those in the other groups. When assessing disease phenotype, the carriage of 2 copies was associated with the presence of anemia, abdominal pain, weight loss, and chronic diarrhea.

Conclusion: The study demonstrates that IgT titers are not significantly influenced by the number of HLA-DQB1*02 copies. Moreover, individuals with at least 1 HLA-DQB1*02 allele tend to have a higher degree of histological damage and different clinical features compared to those carrying other alleles.

Disclosure: Nothing to disclose.

P1219 PERSISTENT VILLOUS ATROPHY AMONG ADULT CELIAC DISEASE PATIENTS ON A GLUTEN-FREE DIET: IS THERE A ROLE FOR SEROLOGY?

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Introduction: Tissue transglutaminase (tTG) antibodies are hallmarks of CD diagnosis. The aim of our study was to assess whether serum IgA-tTG tests are useful to detect villous atrophy in patients with CD treated with gluten free diet (GFD).

Aims and Methods: We performed a prospective study using the information entered into a structured database including adult patients diagnosed with CD hospitalized at the Institute of Gastroenterology and Hepatology, adherent to GFD for at least 12 months after diagnosis. Data from adult patients with CD (diagnosed between January 10, 2010 through December 10, 2015) with biopsy, and tTG-IgA and tTG-IgG antibodies were retrieved from a computerized database. Results of non-invasive tests were compared with the persistence of villous atrophy on follow-up biopsy.

Results: The study group included 81 adult patients with a female: male ratio of 3:1, mean age 40.02 ± 12.14 years. When assessing the serological parameters, IgA-tTG levels (61.45 ± 76.45 u/mL vs 162.02 ± 106.17 u/mL, P = 0.001) correlated with intestinal villous atrophy (Marsh 1–2 vs Marsh 3a-c) in CD patients, with a sensitivity of 82.8% and a specificity of 91.78% for mucosal atrophy upon diagnosis (AUC = 0.99, IC95%: 0.96–0.95). Follow-up biopsy and serology testing were available for 47 (74.6%) treated patients. Twenty-one patients had variable degrees of villous atrophy, and IgA-tTG assay was 51% sensitive and 67.3% specific in identifying Marsh 3 lesions among patients allegedly adherent to GFD with normal IgA-tTG levels.

Conclusion: Increased IgA-tTG levels in the treated population may reflect quantity and frequency of gluten exposure. The diagnostic accuracy of IgA-tTG antibodies for detecting persistent villous atrophy on a GFD is limited, showing relatively high specificity, but low sensitivity. Consequently, the majority of patients with villous atrophy on a GFD had normal levels of IgA-tTG.

Disclosure: Nothing to disclose.

P1230 HLA TYPING AND CELIAC DISEASE IN ROMANIANS

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Introduction: Celiac disease (CD) is considered to have a high heritability involving HLA genes, which provide the genetic risk to develop the disease. The aim of the study was to investigate whether the genetic profile influences age of onset and diagnosis in CD.

Aims and Methods: High-resolution class 2 HLA genotyping was performed in a sample (n = 75) of North-Eastern Romanian residents resident with CD to determine the contribution of DQA1 and DQB1 on the age of diagnosis. The complete inpatient and outpatient medical record of each candidate were carefully reviewed. Age of onset is the age at which the patient first complained of symptoms subsequently explained by CD. Age at diagnosis was established as the date of interpretation of the initial intestinal biopsy or positive serology. Depending on the heterodimers inherited, 3 study groups were identified and compared: high risk (DQ2.5/DQ2.5, DQ2.5/DQ2.2, DQ2.5/DQ8, DQ8/DQ8), moderate risk (DQ2.5/X, DQ2.5/X, DQ8/X, DQ2.2/DQ2.2), and low risk (DQ7/X, DQ7/DQ7, DQ7/DX).

Results: A total of 32 (42.6%) patients had high-risk heterodimers. The age at diagnosis and the age of onset of patient symptoms attributable to CD were significantly lower in high-risk patients compared to moderate and low-risk patients. Nevertheless, patients in group 1 showed more severe histological lesions (Marsh 3a,b) compared to those in the other groups.

Conclusion: Both HLA- DQA1*05 and DQB1*02 alleles are associated with earlier disease onset, diagnosis and disease severity.

Disclosure: Nothing to disclose.

P1231 USEFULNESS OF DOUBLE-BALLOON ENTEROSCOPY FOR DIAGNOSIS OF MCKEEL’S DIVERTICULUM

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Introduction: Meckel’s diverticulum (MD) is a congenital malformation of the gastrointestinal tract. The number of reports of MD observed by balloon assisted enteroscopy is increasing since the development of the double-balloon enteroscopy (DBE) and single-balloon enteroscopy. The present case series describes 14 patients with MD in whom DBE was useful for diagnosis.

Aims and Methods: Thirteen retrograde and one anterograde DBE were performed for fourteen patients (11 men, 3 women) with MD at Kobe City Medical Center General Hospital from May 2004 through October 2017. Results: DBE diagnosed MD in thirteen out of fourteen patients (92.3%), but one patient was misdiagnosed as a lipoma. MD was identified using iodinated contrast medium through the scope during antegrade DBE in one patient. Abdominal computed tomography was performed in all fourteen patients and revealed abnormalities in eight (61.5%), but MD was suspected in only two cases (14.3%). Technetium-99m pertechnetate scintigraphy and capsule endoscopy were carried out in six and four patients, revealing MD in one and two patients, respectively. Surgery was performed in thirteen patients, and endoscopic resection was carried out in one patient (inverted MD) by DBE. Ulcer formation was found in or near MD in eight patients.

Conclusion: Compared with other modalities such as CT scan, Technetium-99m pertechnetate scintigraphy and capsule endoscopy, DBE is excellent for the diagnosis of MD because direct observation of both MD and ulceration is possible. This study shows that DBE is highly useful in the diagnosis of MD either alone or in combination with other methods. In addition, endoscopic resection using DBE could be one method of treatment of inverted MD.

Disclosure: Nothing to disclose.

TUESDAY, OCTOBER 23, 2018

Nutrition II – Hall X1

P1232 ENDOSCOPIC GASTRIC MUCOSAL ABLATION (EGMA) FOR WEIGHT LOSS: THE FIRST HUMAN CASE REPORT

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Introduction: Morbid obesity is an increasing common chronic health problem in the world including in China. Currently, Laparoscopic Sleeve Gastrectomy (LSG) is the most favored surgical bariatric procedure for the treatment of morbid obesity. The LSG procedure requires removal of the greater curvature of the stomach along with its blood vessels and nerves. Inspired by the complication esophageal stenosis after large area Endoscopic Submucosal Dissection (ESD) for the treatment of early esophageal cancer, we hypothesized that ablation of a sufficiently large area of the gastric mucosa might result in permanent contracture and a reduction in gastric volume. We therefore performed Endoscopic Gastric Mucosal Ablation (EGMA) using pigs as an animal model to confirm our hypothesis (manuscript in preparation). EGMA resulted in shrinkage of the pig stomach producing a reduction in gastric volume. Based on the success with animal experiments, we performed EGMA on an obese patient.

Aims and Methods: The patient was a 38-yr-old obese woman (BMI 37.2 kg/m2) with type 2 diabetes (blood glucose level 15–20 mmol/L) who required 25 units of insulin and 850 mg of metformin twice a day. Her total gastric volume was 787.70 mL measured by CT scan before the procedure. EGMA procedure was performed under general anaesthesia with endotracheal intubation. A cap-based single-channel endoscope (GF-Q260J, Olympus, Tokyo, Japan) was used for the procedure. Endoscopic Submucosal Dissection (ESD) and Endoscopic Mucosal Resection (EMR) procedures were performed to resect the mucosal layer of the fundus and body of the stomach. The goal was to rect 80% of the circumference of the anterior, posterior, greater curvature mucosal layer of the stomach (Figure 1a). Small portions of mucosa (mucosal islands) were left to promote wound healing and regeneration of the gastric mucosa after the procedure.
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Introduction: Antibiotic-associates weight gain and risk for obesity. The mechanisms driving this association are not clear. However, dysbiosis has been identified as a potential causative factor for weight gain. Procedures that impact diet, weight, and the gastrointestinal microbiota, such as gastric bypass surgery, have been linked to modified expression of taste receptors on the tongue. Taste receptors are expressed throughout the gastrointestinal tract, and so may be involved in detecting dietary compounds, appetite control and gut motility.

Methods: We, therefore, aimed to assess how antibiotic-induced dysbiosis influenced expression of tas2r114, tas2r116 and tas2r138, three broadly tuned bitter taste receptors, on the tongue and in the colon in a mouse model. Mice (8/group) were housed minimum 2 months, on a five day course, or control conditions. RNA was isolated (TRIZOL) and expression of tas2r114, tas2r116 and tas2r138 assessed by qPCR.

Results: Expression of each receptor assayed was increased in the colon following antibiotic treatment (tas2r114: −0.18 vs 3.39, p < 0.0001; tas2r116: 1.0 ± 0.6 vs 0.657 ± 1.41, p = 0.0001; tas2r138: 1.0 ± 0.20 vs 2.1 ± 0.40, p = 0.05). However, expression of tas2r116 and tas2r138 expression was reduced on the tongue following antibiotic treatment (tas2r116: 0.03 ± 0.36 vs 0.09 ± 0.02, p = 0.03; tas2r138 1.0 ± 0.19 vs 0.4 ± 0.08, p = 0.04). Expression of tas2r144 was not significantly different between the two groups.

Conclusion: The change in expression of taste receptors found may lead to reduced sensation of bitter dietary compounds on the tongue, and increased enteroendocrine signalling in the colon. Further studies are required, to assess the duration of effects, how altered mRNA expression translates into changed protein expression levels, and the consequences for the host.

Disclosure: Nothing to disclose.

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Disclosure: Nothing to disclose.
References


P1236 46Ga-NODAGA-EXENDIN-4 PET/CT FOR IMAGING OF BETA CELLS IN PATIENTS AFTER ROUX-EN-Y GASTRIC BYPASS (RYGB) SURGERY

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Introduction: After undergoing RYGB, remission of type 2 diabetes (T2D) occurs in 60% of patients. The mechanism behind this remission is not completely understood. Beta cell activity (BCA) and beta cell mass (BCM) could possibly play a role. While RYGB is beneficial for the health and quality of life of most patients, a rare complication is hyperinsulinemic hypoglycaemia. Also here the mechanism is not clear, but a role for BCA and BCM is hypothesized. Measuring BCA and BCM could provide useful information on the role of beta cells in patient responses to RYGB and possibly offer predictive value. Exendin-4, a stable analogue of glucagon-like peptide-1, specifically accumulates in the beta cells. Using 46Ga-exendin-4 PET/CT can be used to quantify BCM in vivo and could help to study the role of BCM in changes of glycemic control after RYGB.

Aims and Methods: BCA and BCM were compared between patients with different responses after RYGB. Patients with complete remission of T2D (responders) and without complete remission of T2D (non-responders) after RYGB were included as well as patients with hypoglycaemia after RYGB.

Results: BCA was measured by an arginine stimulation test and either an oral glucose tolerance test (in the hypoglycaemia patients). BCM was measured in all patients as pancreatic uptake of 46Ga-exendin-4 by quantitative analysis of PET/CT scans.

Conclusion: These preliminary data show that measuring BCM in vivo is possible using 46Ga-exendin-4 PET/CT. The data suggest that BCM is lower in patients with incomplete remission of T2D compared to those with complete remission.

Disclosure: Nothing to disclose.

P1237 LIRAGLUTIDE TREATMENT IN OBESE DIABETIC PATIENTS MODULATES GAS PRODUCTION DURING LACTULOSE BREATH TEST: A NEW POTENTIAL TREATMENT TO MODULATE GUT MICROBIOTA

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Introduction: Colonic bacteria fermentation produces hydrogen (H2) and methane, which can be easily measured using breath test method. H2 breath tests (BT) represent a valid and non-invasive diagnostic tool in many gastroenterological disorders. C13 Octanoic Acid breath test, is used to analyze gastric emptying, often altered in various gastrointestinal disorders. To date the link between diabetes and intestinal microbiota is well known. Liraglutide is a human GLP-1 analogue approved for type 2 diabetes, to reduce glycosylated hemoglobin (HbA1c) and achieve better effects on glucose control. Delayed gastric emptying has been previously associated with Liraglutide treatment. So far it has never been analyzed colonic gas production, with lactulose breath test, before and after Liraglutide treatment.

Aims and Methods: Ten obese diabetic patients (age 63.8 ± 12.6; HbA1C 8.1 ± 1.4 %; body weight: 90.5 ± 19.1 kg), candidate to receive GLP-1 treatment, were included in the study. All subjects underwent, before (B) and after 6 weeks of treatment (PT) with liraglutide 1.2 mg, metabolic evaluation including glucose, HbA1c, glucose self-monitoring, Lactulose Breath test (LBT) and Octanoic Acid Breath test in our Gastroenterology Unit. Methane and Hydrogen production, by the area under the time-concentration curve calculation (AUC), and the peak value were calculated, during LBT. Gastric emptying was assessed by C13 Octanoic Acid BT.

Results: All subjects experienced a significant weight loss (6% of the basal body weight; BMI B: 37.5 ± 1.1 kg/m², BMI PT: 27.4 ± 1.5 kg/m² p: 0.05), as well as a significant reduction of fasting plasma glucose (B FPG pre: 149.4 ± 15 mg/dL, FPG PT: 98.2 ± 23 mg/dL p: 0.09) and a HbA1c (B HbA1c 8.1 ± 1.4 %, HbA1c PT 5.4 ± 1.1% p: 0.01). Methane and Hydrogen production (AUC) and peak value were significantly reduced by Liraglutide in the post-treatment group; moreover, the LBT revealed that Liraglutide is able to significantly slow down the Ozo-ecal transit time (OTT). Also Gastric emptying was significantly reduced after Liraglutide treatment.

Conclusion: These results confirm the effect of Liraglutide on delayed gastric emptying and suggest that the glucose lowering effect of this molecule, may be potentially mediated by modulation of intestinal gas production, and OTT. These findings could represent a new potential effect of Liraglutide treatment on the modulation of Gut Microbiota, underlying new potential mechanisms of microbiota-mediated metabolic effects.

Disclosure: Nothing to disclose.

P1238 ROLE OF DIETARY INTERVENTION IN CLINICAL IMPROVEMENT OF NONALCOHOLIC FATTY LIVER DISEASE

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is the main cause of liver diseases worldwide that poses heavy health-related metabolic problems associated with the increasing prevalence of obesity and diabetes. NAFLD is affected by lifestyle practices including nutrition and sedentary life. Therefore, the common treatment is weight loss through dietary restrictions and practicing exercise. However, there is no consensus regarding the best diet to treat NAFLD, not merely focusing on weight loss but to improve the metabolic health of patients.

Aims and Methods: The aim is to study the role of dietary intervention program including dietary and exercise plan in the clinical improvement of NAFLD. 110 patients were recruited from the Hepatology Patient Clinic in the Main Alexandria University Hospital and diagnosed as NAFLD based on Ultrasound examination and exclusion of other causes of acute and chronic liver disease like post viral, alcoholic, autoimmune and metabolic liver diseases. Also, patients with diabetes mellitus type 1 or 2, or receiving hormonal treatment were excluded. Assessment of dietary intake, dietary habits, lifestyle practices, body composition measurements, laboratory investigations, clinical examination and evaluation of liver fat with ultrasound based hepaticorenal index calculations were done. For 12 weeks, each patient received individualized dietary plan based on Mediterranean diet restricted in carbohydrates (40-45%), moderate in fat (35-40%) and protein (15-20%). Physical exercise including aerobic training and abdominal exercises 5 times a week and 2 times twice a week.

Results: The dietary intake of carbohydrate and energy were decreased, while the percent of fat intake were increased. This was associated with reduction of liver fat among 70% of patients as assessed by reduction in HRI scores, improvement of serum transaminases as well as components of metabolic syndrome and gastrointestinal tract symptoms. Moderate reduction in body weight 5-6% with more loss of body fat (12%) and good preservation of muscle mass were observed.

Conclusion: Proper nutrition counseling based on Mediterranean diet restricted in total calories and carbohydrates, has significant impact on improving the metabolic health of NAFLD patients.

Disclosure: Nothing to disclose.

P1239 SAFETY AND EFFICACY OF ELLIPSE BALLOON IN OBESE ADULT PATIENTS: A SINGLE-CENTER PILOT STUDY IN AN ITALIAN TERTIARY HOSPITAL


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Introduction: Obesity represents a paramount clinical problem for short and long-term cardiovascular and metabolic complications, with consistent increasing incidence in many countries. Gastric balloon is a relevant non-surgical option for such patients, but the positioning and the removal requires endoscopic procedure
and sedation. ELIPSE balloon is a novel device that does not require endoscopy and can be swallowed by the patients and spontaneously excreted after a progressive deflation. We conducted a prospective pilot study at S. Giovanni Hospital in Rome, Italy, to evaluate safety and efficacy of ELIPSE balloon in obese adult patients.

Aims and Methods: Eleven consecutive patients (8 females), with mean age 40 ± 5 and BMI 40 ± 4, were included in the study. ELIPSE balloon was swallowed with water, filled with 560 mL of fluid. Patients were followed up by a nutritionist during the study. Body weight were recorded before ingestion and after excretion of the balloon and potential adverse events were monitored at ingestion time and during follow up till the excretion of the balloon.

Results: All the patients successfully swallowed the device, and no major adverse event was recorded during the study. Minor and transient symptoms reported were dyspepsia, constipation, and diarrhea. All the patients spontaneously excreted the balloon after 16 ± 2 weeks. At the end of the study, all the patients had a significant weight loss (mean: 14.4 ± 5 Kg).

Conclusion: In a single-center pilot study, ELIPSE balloon has demonstrated safety and efficacy in adult obese patients. This device do not require endoscopy and sedation and may represent a feasible and effective option even in primary setting. Data confirming efficacy and safety of ELIPSE are increasing, and further studies will better clarify the positioning of this promising device for the treatment of obesity.

Disclosure: Nothing to disclose

P1240 CHANGES IN THYROID HORMONE LEVELS IN OBESE EUTHYROID PATIENTS UNDERGOING BARIATRIC SURGERY
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Introduction: The relationship between obesity and elevated levels of thyroid stimulating hormone (TSH) has been reported. One of the suggested mechanisms is the influence of adipokines, namely adiponectin. Bariatric surgery is a currently recognized technique for the treatment of obesity, with a favorable effect on weight loss; however, the impact of the postoperative period on thyroid function has not been clarified.

Aims and Methods: The aim of this study was to evaluate the changes in TSH and free thyroxine (FT4) in the obese population submitted to bariatric surgery. Prospective analysis of patients undergoing Roux-en-Y gastric bypass (RYGB) for obesity. Clinical and laboratory data were analyzed before and after surgery. Patients with a known history of thyroid disease were excluded. Statistical analyses performed in SPSS V24.

Results: 38 patients were included; mean age was 43.4 ± 11.2 years, 80% were women and mean Body Mass Index (BMI) before surgery was 41.7 ± 5.4 kg/m2. After surgery, patients lost an average of 33.4% of their total body weight and 87.8% of BMI in excess. There was a significant reduction in weight (111 vs 73.7 kg) and BMI (41.2 vs 27.7 kg/m2) before and after surgery (p<0.00). There was also a reduction in FT4 and TSH levels before and after surgery (FT4 0.92 vs 0.87 mg/dL, p<0.02 and TSH 1.13 vs 1.04 μIU/mL, p<0.14). There was also a significant correlation between TSH levels and BMI before surgery (r = 0.37, p< 0.05). After surgery, there was a reduction in FT4 in female subgroup (r = 0.36, p<0.048). There was a significant reduction in TSH levels with increased levels of adiponectin (r = -0.39; p<0.04), but only in the subgroup of women. Changes could be a reduction in thyroid hormone levels due to weight loss after bariatric surgery. Changes in adipokine production, such as adiponectin, in adipose tissue may explain some of the variation in TSH.

Disclosure: Nothing to disclose

P1241 DIAGNOSIS OF LACTOSE MALABSORPTION BY THIRD GENERATION HYDROGEN BREATH TEST: TIME IMPLEMENTATION AND SAMPLES DATA REVIEW
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Introduction: Hydrogen breath test using various substrates like glucose, lactulose, and mannitol are being used more and more to diagnose lactose malabsorption and small intestinal bacterial overgrowth (SIBO). While glucose and lactulose hydrogen breath tests are more acceptable the diagnosis of SIBO, lactulose and fructose hydrogen breath tests are used to diagnose various types of sugar malabsorption and lactose intolerance. Technique and interpretation of different hydrogen breath tests are outlined in this review.

Aims and Methods: The third generation of hydrogen breath test monitors has reached a level of precision which makes such continuous air flow device (Gastrolyzer Bedfont, Scientific Ltd Harrietsham) or Heliprobe (Kilion, Mayoli Spindler) a helpful assist for diagnosis of gastrointestinal disorders.

Gases as H2, CH4 or CO2 are detected in a semi-conductor flow cell an displayed on the monitor. The original sluggish development has now made room for a useful screening test in the cases where lactose intolerance is suspected. Genetic test of lactose intolerance may help to differentiate patients with primary hypolactasia from those with lactose intolerance caused by secondary hypolac- tasia. Also it is useful for differing lactose intolerance from irritable bowel syn- drome (IBS) which has very similar symptoms. So for the differentiation of adult- type hypolactasia from secondary causes of lactose intolerance, hydrogen breath testing (H2BT) might not need further genetic approach. The third generation of H2BT is to prove and establish whether a simplified two or three sample test may reduce time, costs and staff resources without reducing the sensitivity of the procedure.

Data from 32 patients (20 males, 12 females) with a positive 4 h, nine samples H2BT were fully tested. Patients were stratified according to the degree of lactose malabsorption, the occurrence and type of symptoms. Sensitivity in the H2BT was tested taking into account two samples tests (0 and 210 min or 0 and 210 min) or three-sample tests (0 min, 120 min and 180 min or 0 min 120 min and 210 min). Using a two sample test (0 min and 120 min or 0 min and 210 min) the false-negative rate was 35.6% and 27.8% respectively. With a three-sample test (0 min 120 min and 180 min or 0 min 210 min) lactose malabsorption was diagnose in 94.6% (30 of 32) patients and in 97.1% (31 of 32) patients respectively. Of 20 patients with abdominal symptoms, 5 (25%) in one sample test and 2 (12.2%) would have false-negative results with 0 min and 120 min or 0 min and 210 min two-sample tests respectively. The three-sample tests, 0 min, 120 min and 180 min or 0 min, 120 min and 210 min, would have a false-negative rate of 5.9% and 2.1% respectively.

Conclusion: H2BT is an inexpensive, useful, simple and safe diagnostic test in the evaluation of lactose malabsorption. Standardization of the indications, perfor- mance and interpretation of the test still needs to be improved in clinical practice and research.

The third generation quantitative detection of rare gases with the breath expan- sion with three-sample H2BT is time and cost sparing without significant loss of sensitivity for the diagnosis both of lactose malabsorption and lactose intolerance

Disclosure: Nothing to disclose

References
Aims and Methods: We conducted a single-arm, open-label, prospective, multi-center study in which 727 patients (HbA1c 7.5–10.0%; age 25–75y; BMI 24–40kg/m²; using oral glucose lowering medication) received a single DMR procedure. Adverse events and impact on glycemic control (HbA1c and fasting plasma glucose [FPG]), insulin resistance (HOMA-IR), and liver enzymes (AST and ALT) were determined at baseline and 3, 6, 9, 12 months post DMR. Glucose lowering medication was kept stable for ≥ 6 months post DMR but could be adjusted according to care guidelines thereafter. We used ANOVA for repeated measurements with Bonferroni correction for the analysis of the multiple measurements after DMR. Values are mean±SD.

Results: Baseline characteristics (n = 46) are 63% male, mean age of 55 years [range 31–69], mean T2D duration of 6 years [range 0.1–12], and mean BMI 31.6±4.3 kg/m². Additional baseline values are shown in Table 1. DMR was well tolerated in all 46 patients. Eight serious adverse events (SAEs) were reported, of which one was considered procedure-related and non were considered device-related. The single procedure-related SAE was mildly elevated body temperature (38°C) with an increase in C-reactive protein that started one day post DMR and involved one extra day of hospitalization for observation. The 6 and 12 month post DMR follow-up values of HbA1c, FPG, HOMA-IR, weight, ALT and AST with significance levels (as compared to baseline) are shown in Table 1. Change at 12 months are: Δ HbA1c -1.0 ± 0.2% (p < 0.001), Δ FPG -4.1 ± 1.8 mg/dL (p < 0.001), Δ HOMA-IR -5.2 ± 0.9% (p = 0.005), Δ weight -2.7 ± 0.6 kg (p = 0.003), Δ ALT -10 ± 2 (p = 0.005), and Δ AST -6 ± 2 (p = 0.002).

Conclusion: The endoscopic DMR procedure was found to be safe and effective in 46 patients with suboptimally controlled T2D using oral glucose lowering medication. DMR elicited a substantial improvement in parameters of glycaemia as well as a decrease in liver transaminase levels up to 12 months post-procedure, suggesting considerable potential of DMR for the treatment of T2D.

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References

P1244 MICRONUTRITION STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
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Introduction: Micronutrient (MN) status in patients with inflammatory bowel disease (IBD) is important in evaluation of malnutrition. Malnutrition and weight loss are the most common causes of altered status of MN due to reduced food intake, enteric loss of nutrients and malabsorption. A wide range of vitamin and mineral deficiencies has been noticed in IBD patients, with varying degrees of clinical importance.

Aims and Methods: Aim of our study was to investigate levels of micronutrients in IBD patients, as well as assessment of possible correlation of micronutrients levels and disease activity.

A case-control study was performed among 30 newly diagnosed IBD patients and the same number age, sex-matched healthy controls. All patients underwent a full colonoscopy with ileoscopy. Complete blood count was obtained in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR). Serum levels of selenium, copper and magnesium were measured spectro-photometrically, while serum iron was assayed with an electrochemiluminescence immunoassay. Mayo score and CDAI respectively were calculated for each patient.

Results: Serum levels of iron, zinc, magnesium and selenium were significantly lower (p < 0.05) in IBD patients than controls. There was no statistically significant difference in levels of iron and zinc between the two groups (P>0.05).

In patients group mean levels of iron (7.1 ± 2.8 μmol/L), zinc (23.6 ± 5.3 μmol/L), magnesium (0.6 ± 0.2 mmol/L) were reduced below the reference values, while the levels of copper (28.2 ± 24.1 μmol/L) were elevated. Serum levels of copper and zinc negatively correlated with CDAI and Mayo score (P < 0.05), while the levels of iron and magnesium did not show significant correlation with CDAI and Mayo score (P>0.05).

Conclusion: Our results suggest that deficiency of MN can be a result of the inflammatory process, so regular MN monitoring is essential, considering that zinc and iron deficiency could be potential indicators of disease activity.

Disclosure: None to disclose

P1245 DEPELLING MICROBE-HOST COMMUNICATION BASED ON A DIETARY INTERVENTION WITH PARTIALLY HYDROLYZED GUAR GUM – THE PAGODA STUDY
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Introduction: Structural alterations of the intestinal microbiota and its metabolic capacity are associated with various diseases states in humans. There is a need to remodel a dysbiotic microbiome towards a normal shape could improve health. Prebiotics are one possibility to beneficially modulate a dysbiotic microbiome. Despite increasing knowledge, mechanistic insight linking dietary fiber with health benefits, beyond the well-known role of short chain fatty acids (SCFA), is still scarce.

Aims and Methods: This study aimed to decipher novel mechanistic links between a dietary fiber intervention with partially hydrolyzed guar gum (PHGG) and structural and metabolic alterations of the human microbiome. We performed a clinical trial including 19 healthy volunteers (8m, 11f). Stool, serum and urine samples were collected weekly for 9 weeks allowing every study participant to serve as his/her own control. The study included three periods, namely a 3 weeks lead-in period, 3 weeks intervention, and a 3 weeks wash-out phase. During the 3 weeks intervention phase participants received daily dosing of 5g PHGG for 3 days followed by 10g PHGG for four days in the first week, proceeding with two weeks of 15g PHGG per day. A minute medical and nutritional history was taken for every participant at baseline, questions regarding abdominal symptoms were collected weekly and stool habits using the Bristol Stool Chart (BSC) were recorded on a daily basis. Alterations in the structural composition of the microbiome were assessed by 16S metagenomics using both V1-V3 and V3-V4 chemistry. Furthermore, stool metabolomics was studied by magnetic resonance spectroscopy. Data from metagenomics and metabolomics were linked using sparse regression matrices employing the ‘Sparcc’ software module.

Results: As expected, PHGG administration increased stool frequency and reduced stool consistency. Notably, this effect was more pronounced in males than females and persisted during the wash-out period. 16S sequencing revealed an increase in alpha-diversity during and also persisting after the intervention. Beta-diversity with respect to treatment periods was not different due to large inter-individual variability. NMR spectroscopy of the stool metabolome identified 10 signals, principal component analysis again revealed significant gender-specific differences and we identified >150 significantly changed metabolites before, during and after intervention. Interestingly, the concentration of SCFA showed an early peak that was not persistent, in contrast to numerous other metabolites.

Conclusion: In the PAGODA study, we show that a dietary intervention with PHGG induces beneficial and durable alterations of gut microbial structures along with changes in microbiota-derived metabolites. With more than 150 significantly regulated components we propose that microbiota-host communication due to dietary fibers induced metabolites goes far beyond SCFA.

Disclosure: The study was supported by an unrestricted grant form Nestle Health Sciences to ARM. Otherwise there are no potential conflicts of interest regarding this study.
11 healthy female volunteers (age: 22 ± 0.7 y; BMI: 21.7 ± 1.2 kg/m²) participated in a randomized, controlled crossover study. After an overnight fast, a blood sample was taken (20 mL) and centrifuged at 10000 r.p.m. for 10 min prior to administration. Following blood samples were collected every 10 min after administration for a total of 120 min. A control sample was taken at the same points on a visual analogue scale (VAS). Ad libitum milkshake intake was assessed at the end of the experiment and taste was scored on a VAS. Percentage change of SAT and hunger were calculated from baseline. AUC of positive and negative peaks was calculated for both hunger and SAT. Net increment change was calculated by subtracting the negative from the positive area. Data were analyzed using mixed models with planned contrast analysis. Comparisons of interest were QHCl vs placebo and DB vs placebo for both IG and ID administration together with the comparisons ID vs BD for these differences. Observed p-values were corrected for multiple testing with stepdown Bonferroni.

Results: The net increment of hunger was significantly different after IG administration between QHCl and placebo (p = 0.03). There was no significant difference between IG and ID for these differences. Administration of QHCl had the potential to reduce hunger sensations in healthy female volunteers, but without significant effect on the amount of consumed milkshake and on taste scores. The effect was however, site specific as it was only seen after IG administration. SAT release did not differ between the different treatments, suggesting that SAT is not the inhibiting factor of orexigenic hormone secretion after IG bitter administration.

Disclosure: Nothing to disclose.
The quality of life of the SBS-patients through the immun- and nutritional status. These alterations influence greatly the many cases. The surgical shortening of the bowel causes a qualitative-quantitative change of the human microbiome. These alterations lead to a permanent need for parenteral nutrition in absorbing area and shortened transit-time increase the absorption of nutrients, electrolytes and water.

Disclosure: Nothing to disclose

P1249 A NUTRITION SUPPORT TEAM REDUCES INAPPROPRIATE GASTROSTOMY CASE SELECTION AND ALL-CAUSE 30-DAY MORTALITY

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Introduction: In 2004 the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report highlighted the high 30-day mortality related to Percutaneous Endoscopic Gastrostomy (PEG) insertion and the need for careful patient selection. Subsequent studies have demonstrated a higher mortality in certain patient groups, for example severe dementia. In 2010 the British Society of Gastroenterology (BSG) published guidelines recommending a nutrition support team (NST) to identify appropriate cases for PEG insertion.

A NST was set up in a district general hospital providing a review process for PEG referrals. Prior to this, patients were referred to neighbouring trusts for PEGs or to the radiology team for a per-oral inserted gastrointestinal (PIG). A new standard operating procedure and dedicated electronic request form was created. A nutrition nurse was appointed to perform the initial vetting. Complex cases are discussed in a weekly nutrition multidisciplinary team (MDT) and subsequent ward round. Despite recommendations and evidence regarding PEG insertion, for many patients it remains a difficult clinical and ethical decision. Increasing bed pressures with an ageing population have complicated matters further. We have noted increasing demands for PEG to facilitate discharge to care homes.

Aim and Methods: To assess whether the implementation of the NST led to improved patient selection and reduced 30-day all-cause mortality. We conducted a retrospective analysis of all electronic PEG referrals and referral review notes held by the nutrition nurse between 1st December 2015 and 1st April 2017.

Results: We identified 136 referrals in total. Before the review process could be completed by the NST 8 patients died; 7 patients declined to have a PEG and 13 had already recovered their swallow and therefore these patients were excluded. 108 referrals were reviewed in full by the NST. Of the 108 referrals 81 were deemed suitable for gastrostomy insertion and 27 were not thought appropriate.

Conclusion: Having a dedicated NST who review PEG referrals results in a significant reduction in mortality, inappropriate procedures and respects patient autonomy. It is important to maintain the NST and not let decisions surrounding gastrostomy be eroded by increasing pressures on the health care service.

Disclosure: Nothing to disclose

P1250 COMPOSITION OF THE MICROBIOME IN PATIENTS WITH SHORT BOWEL SYNDROME

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Introduction: Short bowel syndrome (SBS) is present when the length of the remnant small intestine after surgical resection is <65 cm. The decreased absorbing area and shortened transit-time increase the absorption of nutrients, electrolytes and water and lead to a permanent need for parenteral nutrition in many cases. The surgical shortening of the bowel causes a qualitative-quantitative change of the human microbiome. These alterations influence greatly the quality of life of the SBS-patients through the immun-, and nutritional status.

Aims and Methods: To investigate the composition of the microbiome of patients with SBS.

Patients: 18 years old with SBS were included. After informed consent anthropometric parameters (weight, height, BMI, body composition Imbody) were registered. To identify the microbiome-composing bacteria, stool samples were collected and the 16r rRNA (member of the subunit of procarctic ribosome 308) of the microorganism was sequenced. Beside evaluating the composition we calculated the Microbiome Diversity Index (MDI) comparing the diversity of the microbiome of patients with SBS to the data derived from the normal population.

Results: 5 female patients with SBS are under care at our clinic (mean age: 49 ± 13, mean body length: 81 ± 65cm; BMI: 17.8 ± 2.1 kg/m²), 3 of 5 patients are on parenteral nutrition permanently. The diversity is extremely reduced compared to the normal population (MDI: 5.5 ± 1.9, 0–30 between percentiles). The main phylum is Firmicutes, and Proteobacterium and Actinobacterium phyla are present, but the ratio of Bacteroides phyla is extremely low. Among Firmicutes the lactate-producing and -consuming bacteria (Lactobacillus, Bifidobacterium, Veillonella) form the majority of the microbiome.

Conclusion: The composition of microbiome of SBS patients differs largely from the normal population; the diversity is extremely reduced. Being able to enrich the diversity of bacteria in patients with SBS has probably therapeutical consequences.

Disclosure: Nothing to disclose

P1251 RAPID DIAGNOSIS OF BLOODSTREAM INFECTIONS IN PATIENTS ON HOME PARENTERAL NUTRITION

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Introduction: Home parenteral nutrition (HPN) patients have an increased risk of catheter-related bloodstream infections. Early identification of causative microorganism (s) is critical to optimize patient care and antimicrobial use. The droplet digital polymerase chain reaction (ddPCR) is a novel culture-independent molecular technique to rapidly identify pathogens in whole blood.

Aims and Methods: The aim of this study was to measure the diagnostic accuracy of the ddPCR in the HPN-setting in comparison with the current gold standard blood cultures. We analyzed a set of historically collected frozen blood samples from adult HPN patients with a suspected bloodstream infection, and compared these with blood cultures drawn on the same day. In a relative short procedure (15 minutes) whole blood samples were isolated and analyzed with ddPCR. The analyses were independently performed by two research analysts, without knowledge of the blood culture results. Study outcomes included sensitivity, specificity, the positive- and negative predictive value and the positive- and negative likelihood ratio of the ddPCR.

Results: In total, 40 blood samples were analyzed (Table 1). The sensitivity was 89% (95%CI 44–97) and the specificity 85% (95%CI 65–94). The positive- and negative predictive value were 62% (95%CI 40–79) and 93% (95%CI 78–98), respectively. The positive- and negative likelihood ratio were 4.8 (95%CI 2.0 11.3) and 0.24 (95%CI 0.07–0.84), respectively.

Disclosure: Nothing to disclose

P1252 EFFECT OF ROSUVASTATIN ON HEPATIC STEATOSIS AND FIBROSIS IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS: A DOUBLE BLIND RANDOMIZED CLINICAL TRIAL

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Introduction: Non-alcoholic steatohepatitis is a serious and progressive disease, with no definitive treatment for it. Statins, as cholesterol-lowering drugs, are one of the treatments for this disease.

Aims and Methods: The aim of the present study is to determine the effect of rosuvastatin on steatosis and fibrosis in patients with non-alcoholic steatohepatitis. In this double-blind clinical trial, 44 patients with non-alcoholic steatohepatitis without metabolic syndrome, non-diabetic and BMI less than 30 were randomly divided into intervention (6 months daily 10 mg of rosuvastatin with nutrition and lifestyle education) and control (Placebo with the same protocol) groups. The condition of liver fibrosis and steatosis were evaluated by transient elastography (FibroScan) at the beginning and the end of the study.

Results: After 6 months, the percentage of steatosis in both groups was lower than the beginning of the study, which was significant in the intervention group (P = 0.014). At the beginning of the study, the liver fibrosis index in the control group was significantly lower than intervention group (P = 0.01) and at the end of the study, this difference was maintained between the two groups (P = 0.002). In the intervention group, the index of fibrosis decreased, although this difference was not significant (P = 0.22).

Conclusion: The use of rosuvastatin can affect the reduction of steatosis and may prevent the progression of liver fibrosis.

Disclosure: Nothing to disclose

[Table 1]
P1253 MICRONRA-199A-3P PROMOTES THE ACTIVATION OF HEPATIC STELLATE CELLS AND LIVER FIBROSIS BY SUTPPRESSING CAVOLEIN-2

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Introduction: There is limited therapy for liver cirrhosis although it constitutes a large and growing problem in the Western world. The activation of hepatic stellate cells (HSCs) is known as the key contributors to liver fibrosis/cirrhosis. MicroRNAs have been widely reported to regulate various diseases including liver fibrosis, and are promised to be novel therapeutic targets. Aims and Methods: The aim of the study is to investigate the role of miR-199a-3p and its target caveolin-2 (CAV2) in liver fibrosis and the underlying mechanisms. Rat HSCs was isolated by in situ perfusion with pronase and collagenase B, followed by Nycodenz density gradient centrifugation. We perform microRNA microarray to detect microRNA expression profile in quiescent and activated rat HSCs. We validated the microarray data by qPCR in rat HSCs, and further examine the expression in rat and human liver fibrotic tissues. Based on these results, the inhibitors of miR-199a-3p in both activated HSCs and liver fibrotic tissues was selected for further analysis. The human liver line, LX-2, and rat HSCs were transfected with miR-199a-3p mimics and antagonist, followed by qPCR and western blot to examine the expression of fibrotic markers. Moreover, miR-199a-3p and its antagonist were used to detect the regulation of fibrogenesis of HSCs. The targets of miR-199a-3p were predicted by Targetscan and miranda. The effect of miR-199a-3p in vivo was assessed in mice liver fibrosis model induced by CCL4.

Results: miR-199a-3p dramatically up-regulated during HSCs activation and liver fibrotic tissues from both rat and human. Forced expression of miR-199a-3p in LX-2 and rat HSCs significantly increased fibrotic markers expression. Additionally, inhibition of miR-199a-3p reduced fibrotic markers expression. Moreover, CAV2 and CAV2 protein expression was down-regulated by miR-199a-3p. Further study revealed that CAV2 obviously inhibited fibrotic markers expression and the proliferation of HSCs. We then found the protein expression of TGFβRI, a key receptor in TGFβ signaling pathway, was reduced by CAV2. Interestingly, Twist1 could bind with the promoter sequences of miR-199a-3p to drive miR-199a-3p expression in HSCs, then promoting liver fibrosis. More importantly, we provided evidence that antagonist-miR-199a-3p injection relieved mice liver fibrosis induced by CCL4.

Conclusion: These results indicate that miR-199a-3p mediates the regulation of liver fibrosis by suppressing CAV2 expression, and promoting TGFβ signaling pathway probably through increasing TGFβRII expression. Thus miR-199a-3p may represent potential targets for novel therapeutic strategies against hepatic fibrogenesis and also might evolve as biomarkers in the diagnosis of liver fibrosis.

References: none

Disclosure: Nothing to disclose

Aims and Methods: The aim of this study was to identify novel non-invasive markers that are associated with key histology lesions of progressive NAFLD. Therefore, patients with biopsy-proven NAFLD (n = 74) and healthy controls (n = 62) were recruited; among the NAFLD patients, 13 had advanced fibrosis (F ≥ F2) and 61 had no or mild fibrosis (F0-F1). EDTA plasma samples were obtained from blood by centrifugation and analyzed by targeted metabolomics using ultra-performance liquid chromatography-tandem mass spectrometry-based metabolomics. Statistical analysis was performed by multivariate (random forest, elastic net, and linear discriminant analysis) as well as univariate (analysis of variance) algorithms, and peak signals were compared to key histology lesions of NAFLD, i.e. fibrosis, activity, and steatosis.

Results: We identified a metabolite panel that successfully distinguishes between patients with fibrosis stage ≥ F2 and those with fibrosis stage F ≤ F1. Our biomarker panel consists of 9 metabolites newly discovered under the curve (AUC) value of 0.95 (sensitivity of 0.92, specificity of 0.90), outperforming current non-invasive diagnostic tests, including the measurement of cys-Cleaved keratin 18 levels (AUC ≤ 0.68), the fibrosis-4 index (F4-test, AUC = 0.82).

Conclusion: Our results proved that metabolomics is a powerful technology platform for studying complex disease mechanisms. By using whole metabolite profiling, we could identify a biomarker that is strongly associated with the stage of liver fibrosis in NAFLD patients. Since it provides a non-invasive tool in the detection of fibrosis in plasma samples from NAFLD patients, it can serve as a new non-invasive screening tool for NAFLD patients.

Disclosure: Nothing to disclose

P1254 THE COMBINATION OF AN ANDROGEN, A BILE ACID AND AN EICOSANOID IS A PROMISING BIOMARKER FOR LIVER FIBROSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) affecting about 25% of population, is becoming the leading and growing cause of mortality worldwide. The prevalence of NAFLD is growing rapidly due to western life style, and increasing incidences of diabetes and obesity. 30% of affected people develop liver inflammation or non-alcoholic steatohepatitis (NASH) which further progresses to advanced fibrosis or cirrhosis to hepatocellular carcinoma. Currently, there is an unmet need for the effective and safe therapies for the treatment of this disease. Inflammatory macrophages play a crucial role in the pathogenesis of NASH. Therefore, development of a therapeutic strategy (e.g. pharmacologic agent) that diminishes or ameliorates macrophage activation would be highly promising therapy for the treatment of NASH.

Aims and Methods: Transcriptome analyses in NASH patients and inflammatory macrophages revealed Src kinase, a tyrosine-protein kinase, as a prospective therapeutic target in inflammatory macrophages. To address this study, we investigated the implication of Src signaling pathway inhibition in inflammatory macrophages and NASH. We further developed a PLGA nanoparticles delivery system to target Src kinase inhibitors for improved pharmacokinetic profile and therapeutic efficacy, to inhibit M1 macrophages thereby ameliorating liver inflammation and NASH.

To accomplish the goals of this project, we used KX2-391, a small-molecule Src kinase inhibitor. We tested the efficacy, toxicity and efficacy of KX2-391 in the differentiated inflammatory RAW macrophages and bone marrow derived macrophages. Thereafter, we synthesized PLGA nanoparticles to deliver Src kinase inhibitor (KX2-391) to increase the drug pharmacokinetics for the efficient treatment of liver inflammation. We investigated the efficacy of KX2-391-PLGA nanoparticles in differentiated RAW macrophages, bone marrow derived macrophages and murine precision cut liver slices (PCLS). Finally, we evaluated the therapeutic effects of KX2-391 and KX2-391-PLGA nanoparticles in vivo in Mdr1a−/− mice which is a model of NASH.

Results: Analysis of livers from NASH patients showed a highly significant induction of Src kinase expression that correlated with the increasing NAS score as compared to normal livers as determined from transcriptome analysis (GEO accession number: GSE48452). Expression of Src kinase and M1-specific genes (iNOS, IL-1β, CCL2, FcyRI) was found to be significantly upregulated in inflammatory macrophages. Src kinase pathway activation (Src phosphorylation) was confirmed in inflammatory macrophages. KX2-391 dose-dependently inhibited Src phosphorylation and Src and c-Abl tyrosine phosphorylation. Furthermore, KX2-391 significantly attenuated M1-induced Nitric oxide (NO) release (an indicator of M1 activation) and expression of M1 markers in RAW macrophages, BMDMs and murine precision cut liver slices (PCLS). PLGA loaded with Src inhibitor KX2-391 showed improved entrapment efficiency. KX2-391-PLGA inhibited NO release and M1-specific markers expression in RAW macrophages and BMDMs. KX2-391 and KX2-391-PLGA showed significant inhibition of M1 macrophage markers in PCLS without inducing toxicity. Recently, we have performed an in vivo study on MCD diet-induced murine model of NASH and preliminary results suggests inhibition in liver inflammation as assessed by quantitative PCR. Further analyses are currently ongoing.
Conclusion: Inhibition of Src signaling pathway in inflammatory macrophages suggests a potential therapeutic approach to treat non-alcoholic steatohepatitis.

Disclosure: Nothing to disclose

References:

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Introduction: In cirrhotic patients, portal hypertension, hypophatemia, intestinal mucosal hyperemia and edema, dyskinesia, dysfunction of bile salt transporters and other factors could influence the species, colonization and metabolism of bacteria undergo microbiota. While, endotoxin release and intestinal inflammatory mediated-damage, intestinal dysbiosis could further aggravate liver damage. It has been found that TLR2,TLR4 and CD14 are the main endotoxin receptor. This study was to evaluate the effect of SIBO by lactulose hydrogen breath test, measure the plasma concentrations of endotxin, and TLR2,TLR4 expression to determine the relationship among SIBO, endotoxia and TLR2,TLR4 expression. Small intestinal bacterial overgrowth (SIBO) gets great attention because of its clinical significance in systemic and local complications in patients with liver cirrhosis, but there are still many controversies about the mechanisms.

Methods: To determine the frequency of SIBO in cirrhics and correlate with endotoxia, TLR2,TLR4 expression.

Between July 2015 and December 2016, there were 59 cirrhitic patients enrolled in our department. Based on the Child-Pugh classification, there were 18 cases of Child-Pugh grade A, 17 cases of grade B and 23 cases of grade C.36 males and 23 females, aged between32 and 78 year; mean age, 42.25 ± 14.18 years. Patients were included in the study if they had not been using any antibiotics, lactulose, antacids, or other drugs affecting gastrointestinal motility in the past 4 weeks. The serum endotoxins were tested by TAL chromogenic substrate Assay. The expression of TLR2,TLR4 on the surface of PBMC were measured by flow cytometry. Small-intestinal bacterial overgrowth was determined by LBHT. A rise of ≥20 p.p.m from baseline or a rise of ≥20 p.p.m from baseline in hydrogen by 90 min should be considered SIBO positive test. Hydrogen breath tests were also measured in all subjects who exhaled gas within 90 minutes (LBHT set-value). The LBHT set-value is expressed by the sum of the seven measured values in 90 minutes or before the second peak. In addition, it can be used as an indicator to indirectly reflect the growth of bacteria in the small intestine.

Results: Of the 38 cirrhotics, 25 (65.7%) had SIBO positive, compared to two (7.49%) control (x² = 10.32, P < 0.001). The LBHT inteset value set,seum endotoxin level and the expression of TLR2,TLR4 on the surface of PBMC in cirrhosis were obviously higher than the control group (t = 11.573, P < 0.05; t = 9.958, P < 0.05; t = 12.380, P < 0.05; t = 10.319, P < 0.05). It was shown by Pearson correlation analysis that LBHT inteset value was positive correlation with endotoxin level and the expression of TLR2,TLR4 among cirrhotic patients and live cirrhosis with SIBO-negative.

Disclosure: Nothing to disclose

P2128 THE RELATIONSHIP BETWEEN SMALL INTESTINAL BACTERIAL OVERGROWTH, ENDOXENIA LEVELS AND TLR2,TLR4 EXPRESSION IN PATIENTS WITH CIRRHOSIS

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Introduction: Cirrhotic patients, portal hypertension, hypophatemia, intestinal mucosal hyperemia and edema, dyskinesia, dysfunction of bile salt transporters and other factors could influence the species, colonization and metabolism of bacteria undergo microbiota. While, endotoxin release and intestinal inflammatory mediated-damage, intestinal dysbiosis could further aggravate liver damage. It has been found that TLR2,TLR4 and CD14 are the main endotoxin receptor. This study was to evaluate the effect of SIBO by lactulose hydrogen breath test, measure the plasma concentrations of endotxin, and TLR2,TLR4 expression to determine the relationship among SIBO, endotoxia and TLR2,TLR4 expression. Small intestinal bacterial overgrowth (SIBO) gets great attention because of its clinical significance in systemic and local complications in patients with liver cirrhosis, but there are still many controversies about the mechanisms.

Methods: To determine the frequency of SIBO in cirrhics and correlate with endotoxia, TLR2,TLR4 expression.

Between July 2015 and December 2016, there were 59 cirrhotic patients enrolled in our department. Based on the Child-Pugh classification, there were 18 cases of Child-Pugh grade A, 17 cases of grade B and 23 cases of grade C.36 males and 23 females, aged between32 and 78 year; mean age, 42.25 ± 14.18 years. Patients were included in the study if they had not been using any antibiotics, lactulose, antacids, or other drugs affecting gastrointestinal motility in the past 4 weeks. The serum endotoxins were tested by TAL chromogenic substrate Assay. The expression of TLR2,TLR4 on the surface of PBMC were measured by flow cytometry. Small-intestinal bacterial overgrowth was determined by LBHT. A rise of ≥20 p.p.m from baseline or a rise of ≥20 p.p.m from baseline in hydrogen by 90 min should be considered SIBO positive test. Hydrogen breath tests were also measured in all subjects who exhaled gas within 90 minutes (LBHT set-value). The LBHT set-value is expressed by the sum of the seven measured values in 90 minutes or before the second peak. In addition, it can be used as an indicator to indirectly reflect the growth of bacteria in the small intestine.

Results: Of the 38 cirrhotics, 25 (65.7%) had SIBO positive, compared to two (7.49%) control (x² = 10.32, P < 0.001). The LBHT inteset value set,seum endotoxin level and the expression of TLR2,TLR4 on the surface of PBMC in cirrhosis were obviously higher than the control group (t = 11.573, P < 0.05; t = 9.958, P < 0.05; t = 12.380, P < 0.05; t = 10.319, P < 0.05). It was shown by Pearson correlation analysis that LBHT inteset value was positive correlation with endotoxin level and the expression of TLR2,TLR4 among cirrhotic patients and live cirrhosis with SIBO-negative.

Disclosure: Nothing to disclose

References:

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Coffee upregulated the expression of ABCA1, ABCG1, FFAR-1, Zonulin, and PPAR-M. Guido3, M. Savoia4, N. Caporaso1, F. Morisco1

C. 1 and 2, Occludin and ZO-1 in colonic mucosa were markedly downregulated in NF73-1 treated mice compared with NF23-1 and NF4-1 groups. Similar with in vivo staining, the mRNA levels of Occludin and ZO-1 in HT-29 cells were lowest in NF73-1 group.

Conclusion: Mucosal-adherent Escherichia coli NF73-1 induces more serious liver injury than other isolates NF23-1 and NF4-1, indicating that NF73-1 might be a critical strain in NAFLD. Our research shed some light on diagnosis and treatment of NAFLD and specific bacterial strain.

Disclosure: Nothing to disclose.

P1260 DOES THE COFFEE VIA GUT-LIVER AXIS PLAY A BENEFICIAL EFFECT ON LIVER DAMAGE?

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Introduction: Metabolic syndrome is one of the most important health issues worldwide. Its liver phenotype is called non-alcoholic fatty liver disease (NAFLD). We have previously demonstrated that high fat diet (HFD)-induced liver damage is reverted by coffee consumption thought a reduction of fat deposition in the liver and an amelioration of antioxidant and anti-inflammatory status. Aim: We hypothesized that the first target organ of coffee in the gut is protecting the effective on the liver by modulating the gut permeability and contributing to the concept of relevant role of gut-liver axis. Twenty-four C57BL/6 mice were divided into 3 groups of 8 mouse each: one group received standard diet (3D: 33 Kcal,g; 5% from fat), one group received HFD (5.5 Kcal, 58% from fat), and a third group received HFD plus decaffeinated coffee solution (HFD+Coffee) for 12 weeks. Coffee daily dosage corresponded to 2 cups of espresso coffee or 2 cups of filtered coffee for a 70 kg person. At the end of treatment, mouse liver was harvested, and a well-known ratio for cardiovascular disease (CVD). In a previous cross-sectional study, we reported a strong relationship between the combination of fatty liver and an elevated serum GGT level and the presence of carotid plaque (J Atheroscler Thromb. 2015; 22(10): 1051–60).

Conclusion: The median SFA per steatosis grade was: grade 0 1.41% (IQR 1.03–1.80%); grade 1 4.99% (IQR 2.97–9.31%); grade 2 13.65% (IQR 10.90–16.10%); and grade 3 16.34% (IQR 14.48–20.54%). SFA correlated significantly with steatosis grade (Rs = 0.85, C.I. 0.749–0.902, p < 0.001). In post-hoc analyses, SFA increased significantly with each individual steatosis grade, except between grades 2 and 3. Median fat droplet size increased with steatosis grade (grade 0 108 um2 (IQR 94–124); grade 1 170 um2 (IQR 138–233); grade 2 249 um2 (IQR 218–309); grade 3 226 um2 (IQR 187–321), p < 0.001). Number of fat droplets (median 169.8 (IQR 136.1–304.2)) did not increase with steatosis grade.

Conclusion: We have developed a novel digital analysis algorithm that accurately quantifies steatosis in whole liver slides. SFA percentages were in all cases lower than the percentage range resembled by the steatosis grade. This underlines the variability, typically associated with visual examination. Automated analyses of whole slide images benefits from objective and labor-free analysis. This algorithm can be incorporated when quantification of steatosis is warranted, such as in clinical trials studying efficacy of new therapeutic interventions in NAFLD.

Disclosure: Nothing to disclose.

P1261 FATTY LIVER PROMOTES GAMMA-GLUTAMYL TRANSPEPTIDASE ACTIVITY-INDUCED ARTERIAL PLAQUE FORMATION

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Introduction: Recent studies have provided evidence for a pivotal role of gamma-glutamyl transpeptidase (GGT) activity in arterial plaque formation. Furthermore, many studies have suggested a positive association of fatty liver with cardiovascular diseases, a well-known risk factor for cardiovascular disease (CVD). In a previous cross-sectional study, we reported a strong relationship between the combination of fatty liver and an elevated serum GGT level and the presence of carotid plaque (J Atheroscler Thromb. 2015; 22(10): 1051–60).

Conclusion: Coffee modulates the intestinal permeability and molecular expression of fatty acids mediators increasing fat oxidation and ameliorating fatty acids efflux. Coffee via gut-liver axis exerts a beneficial effect on the liver reducing hepatic steatosis.

Disclosure: Nothing to disclose.

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Introduction: Progression from non-alcoholic fatty liver disease (NAFLD) to steatohepatitis is associated with severity of steatosis. Accurate assessment of hepatic steatosis in liver biopsy specimens is thus important. Steatosis is graded using the semi-quantitative Brunt score (grade 0=0–5%; grade 1=5–33%; grade 2=33–66%; grade 3=66–90% of fatty droplets in a variable number of liver acinar fields). This assessment is labor-intensive which may affect reproducibility and accuracy of results. Digital quantification of the whole liver tissue slide, in contrast to random area selection, has the potential to overcome this.

Aims and Methods: We aim to develop and validate a steatosis quantification algorithm for automated digital analysis of whole slide images. For the training and validation cohort, hepatocellular-stained liver tissue slides from patients with or without NAFLD are included and digitally scanned at 20x magnification. Steatotic areas are manually annotated in representative biopsies from each steatosis grade. Next, thresholds for size and roundness parameters are identified by logistic regression to discriminate steatosis from surrounding liver tissue. The resulting algorithm produces a steatosis proportionate area (SPA; ratio of steatotic area to total tissue area described as percentage) which will be correlated to the steatosis grade. The software is implemented as a Java plugin in FIJI, in which digital whole slide images can be processed automatically with use of the Pathomation extension.

In liver tissue specimens of 61 NAFLD patients and 18 controls were included. The area under the curve of correctly classified steatosis by the algorithm was 0.970 (95% CI 0.968–0.973), p < 0.001. Accuracy of the algorithm was 91.9%, with a classification error of 8.1%. The median SFA per steatosis grade was: grade 0 1.41% (IQR 1.03–1.80%); grade 1 4.99% (IQR 2.97–9.31%); grade 2 13.65% (IQR 10.90–16.10%); and grade 3 16.34% (IQR 14.48–20.54%). SPA correlated significantly with steatosis grade (Rs = 0.85, CI. 0.749–0.902, p < 0.001). In post-hoc analyses, SFA increased significantly with each individual steatosis grade, except between grades 2 and 3. Median fat droplet size increased with steatosis grade (grade 0 108 um2 (IQR 94–124); grade 1 170 um2 (IQR 138–233); grade 2 249 um2 (IQR 218–309); grade 3 226 um2 (IQR 187–321), p < 0.001). Number of fat droplets (median 169.8 (IQR 136.1–304.2)) did not increase with steatosis grade.

Conclusion: We have developed a novel digital analysis algorithm that accurately quantifies steatosis in whole liver slides. SPA percentages were in all cases lower than the percentage range resembled by the steatosis grade. This underlines the variability, typically associated with visual examination. Automated analyses of whole slide images benefits from objective and labor-free analysis. This algorithm can be incorporated when quantification of steatosis is warranted, such as in clinical trials studying efficacy of new therapeutic interventions in NAFLD.

Disclosure: Nothing to disclose.
P1263 THE ASSOCIATION BETWEEN NONALCOHOLIC FATTY LIVER DISEASE AND MILD COGNITIVE IMPAIRMENT IN THE ELDERLY

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Introduction: Up to now, more and more researchers have found that metabolic syndrome (MS) and its elements are closely related to cognitive impairment. Since nonalcoholic fatty liver disease (NAFLD) was regarded as an element of MS in elderly subjects and could be a risk factor for cognitive impairment. Our goal was to assess the correlation between NAFLD and cognitive impairment in the elderly and the underlying mechanisms had not been revealed. Considering the elderly is the major population affected by cognitive impairment, and we lack effective treatment for serious cognitive impairment as dementia, MCI may be a good period to prevent serious cognitive impairment. Aims and Methods: We aimed to investigate the association between NAFLD and MCI and the possible underlying mechanisms in the elderly. A total of 392 elderly objects (60 years), with and without NAFLD were enrolled in this study and were subdivided into NAFLD group (n=191) and non-NAFLD group (n=201). Their clinical data including medical history, medica-
tions, blood pressure, body mass index (BMI), liver function, kidney parameters, glucose metabolism parameters, serum lipid profile, NAFLD fibrosis score and carotid plaques were collected, and logistic regression analysis was used to inves-
tigate the association between NAFLD and MCI.

Result: Detection rate of MCI in NAFLD group is significantly higher than that in non-NAFLD group (19.9% vs 10.4%, 2.6 vs 6.83, P=0.009) and NAFLD is an independent risk factor (OR =2.625, 95% confidence interval (CI) 1.250-5.512, P=0.001) for MCI after adjusting confounding variables such as age, gender, edu-
cation, cardiovascular disease and its risk factors. In addition, female (OR =2.775, 95%CI 1.363-5.651, P=0.005), unstable plaques of carotid (OR =2.736, 95%CI 1.311-6.620, P=0.026), history of stroke (OR =4.122, 95%CI 1.374-12.363, P=0.011), serum albumin (OR =0.908, 95%CI 0.840-0.982, P=0.015), fast glucose (OR =1.268, 95%CI 1.076-1.493, P=0.004), serum AST/ALT ratio (OR =1.370-5.900, P=0.001) were also indi-
cated with MCI in elderly. Among them, female, unstable plaques of carotid, a history of stroke, higher levels of fasting serum glucose and ALT/AST ratio were independent risk factors for MCI in the elderly.

Conclusion: NAFLD is independently associated with MCI in the elderly.

Disclosure: Nothing to disclose.

P1264 NONINVASIVE FIBROSIS SCORES (APRI, FIB 4 INDEX, BARD)-USEFUL TOOLS FOR EVALUATING FATTY LIVER DISEASE

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Introduction: Several noninvasive fibrosis assessment tests were developed in order to replace liver biopsy.

Aims and Methods: Our goal was to assess the correlation between APRI, FIB 4 Index and BARD score with transient elastography (TE) in diabetic patients with fatty liver disease. We conducted a prospective study from October 2016- December 2017 which included 413 diabetic patients out of which 353 had liver steatosis (mean age 61±8.5 years, 55.8% females, 44.2% males) evaluated by both serum markers (APRI, TE, plaquetes) as well as LSM (by TE: Fibroscan, Echosense,Paris, France, with incorporated CAP function). Based on specific formulas we calculated APRI, FIB 4 index and BARD score. We excluded all patients without liver steatosis at ultrasound. Liver stiffness measurement was considered reliable only if 10 valid values were obtained, with an IQR <30% and a success rate >60%. For differentiation between different stages of liver fibrosis, the following cut-off values were used: F2-F3: 7.10 kPa, F4:10.3 kPa. We considered mild steatosis if CAP =230-2575dB/m, moderate steatoses-
sis CAP >2575 dB/m, severe steatosis CAP >300 dB/m.

Results: Severe steatosis according to CAP measurements prevailed: 68.7% of patients, whereas the distribution between mild and moderate steatosis was similar -7.5% vs 14.1% (p <0.05). The patients' distribution regarding the different stages of fibrosis was the following: F0-F1=202 patients (57.2%), F2-F3=78 patients (22.2%), F4=73 patients (20.6%). Out of the 353 patients, 27.1% of them were overweight (BMI 25-29.9 kg/m2), whereas 64% patients were obese (BMI>30 kg/m2).

Conclusion: An APRI score <2, an FIB 4 score <2 and BARD score <2 can rule out advanced fibrosis quite accurately. These simple scores can be used as first line tests to rule out patients without advanced fibrosis in diabetic patients with fatty liver disease.

Disclosure: Speaker Fee: General Electric; Philips

Reference

P1265 ENHANCED LIVER FIBROSIS (ELF) SCORE FOR NONINVASIVE DIAGNOSIS OF NONALCOHOLIC STEATOHEPATITIS (NASH) WITH ADVANCED FIBROSIS

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Introduction: The Enhanced Liver Fibrosis (ELF) test is a noninvasive fibrosis panel composed of hyaluronic acid (HA), procollagen-3 N-terminal peptide (P3NP), and tissue inhibitor of metalloproteinase-1 (TIMP1). Nonalcoholic steato-
hepatitis (NASH) with advanced fibrosis is a significant risk factor for liver-related mortality. Noninvasive tests are needed to identify patients with these advanced stages of NASH who require lifestyle intervention and/or are eligible for enrolment in clinical trials.

Aims and Methods: Aim of the present study was to determine the diagnostic accuracy of ELF score for prediction of NASH with advanced fibrosis/cirrhosis. We enrolled consecutive patients with NASH admitted to two Austrian outpatient liver clinics who underwent liver biopsy. Histological NASH was defined according to the 2005 NASH diagnostic criteria and advanced fibrosis/cirrhosis was defined according to the 2008 NASH-CI, 2010 NASH/CSS, and 2016 ELFS scores. Patients with any recent or chronic viral infection, primary biliary cirrhosis, primary sclerosing cholangitis or autoimmune hepatitis, or who had undergone a liver transplant were excluded. Sensitivity, specificity, positive and negative predictive values were calculated for each diagnostic threshold using the Youden index. The optimal cut-off value was chosen as the best cut-off diagnostic threshold for ELF score in prediction of NASH with fibrosis stage F3-4. The ELF score >9.5 was identified by Youden index as the best cut-off for diagnosis of NASH with fibrosis stage F3-4 (sensitivity 86%, specificity 80%, PPV 51%, NPV 96%).

Conclusion: Based on our findings, ELF score shows high accuracy for noninvasive diagnosis of NASH with advanced fibrosis among patients with NASH. An ELF score >9.5 was found to reliably rule out NASH with fibrosis stage
P1265 THE ROLE OF CXCL10 FOR PREDICTING THE Cardiac Risk and THE OCCURRENCE OF THE METABOLIC SYNDROME IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Patients who have undergone liver transplantation often develop metabolic syndrome (MetS) and de-novo non-alcoholic fatty liver disease (NAFLD).

Aims and Methods: Our aim was to evaluate the cardiovascular risk in these patients using CXCL10, a serum biomarker whose expression levels have been associated with inflammatory diseases. CXCL10 was chosen considering that early changes of immune biomolecules in peripheral blood, reflecting immune status, could be candidate biomarkers able to diagnose or predict cardiovascular complications.

60 liver transplant recipients were assessed for clinical and biological features, performing abdominal ultrasound and transient elastography (TE) with controlled attenuation parameter (CAP), calculated non-invasive scoring systems for advanced fibrosis and NAFLD (APRI, FIB-4, NAFLD score). The cardiovascular risk was assessed using the Framingham risk score and the presence of metabolic syndrome.

Results: The main indication for liver transplantation was HCV (69% of patients) and the mean age 56 years. The paired t-test showed a significant association of CXCL10 with the presence of the metabolic syndrome (p < 0.001) and also with the non-invasive scores for advanced fibrosis and NAFLD. The metabolic syndrome was present in 51% of patients. 23% of patients had a Framingham risk score higher than 12 (10% mortality in 10 years) and 13% a score higher than 17 (30% mortality in 10 years). The multivariate analysis indicated as independent prediction factors for higher values of the Framingham score the serum levels of ferritin (p = 0.02) and urea (p = 0.03). The Spearman rank correlation test showed a significant association between the serum levels of CXCL10 and ferritin (p = 0.04), urea (p = 0.003), but also with uric acid (p = 0.04), an already established risk factor for cardiovascular mortality.

Conclusion: Serum CXCL10 could have an important role in assessing the cardiovascular risk in liver transplant recipients, especially when features of the metabolic syndrome are present. Our study is ongoing, aiming to establish the role of biomarkers, including CXCL10 in cardiovascular related mortality in these patients.

Disclosure: Nothing to disclose

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Non-alcoholic fatty liver disease (NAFLD) is considered to be the hepatic manifestation of metabolic syndrome (MS). A definition that includes NAFLD among the mandatory criteria for defining MS is still missing. In patients with NAFLD, the cardiovascular disease is the primary cause of death. Classical cardiovascular risk scores underestimate the cardiovascular risk in patients with MS. Aims and Methods: Our aim was to identify objective criteria in order to include NAFLD among the mandatory criteria for the definition of MS. We included 4 groups of patients: NAFLD with MS patients, NAFLD without MS patients, MS patients, and controls. We diagnosed with the presence of any three out of the five criteria (abdominal obesity, hypertriglyceridemia, hipo-HDL-cholesterolemia, impaired fasting glucose or T2DM), NAFLD diagnosis was established based on clinical examination and ultrasonography. Diagnosis of non-alcoholic steatohepatitis (NASH) was based on Fibronectin determination. For the cardiovascular risk (CVR) assessment, ultrasonic measurement of carotid intima-media thickness (CIMT-in cm, normal value 0.707 cm) was used. Anthropometric parameters and usual paraclinical parameters were recorded. Results: The CIMT values were higher than normal, except the control group (NAFLD + MS 0.134 ± 0.099, MS 0.149 ± 0.086, NAFLD 0.076 ± 0.051, controls 0.061 ± 0.023), with statistical difference between NAFLD + SM vs NAFLD patients (p = 0.002), but no statistical difference between NAFLD+SM vs SM patients (p = 0.21). In patients with NAFLD, the presence of NASH implied higher values of CIMT, statistically significant (0.09 vs. 0.06, p = 0.025).

Of the histological changes of NAFLD, there was a correlation between the presence of 2D CIMT values (p = 0.095, p = 0.004). The presence of T2DM nor impaired fasting glucose did not correlate statistically significantly with higher CIMT values in all the four groups of patients included in the study (p = 0.193, p = 0.345, p = 0.430, p = 0.261).

Of the classical metabolic risk factors, in patients with NAFLD, with and without MS, there was a statistically significant correlation between CMT values and abdominal circumference (p = 0.284, p = 0.005), body mass index (p = 0.227, p = 0.027), hypertension (p = 0.446, p < 0.001), and between the presence of hypertension and CIMT values in patients with NAFLD and MS (p = 0.497, p < 0.001).

Conclusion: The patients with NAFLD are a particular set of patients regarding cardiovascular risk. Taking into account the particularities of the patients with metabolic syndrome related to cardiovascular diseases development, we propose a new definition for MS. The current MS ordinances to be marked with 1 point (including impaired fasting glucose), except for the presence of T2DM, which is to be marked with 2 points, NAFLD – 1 point, and NASH – 2 points. The development there are less than 10% (8.7%, 10% possible). Of course, it is mandatory for this new model to be validated in further studies.

Disclosure: Nothing to disclose.

References


P2170 CLINICAL IMPACT OF COMORBIDITIES IN AN ITALIAN NAFLD COHORT

Introduction: Metabolic syndrome (MS) is a set of metabolic and cardiovascular risk factors, each of which contributes to predict chronic diseases, especially type 2 diabetes mellitus (T2DM) risk development than its individual components. Non-alcoholic fatty liver disease (NAFLD) is considered to be the hepatic manifestation of metabolic syndrome (MS). A definition that includes NAFLD among the mandatory criteria for defining MS is still missing. In patients with NAFLD, cardiovascular disease is the primary cause of death. Classical cardiovascular risk scores underestimate the cardiovascular risk in patients with MS. Aims and Methods: Our aim was to identify objective criteria in order to include NAFLD among the mandatory criteria for the definition of MS. We included 4 groups of patients: NAFLD with MS patients, NAFLD without MS patients, MS patients and controls. MS was diagnosed with the presence of any three out of the five criteria (abdominal obesity, hypertriglyceridemia, hipo-HDL-cholesterolemia, impaired fasting glucose or T2DM). NAFLD diagnosis was established based on clinical examination and ultrasonography. Diagnosis of non-alcoholic steatohepatitis (NASH) was based on Fibronectin determination. For the cardiovascular risk (CVR) assessment, ultrasonic measurement of carotid intima-media thickness (CIMT-in cm, normal value 0.707 cm) was used. Anthropometric parameters and usual paraclinical parameters were recorded.

Results: The CIMT values were higher than normal, except the control group (NAFLD + MS 0.134 ± 0.099, MS 0.149 ± 0.086, NAFLD 0.076 ± 0.051, controls 0.061 ± 0.023), with statistical difference between NAFLD + SM vs NAFLD patients (p = 0.002), but no statistical difference between NAFLD+SM vs SM patients (p = 0.21). In patients with NAFLD, the presence of NASH implied higher values of CIMT, statistically significant (0.09 vs. 0.06, p = 0.025).

Of the histological changes of NAFLD, there was a correlation between the presence of 2D CIMT values (p = 0.095, p = 0.004). The presence of T2DM nor impaired fasting glucose did not correlate statistically significantly with higher CIMT values in all the four groups of patients included in the study (p = 0.193, p = 0.345, p = 0.430, p = 0.261).

Of the classical metabolic risk factors, in patients with NAFLD, with and without MS, there was a statistically significant correlation between CMT values and abdominal circumference (p = 0.284, p = 0.005), body mass index (p = 0.227, p = 0.027), hypertension (p = 0.446, p < 0.001), and between the presence of hypertension and CIMT values in patients with NAFLD and MS (p = 0.497, p < 0.001).

Conclusion: The patients with NAFLD are a particular set of patients regarding cardiovascular risk. Taking into account the particularities of the patients with metabolic syndrome related to cardiovascular diseases development, we propose a new definition for MS. The current MS ordinances to be marked with 1 point (including impaired fasting glucose), except for the presence of T2DM, which is to be marked with 2 points, NAFLD – 1 point, and NASH – 2 points. The development there are less than 10% (8.7%, 10% possible). Of course, it is mandatory for this new model to be validated in further studies.

Disclosure: Nothing to disclose.

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P2171 N-3 POLYUNSATURATED FATTY ACIDS IN NAFLD (A DOUBLE-BLIND RANDOMISED PLACEBO-CONTROLLED STUDY)

Introduction: Non-alcoholic fatty liver disease (NAFLD) represents the most common chronic liver disease in western countries with a global prevalence of 25% in adults. It encompasses a wide spectrum of liver damage ranging from benign simple steatosis, to non-alcoholic alcoholic steatohepatitis (NASH), liver fibrosis and cirrhosis. The detailed pathogenetic mechanisms involved in the development of NAFLD remain unclear. There is no established pharmacological treatment of NAFLD. Weight reduction and lifestyle modification with increased physical activity stay the only effective therapeutic measures, but they are difficult to achieve and sustain. It has been reported that n-3 polyunsaturated fatty acids (PUFAs) are able to ameliorate hepatic steatosis and insulin resistance, whereas a diet deficient in PUFA with a high n-6/n-3 ratio could induce fatty liver. Up to date published papers using PUFA have yielded contradictory results.

Aims and Methods: The aim of the study was to assess the effects of administration of PUFA in development of NAFLD in patients during one year follow-up. We have examined 60 patients with metabolic syndrome and NAFLD in different stage of disease (simple steatosis (NASH=n=53) liver cirrhosis (n=5)). Patients were randomized into two groups: 30 used PUFA in daily dose 1.8 g (1.36 g of eicosapentaenoic acid and 1.36 g of docosahexaenoic acid in four divided doses; 30 patients used placebo in the same scheme. During one year follow-up were patients periodically examined – anthropometry (weight, waist circumference, or BMI) were observed in the patients enrolled in the study. On the other hand, there was a significant decrease in GGT activity in the placebo group (2.27 ± 2.11 vs. 1.43 ± 1.55 U/L, p = 0.0397), without any change in the placebo group (2.31 ± 3.57 vs. 2.03 ± 2.8 U/L, p = 0.664). Other observed biochemical parameters (ALT, AST, AIP, and bilirubin) remained unchanged in both groups. During the follow-up liver elastography did not change in either group, as well as percentage of fat in hepatic tissue measured by MRS with a high n-6/n-3 ratio could induce fatty liver. Up to date published papers using PUFA have yielded contradictory results.

Results: Of the 60 patients enrolled in the study were 45 men and 15 women, the mean age was 51.9 ± 12.2 years, the weight was 97.1 ± 15.2 kg and the mean BMI was 31.25 ± 4.23. There was no significant difference in any of these parameters among the monitored groups (PUFA versus placebo) at the beginning of the study. Similarly, between both groups there was no significant difference in other key parameters – ALT, GGT, or the percentage of fat in the liver tissue determined by MRS. After one year follow-up, no changes in anthropometric data (weight, waist circumference, or BMI) were observed in the patients enrolled in the study. On the other hand, there was a significant decrease in GGT activity in the PUFA group (2.27 ± 2.11 vs. 1.43 ± 1.55 U/L, p = 0.0397), without any change in the placebo group (2.31 ± 3.57 vs. 2.03 ± 2.8 U/L, p = 0.664). Other observed biochemical parameters (ALT, AST, AIP, and bilirubin) remained unchanged in both groups. During the follow-up liver elastography did not change in either group, as well as percentage of fat in hepatic tissue measured by MRS in both groups (PUFA 13.44 ± 7.7%, placebo 13.24 ± 9.1%).

Conclusion: We observed significant decrease in GGT serum activity after 12 months of PUFA administration, the total amount of liver fat remained unchanged. We conclude that PUFA could represent a potential agent in preventing the development of NAFLD in patients with metabolic syndrome. This work was supported by grants: AZV 15-28745A SVV 260370/2018

Disclosure: Nothing to disclose.
Introduction: Fatty liver is classified as alcoholic and nonalcoholic according to the amount of alcohol consumed. In some cases, however, both drinking and overnutrition are involved in the development of fatty liver. Furthermore, epidemiological studies have demonstrated that light to moderate alcohol consumption appears to protect against fatty liver. The relation between alcohol and fatty liver possibility varies in each patient, depending on several cofactors. To make recommendation to modify patients' lifestyle, it may be not appropriate to distinguish alcoholic fatty liver and nonalcoholic fatty liver by a simple quantitative threshold of alcohol intake.

Aims and Methods: To answer whether they should drink or stop drinking, we aimed to distinguish alcohol-induced fatty liver and nutrition-induced fatty liver among drinkers. We obtained clinical and laboratory data from 8,879 Japanese subjects who underwent ultrasonography as a part of systematic health checkups at Junpaku Health Maintenance Center between 2006 and 2010, excluding individuals with the concurrent liver disease, any missing components of data, or missing follow-up study. The amount of alcohol consumed was stratified into following 5 groups: <70 g/week, 70-140 g/week, 140-280 g/week, 280-420 g/week, >420 g/week. We hypothesized that drinking cut down on alcohol intake would be required for remission of the alcohol-induced fatty liver and that remission of fatty liver without cutting down on alcohol consumption would indicate nutrition-induced fatty liver. Among patients who had remission of fatty liver, we compared those with cutting down on alcohol consumption (group A) and those without (group N) to elucidate the difference between them.

Results: In 8879 examiners, 31% had fatty liver and 60% reported habitual drinking at baseline. The prevalence of fatty liver in drinkers was significantly lower than that in non-drinkers (40% vs. 60% for men and 15% vs. 20% in women). During the observation period, the remission of fatty liver was observed in 345 out of 1,756 drinkers with fatty liver at baseline (20%). While the median amount of alcohol consumed had decreased from 154 g/week to 132 g/week in group A (n = 30), it increased from 132 g/week to 154 g/week in group N (n = 265). In comparison between group A and group N, significant differences were found in high-density lipoprotein levels (60 mg/dl vs. 55 mg/dl as median, P < 0.025) and in uric acid levels (6.4 mg/dl vs. 6.2 mg/dl, P = 0.025). When cases were stratified by the amount of alcohol consumed at baseline, the difference in HDL levels remained significant in cases with alcohol intake of >420 g/week (81 mg/dl vs. 56 mg/dl, P = 0.029). Among those without medication for dyslipidemia or hyperuricemia (n = 316), receiver operating characteristic analysis indicated that the optimal cut point for high-density lipoprotein level and uric acid level to distinguish group A and group N is 63 mg/dl (AUC = 0.570) and 7.0 mg/dl (AUC = 0.587), respectively. In cases with high-density lipoprotein levels >63 mg/dl and uric acid levels >7.0 mg/dl, group A accounted for 80%.

Conclusion: High-density lipoprotein levels and uric acid levels are useful to judge whether the fatty liver was induced by alcohol consumption or by overnutrition. Abstinence or cutting down on alcohol intake may resolve fatty liver in patients with high-density lipoprotein levels >63 mg/dl and uric acid levels >7.0 mg/dl.

Disclosure: Nothing to disclose

References

P1273 GENDER DIFFERENCES IMPACT THE PD-1 AND PD-L1 EXPRESSION ON PERIPHERAL T AND B CELLS IN PATIENTS WITH ALCOHOLIC LIVER DISEASE

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Introduction: Exposure to excessive alcohol consumption, its breakdown metabolites and gut-derived endotoxins dysregulates immune signaling. As a result the number of regulatory response and immunopathological tract and other organs may occur. The programed cell death (PD-1) receptor and its ligand PD-L1 play a critical role in inhibition of self-reactive and inflammatory effector cells and the protection against immune-mediated tissue damage. Analysis of expression of the PD-1/PD-L1 expression on peripheral T and B lymphocytes, its correlation with markers of inflammation and the severity of liver dysfunction in the course of alcoholic liver disease (ALD).

Fifty six inpatients with ALD (38 males, 18 females, aged 49.23 ± 10.66) were prospectively enrolled and assigned to subgroups based on their: 1) gender, 2) severity of liver dysfunction (Child-Pugh, MELD scores, mDF), 3) presence of ALD complications, and followed for 30 days. Twenty five age- and gender-matched healthy volunteers, who consumed no more than 10 g alcohol per day, served as the control group. Flow cytometric analysis of the PD-1/PD-L1 expression on peripheral lymphocyte subsets were performed.

Results: The general expression of PD-1 and PD-L1 on T and B cells did not differ between the ALD and control group. Although, when the groups were analyzed based on their gender, significantly higher expression of PD1 and PD-L1 was observed in females compared to controls. ALD females with severe alcoholic hepatitis (AH) and mDF>32 or MELD>20 showed significantly higher expression of PD-1 on CD19+ B cells and PD-L1 on all studied T and B subsets. The same pattern of the PD-1/PD-L1 expression was observed when ALD females were compared with ALD males, including the subgroups with mDF>32 and MELD>20. No correlations of PD-1+/PD-L1+ expression with mDF, CTP and MELD scores, nor with complications of ALD were observed, but significant correlations of CD19+PD-L1+ frequencies with all conventional markers of inflammation (i.e. white blood cell and neutrophil counts, C-reactive protein and neutrophil-to-lymphocyte ratio) were found.

Conclusion: Gender-related differences in the PD-1/PD-L1 expression on peripheral T and B cells may account for the different susceptibility to ethanol-related liver damage in males and females. Upregulation of PD-1/PD-L1 expression paralleled the severity of AH and liver dysfunction in females with ALD.

Disclosure: Nothing to disclose
P1275 CALCULATION OF LILLE MODEL BETWEEN DAY 3 AND 4 CAN ACCURATELY PREDICT CORTICOSTEROID RESPONSE: A SINGLE-CENTER RETROSPECTIVE STUDY

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Introduction: Patients with severe alcoholic hepatitis (SAH) should be treated with corticosteroids (CT). Response to CT is assessed at 1 week using the Lille Model score (LM). Adverse effects of CT specially the risk of infections raise concerns among practitioners. A recent study demonstrated that LM calculated at day 4 is as accurate as LM calculated at day 7. This finding needs further validation.

Aims and Methods: To assess the accuracy of the LM calculated between day 3 and 4 in predicting CT response compared with the standard day 7.

Single-center retrospective study that included all patients admitted between January 2012 and December 2017 with a diagnosis of SAH defined by clinical and laboratory evidence and a Maddrey Discriminant Function (DF) ≥ 32. Response to CT treatment was determined by calculation of the LM score at days 3 and 4 and then at day 7 according to the cutoff > 0.45. Statistical analysis was performed with SPSS v.24 Agreement between LM3-4 and LM7 was assessed by the Cohens kappa (κ). Receiver operating characteristics (ROC) curves were used to compare accuracy between LM3-4 and LM7 in predicting 30-day mortality.

Results: 49 patients with SAH were included in the study. 81.6% were male and the mean age at the time of treatment was 60 (± 8.73) years. Median DF was 71.2 (40-195.2). 30 patients were treated with corticosteroids (CT). 16 patients had their LM score calculated at day 3, 12 at day 4 and 26 at day 7. Median LM3-4 and LM7 for patients who received CT was 0.45 (0.10-0.97) and 0.37 (0.10-0.98) respectively (p = 0.036). A substantial agreement was found between the two scores in predicting CT treatment (κ = 0.92, p < 0.0005). 30-day mortality was 40.8% (n = 20). There were no significant differences between LM3-4 and LM7 in predicting 30-day mortality (AUC 0.750 vs. 0.735 p = 0.615, respectively).

Conclusions: In the context of new treatment alternatives for SAH, the Lille Model score can be an important tool for clinical practice.

Disclosure: Nothing to disclose

References

P1276 SIGNIFICANCE OF CIRCULATING MEDIATORS RELEASED FROM ACTIVATED NEUTROPHILS IN PATIENTS WITH ALCOHOLIC LIVER DISEASE

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Introduction: Neutrophils are the first-line effectors of human innate immune system. Inflammatory dysregulation and neutrophil infiltration are hallmarks of alcoholic liver disease (ALD). Given their destructive potential, extracellularly released neutrophil enzymes should be carefully controlled to avoid damage to the liver.

Aims and Methods: Assessment of the systemic profile of neutrophil-derived mediators i.e. neutrophil elastase (NE), myeloperoxidase (MPO), as well as alpha-antitrypsin (AAT)- a potent inhibitor of neutrophil proteases, with emphasis on their potential relevance in the course of ALD.

Sixty-two patients with ALD (47 males, 15 females, aged 49.2±9.9) were prospectively recruited and assigned to subgroups based on their 1/2 severity of liver dysfunction (Child-Pugh, MELD scores, mDF). 3/ presence of ALD complications, and followed for 30 days. Twenty four age-, sex- and ethnicity-matched healthy volunteers served as the control group. Selected plasma markers of neutrophil activation were quantified using immunoenzymatic ELISAs. Correlation coefficients between their blood concentrations and (i) indicators of systemic inflammation (the neutrophil-to-lymphocyte ratio, C-reactive protein, white blood cell and neutrophil counts), (ii) liver dysfunction severity scores (Child-Pugh, MELD, mDF) and (iii) ALD complications were calculated.

The receiver operating curves (ROC) for studied molecules were constructed and their areas under the curve (AUCs) checked in order to assess their accuracy in predicting the degree of liver failure and the development of ALD complications.

Results: Concentrations of MPO and NE were significantly increased in the blood of patients with ALD in comparison with controls, but the AAT level was not different. ALD females presented with higher MPO levels in comparison with ALD males. There were no gender-related differences in NE levels in ALD group. NE, but not MPO, correlated with MELD and mDF scores. MPO, but not NE correlated with standard ALD complications. ALD subgroups with mDF > 32, Child class C and hepatic encephalopathy presented with significantly higher NE, but not MPO levels.

Conclusion: Our results support the value of MPO and NE in the ALD assessment. MPO seems to be an inflammatory marker, while NE the disease severity indicator. The higher systemic NE/AAT ratio in the course of ALD may facilitate the expansion of the inflammatory cascade. Gender-related differences in neutrophils’ activation in ALD may impact the different susceptibility to toxic injury in male and females.

Disclosure: Nothing to disclose

References

P1277 EVALUATION OF CYTOSTATIC-INDUCED LIVER INJURY RISK IN PATIENTS WITH ACUTE MYELOID LEUKAEMIA

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Introduction: Chemotherapy (CHT) for acute myeloid leukaemia (AML) is accompanied by the risk of hepatotoxic reactions, severity of which influences patients’ further management and leads to the need of drugs dose reduction. The main
negative prognostic factor, which does not depend on tumor morphology and patients' state of health. Moreover, adherence to the dosage and administration regimens of cytostatic agents. Timely performed diagnostics of hepatotoxic reactions, induced by cytostatic agents, and their prophyllaxis play the main role.

**Aims and Methods:** to study the frequency and character of hepatotoxic reactions in patients with AML depending on morphologic variant according to the FAB classification and prescribed CHT scheme.

A total of 63 patients with firstly diagnosed AML and normal liver function tests were examined, 29 (46%) of them were females and 34 (54%) – males. ECOG performance status was I-II, Karnofsky index was 60–80%. Patients were divided into groups: I (n = 27) – patients with AML M0, M1, M5 according to FAB-criteria; II (n = 36) – patients with AML M2, M3 according to FAB-criteria.

Results: Conduction of the 1-st remission induction course in AML patients with M0-M1 was accompanied by the 1-st grade hepatotoxic reactions in 2 (7.4%) patients and in AML patients with M2-M3 variants – in 11 (30.5%) patients, in 8 (22.2%) out of them the grade I of severity was detected, in 3 (83%) – grade II. Hepatotoxic reactions in 2 (7.4%) patients with AML M0, M1 and 3 patients with the group I were characterized as cytolytic. Among the patients of the group II with AML M0 and M3 variants the next types of hepatotoxic reactions were registered: in 2 (5.5%) – cytolytic, in 4 (11.1%) – cholestatic, and in 5 (13.9%) – mixed.

Hepatic function state was restored until 28-th day in all groups of comparison, where liver tests disturbances were observed on the 7-th and 14-th days.

**Conclusion:** M0-M1, M0-M3 variants of AML are associated with an increased risk of hepatotoxic reactions, that is determined by hemoblastosis morphology and higher toxicity of CHT regimens with etoposide inclusion.

Disclosure: Nothing to disclose.

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**P1279 PREVALENCE AND PREDICTIVE FACTORS OF CIRRHOTIC CARDIOMYOPATHY IN A COHORT OF CIRRHOTIC PATIENTS**

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**Introduction:** Cirrhotic cardiomyopathy (CCM) is a relatively new concept that currently appears as a particular clinical entity, characterized by impaired contractile response to stress, diastolic dysfunction and electrophysiological abnormalities in the absence of a known cardiac disease. Data on the epidemiology and natural history of CCM is still lacking.

**Aims and Methods:** We aimed to determine the prevalence of CCM and investigate its predictive factors in patients with liver cirrhosis. This cross-sectional study was conducted on all cirrhotic patients (N=109) who were admitted in our department from September 2016 to May 2017. Patients were divided into two groups: liver cirrhosis due to alcohol and/or non-alcoholic, severe anemia (Hemoglobin <7 g/dl) or recent bleeding (<1 month) were excluded (N=33). Resting ECG was done in all patients. QTc interval of >0.44 sec was considered as prolonged. A detailed two-dimensional echocardiography was also performed in all patients. CCM was considered present when diastolic and/or systolic dysfunction was diagnosed at rest, together with supporting criteria such as electrophysiological abnormalities, based on the criteria of the Montreal 2005 consensus. A stepwise Cox regression model was fitted to determine factors associated with the diagnosis of CCM. All statistical analyses were performed using the SPSS 21.0 version.

Results: A total of 76 patients were included in this study, out of which 45 (59%) were males and 31 (41%) were female. The mean age was 54 years (±5.2). The most common etiology was hepatitis B (38.2%). Median Child Pugh and MELD scores were 7[5-12] and 11[7-33], respectively. Twenty-five patients (32.9%) had ascites. Diastolic dysfunction was noted in 39 patients (51.3%) while 4 patients (5.3) showed evidence of systolic dysfunction. A prolonged QT interval was found in 33 patients (43.5%) while CCM was then diagnosed in 11 patients (53.9%). In multivariate analysis, 3 independent predictive factors were identified: age>50 years (OR 1.05; CI 95% :1.003–1.103; p = 0.039), female gender (OR 3.06; CI 95%; 1.029–8.778; p = 0.044) and Child Pugh score >9 (OR 4.36; CI 1.328–14.331; p = 0.014).

**Conclusion:** Cirrhotic cardiomyopathy is a frequent complication of cirrhosis. Given its association with the severity of liver disease, we recommend cardiac assessment in all Child Pugh B and C cirrhotic patients.

Disclosure: Nothing to disclose.
P1281 Endoscopic Variceal Ligation Followed by Argon Plasma Coagulation against Endoscopic Variceal Ligation alone: Results of 5.5-Year Follow Up
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Introduction: Our group had started a randomised controlled trial in April 2012 to study the effect of argon plasma coagulation (APC) after esophageal varices eradication using endoscopic variceal ligation (EVL) on recurrence of esophageal varices after previous bleeding episode. Recurrence of esophageal varices during 2.5 years was 21% in the APC group against 68% in the EVL only group. (P = 0.003). No one in the APC group needed rebleeding while 63.2% of the EVL only group underwent rebleeding (P = 0.001). These results were published (1).

Aims and Methods: To continue the follow up of both groups to determine the ability of Argon plasma coagulation to maintain its efficacy in prevention of esophageal varices recurrence over a longer period (5.5 years). Endoscopic follow up intervals in the APC group were increased to be every 12 months, while in the EVL only group they became every 6 months if there were no recurrent varices and every 3 months if there were small recurrent varices without risk of rebleeding.

Results: In the APC group 35.3% of cases experienced recurrence of esophageal varices during the 5.5-year follow up against 93.8% of cases in the EVL only group (P < 0.001). Still no one from the APC group needed rebleeding as all recurrent varices were small and without risk signs. In the EVL only group 71.1% of cases needed rebleeding.

Conclusion: APC after esophageal varices eradication using EVL can decrease the risk of esophageal varices recurrence and the need for rebleeding over long period with the possibility of decrease in endoscopic follow up intervals. This also can decrease the burden on endoscopic units especially in countries where liver diseases are endemic.

Disclosure: Nothing to disclose.

Reference

P1282 GLOMERULAR FILTRATION RATE BASED ON SERUM CREATININE IN DECOMPENSATED LIVER CIRRHOSIS – COMPARATIVE STUDY WITH THE “ROYAL FREE HOSPITAL” FORMULA

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Introduction: Renal dysfunction is a marker of poor prognosis in liver cirrhosis. Serum creatinine tends to overestimate the true value of the glomerular filtration rate (GFR) in these patients. The GFR measured by the RFH formula performed in cases of decompensated liver cirrhosis admitted to a tertiary center during a 7-year period. Renal dysfunction was considered clinically significant for GFR lower than 30 mL/min/m², being that this GFR values generally imply modification of therapeutic strategies in clinical practice.

Results: A total of 418 cases were evaluated [78.7% men (n = 329), mean age 66.25 ± 11.79 years]. The median serum creatinine was 0.91 mg/dL (IQR 0.7–1.36 mg/dL). Death occurred within the first 100 days after admission in 20.1% of the patients. At admission, the GFR was less than 30 mL/min/m² in 15.3% (MDRD-4), 19.6% (MDRD-6), 16% (CKD-EPI) and 21.5% (RFH) of the cases.

The GFR measured by the RFH formula showed a strong correlation with the other formulas (MDRD-4: r = 0.97; p < 0.001; MDRD-6: r = 0.98; p < 0.001; CKD-EPI: r = 0.95; p < 0.001).

Active infection and ascites were associated with the lowest mean value of GFR measured in all formulas (Active disease, MDRD-4 p = 0.008; MDRD-6 p = 0.003; CKD-EPI p < 0.001; RFH p = 0.007; Ascites: MDRD-4 p = 0.001; MDRD-6 p = 0.001; CKD-EPI p = 0.001; RFH p = 0.001).

The data concerning early mortality (< 100 days) showed that average survival was significantly lower for GFR < 30 mL/min/m² calculated by RFH (GFR > 30, mean 47.2 ± 28.2 mL/min/m²; GFR < 30, mean 32.8 ± 28.4 mL/min/m²; p = 0.040), but not when the GFR was estimated by CKD-EPI (GFR > 30, mean 46.01 ± 29.04 mL/min/m²; GFR < 30, mean 30.53 ± 24.91 mL/min/m²; p = 0.06), MDRD-4 (GFR > 30, mean 45.59 ± 29.05 mL/min/m²; GFR < 30, mean 31.57 ± 25.51 mL/min/m²; p = 0.097) and MDRD-6 (GFR > 30, mean 46.73 ± 28.42 mL/min/m²; GFR < 30, mean 32.10 ± 27.95 mL/min/m²; p = 0.05) equations.

Conclusion: In this study, the new RFH formula had a strong correlation with the other formulae based estimated glomerular filtration rate equations. This supports that the most common formulas can still be used in the clinical management of patients with cirrhosis.

However, a GFR under the value of 30 mL/min/m² estimated by the RFH formula (in comparison with other formulas) was related with a lower survival at 100 days.

Disclosure: Nothing to disclose.

Reference
P1285 THE NEW RECOMMENDED CRITERIA FOR SEPSIS ARE INAPPROPRIATE FOR PATIENTS WITH DECOMPENSATED CIRRHOSIS

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Introduction: The new criteria of sepsis published in 2016, based on the SOFA Syndrome (Systemic Inflammatory Response Syndrome) score, do not have a specific focus on infection and sepsis. Early diagnosis of sepsis is crucial in patients with decompensated cirrhosis. Recent studies have shown a good performance of presepsin and resistin as early diagnostic tools for sepsis but their performances in patients with cirrhosis is not known.

Aims and Methods: The aims of the study were: 1) to identify the most accurate definition for sepsis diagnosis in cirrhosis using the 28-day mortality as endpoint; 2) to compare the diagnostic performances of presepsin, resistin and as early markers in patients with decompensated cirrhosis.

Results: Eighty-two patients were included with a sex-ratio at 0.9 and a mean age of 59±9 years (23–74). The main comorbidities were diabetes mellitus (25%) and hypertension (20%). Hepatitis C was the most common etiology of cirrhosis (42%). Child-Pugh score was mainly C (63%) and 13±3. Main MELD score was 10±6. Bacterial infection was the main cause of decompensating (27%) 30-day mortality was 16%. In comparison with the surviving group, deceased patients had similar demographic characteristics. NACELD-ACLF was ≥2 in 15% of patients. Patients who met criteria for NACELD-ACLF had an overall 20% 30-day survival vs 85% in patients without NACELD-ACLF (p < 0.001). RR was 22 (95% CI 3·47–91·15).

Conclusion: NACELD-ACLF might predict 30-day mortality in cirrhotics in decompensation with a good sensitivity and specificity. However, it concerns only 15% of patients admitted for acute decompensation of cirrhosis which makes it a very restrictive score.

Disclosure: Nothing to disclose

P1286 LIMITED DIAGNOSTIC PERFORMANCE OF CONTROLLED ATTENUATION PARAMETER FOR ASSESSING HEPATIC STEATOSIS IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE AND PORTAL HYPERTENSION

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Introduction: Transient elastography (TE) assesses liver stiffness as a measure of liver fibrosis but is influenced by hepatic perfusion pressure. TE-based controlled attenuation parameter (CAP) is an non-invasive marker for hepatic steatosis. However, the diagnostic performance of CAP has yet to be investigated in patients with advanced chronic liver disease (ACLD)/portal hypertension (PH); hepatic venous pressure gradient (HVPG) ≥6 mmHg.

Aims and Methods: Eighty-two patients with liver stiffness values ≥10 kPa and/or HVPG ≥6 mmHg undergoing simultaneous liver biopsy, CAP and HVPG measurement were included in this retrospective analysis. Steatosis (S) was histologically graded according to the Banff classification.

Results: Sixty-four (77.2%) Child-Pugh B and 8 (9.1%) Child-Pugh C patients with a mean MELD Score of 11 (SD ±4) points were included. The underlying causes of liver disease were viral hepatitis in 22 (25.0%), non-alcoholic fatty liver disease in 12 (13.6%) and alcoholic liver disease in 11 (12.5%) patients. Twenty-two (25.0%) patients had other etiologies, while the cause was cryptogenic in 21 (23.9%). Median HVPG was 16 (IQR:10–19) mmHg, median liver stiffness was 27±4 (IQR:16.2–48.9) kPa and mean CAP value was 221 (SD ±75) dB/m.

According to histology, 47 (53.4%) patients had no steatosis (S0), 28 (31.8%) had S1, 11 (12.5%) had S2, and 2 (2.3%) had S3. CAP was significantly different between patients with any hepatic steatosis (S1/S2/S3 vs. S0): 25±22 (SD ±70) kPa and with S0: 20±2 (SD ±72) kPa (p = 0.002). The AUROC for diagnosing any hepatic steatosis (S1/S2/S3 vs. S0) was 0.692 (95% CI: 0.582–0.802) in the overall cohort, 0.667 (95% CI: 0.552–0.783) in patients with PH, 0.629 (95% CI: 0.497–0.761) in the subgroup with clinically significant portal hypertension (CSPH, HVPG≥10mmHg; n = 69). Among patients with cirrhosis diagnosed by histology (n = 56), the AUROC was 0.607 (95% CI: 0.459–0.756). Applying the previously defined cut-off of 248 dB/m, sensitivity and specificity of CAP for diagnosing any steatosis (S1/S2/S3 vs. S0) was 83±% and 76.6% with a positive predictive value (PPV) and a negative predictive value (NPV) of 64.5% and 63.2% in the overall cohort.

CAP correlated with the percentage of steatotic hepatocytes (Spearman’s ρ = 0.402, p = 0.001) and liver stiffness (ρ = 0.225, p = 0.035). HVPG neither correlated with percentage of steatotic hepatocytes (p=0.055; p=0.654), histological steatosis grade (p=0.026; p=0.829), nor with CAP values (p=0.054; p=0.653).

Conclusion: The diagnostic performance of CAP for assessing hepatic steatosis seems to be limited in patients with ACLD/PH, especially in patients with CSPH or cirrhosis based on histology.

Disclosure: Nothing to disclose

P1287 THE VALUE OF ULTRASOUND-BASED ELASTOGRAPHIC METHODS FOR RULING OUT THE PRESENCE OF ESOPHAGEAL VARICES IN LIVER CIRRHOTIC PATIENTS

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Introduction: Ultrasound-based elastographic methods are non-invasive techniques for the evaluation of liver stiffness that might have also a place in the assessment of portal hypertension.

Aims and Methods: The aim of this study was to evaluate the value of 5 ultrasound-based elastographic methods for rule out the presence of esophageal varices in patients known with liver cirrhosis.

The study included 69 consecutive subjects diagnosed with liver cirrhosis (patients known with history of chronic liver disease with clinical, biological, ultrasound, endoscopic or histological signs of liver cirrhosis), in whom liver stiffness (LS) was evaluated in the same session by means of 5 elastographic methods and for 2D-SWE and the LogiqE9, a Cardiovascular Machine (GE). Reliable LS measurements were defined as follows: for TE, ElastIQ, TQO and 2D-SWE.GE: the median value of 10 measurements and for 2D-SWE.SI the mean value of 3 measurements acquired in a homogenous area.

Results: In 50 patients out of 69, all 5 elastographic methods had valid measurements and were included in the final analysis. 19/50 patients from the study group had varices, while 31/50 did not have varices.
The best cut-off values for “rule out” esophageal varices for the 5 different techniques are presented in the following table:

<table>
<thead>
<tr>
<th>Method</th>
<th>Cut-off</th>
<th>Se</th>
<th>Sp</th>
<th>PPV</th>
<th>NPV</th>
<th>LR+</th>
<th>LR-</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE (1)</td>
<td>≤21.5 kPa</td>
<td>85.7%</td>
<td>73.9%</td>
<td>66.7%</td>
<td>89.5%</td>
<td>0.54</td>
<td>1.2</td>
<td>0.67</td>
</tr>
<tr>
<td>VTT (2)</td>
<td>≤1.88 m/s</td>
<td>90%</td>
<td>23.3%</td>
<td>43.9%</td>
<td>77.8%</td>
<td>0.48</td>
<td>1.1</td>
<td>0.57</td>
</tr>
<tr>
<td>ElastPQ (3)</td>
<td>≤10.4 kPa</td>
<td>95%</td>
<td>43.2%</td>
<td>82.2%</td>
<td>80%</td>
<td>1.1</td>
<td>0.38</td>
<td>0.66</td>
</tr>
<tr>
<td>2D-SWE:SS (4)</td>
<td>≤13.2 kPa</td>
<td>95%</td>
<td>33.3%</td>
<td>45.2%</td>
<td>87.5%</td>
<td>0.24</td>
<td>1.24</td>
<td>0.58</td>
</tr>
<tr>
<td>2D-SWE:GE (5)</td>
<td>≤12.2 kPa</td>
<td>95%</td>
<td>53.3%</td>
<td>51.7%</td>
<td>76.2%</td>
<td>0.48</td>
<td>1.61</td>
<td>0.68</td>
</tr>
</tbody>
</table>

[The best cut-off values for “rule out” esophageal varices for the 5 different elastography techniques]

Conclusion: Ultrasound based elastographic methods seem to have the same performance for rule out the presence of esophageal varices in patients with liver cirrhosis.

Disclosure: Speaker fee from General Electric; Philips

P1288 TRANSJUGULAR LIVER BIOPSY PERFORMED BY HEPATOLOGISTS TREATED IN HEPATIC VENOUS PRESSURE GRADIENT MEASUREMENTS IS SAFE AND PROVIDES IMPORTANT DIAGNOSTIC AND PROGNOSTIC INFORMATION

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Introduction: Transjugular liver biopsy (TJLBX) represents an alternative to percutaneous liver biopsy, especially in patients with impaired coagulation. Here we describe our experience with TJLBX performed by hepatologists being experienced in HVPG measurements.

Aims and Methods: 445 TJLBX (16G Menghini aspiration needle) of 399 adult patients with a diagnosis of liver cirrhosis. Complications occurred in 28 patients (6.3%) including 22 (4.9%) with minor complications (subcapsular capsule perforation in 11, hematomas in 7, extraperitoneal bleeding in 3, small pleural effusion in 2, abdominal pain in 2, chest pain in 2, subcapsular hematoma in 1), and 6 (1.5%) with major complications (subcapsular hematoma in 4, hepatic abscess in 1, major hemorrhage in 1). No deaths due to TJLBX were observed.

Aim of the study was to assess the diagnostic and prognostic value of TJLBX in patients with liver cirrhosis. The diagnostic performance of rule out high-risk varices for the 5 different

Disclosure: Nothing to disclose

P1289 DIAGNOSTIC ACCURACY OF BAVENO VI CRITERIA FOR SCREENING OF VARICES IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE – A META-ANALYSIS

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Introduction: The Baveno VI criteria based on platelet count > 150x10^9 cells/L and a portal pressure measurement (HVPG) <20 kPa have been proposed for identification of compensated advanced chronic liver disease (cACLD) patients who could safely avoid screening endoscopy. However, evidence are inconsistent. We performed a systematic review and meta-analysis to assess the diagnostic accuracy of the Baveno VI criteria for diagnosis of any size varices and varices needing treatment in patients with cACLD.

Methods: We systematically searched MEDLINE, EMBASE, Cochrane Library and grey literature sources through April 2018. We included diagnostic studies that assessed the accuracy of the Baveno VI criteria for any varices or high risk varices (HRVs), as defined by the authors, in patients with cACLD. We evaluated studies that utilized upper endoscopy as reference standard. We evaluated study quality by using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool.

Results: We included 27 studies with 5091 participants. Fourteen studies (2916 patients) provided data for varices of any size and 17 studies (3175 patients) evaluated the criteria for HRVs. All studies were cross-sectional with sample size ranging from 32 to 774 patients. Time interval between liver stiffness measurement and endoscopy was usually 6 to 12 months. The median prevalence of varices of any size was 0.38 (range 0.15–0.72) and the median prevalence of HRVs was 0.10 (ranged from 0.04 to 0.20). Most of the studies were retrospective and deemed at unclear risk of bias. Pooled sensitivity of Baveno VI criteria for diagnosis of any varices was 88% (95% CI 82 to 92), specificity 43% (95% CI 32 to 55), positive likelihood ratio (LR+) 1.5 (95% CI 1.3 to 1.8), negative likelihood ratio (LR-) 0.27(95% CI 0.22 to 0.34), pooled sensitivity for HRVs was 98% (95% CI 93 to 99), specificity 27% (95% CI 22 to 33), positive likelihood ratio (LR+) 1.3 (95% CI 1.2 to 1.4), negative likelihood ratio (LR-) 0.09(95% CI 0.03 to 0.27).

Conclusion: The Baveno VI recommendations can adequately rule out the presence of clinically significant varices in cACLD patients. They could be used as a triage test since they can identify low risk patients who could safely avoid screening endoscopy.

Disclosure: Nothing to disclose

P1290 ABILITY OF MELD SCORE AND PLATELET COUNT FOR RULING-OUT HIGH-RISK VARICES IN COMPENSATED LIVER CIRRHOSIS PATIENTS

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Introduction: Portal hypertension is a major pathological alteration in liver cirrhosis. Upper gastrointestinal (GI) endoscopy is generally required in these patients since their management is defined by the presence and type of esophageal varices. Since Baveno VI, the use of fibroscan and platelets count is recommended to avoid endoscopy in some low-risk patients. Recently, new evidence about the usefulness of MELD score and platelets count to avoid endoscopy mainly in patients with HCV-related cirrhosis has been published.

Aims and Methods: We aimed at assessing the accuracy of MELD and platelets count to rule out high-risk varices in a population of mainly alcohol-related cirrhosis. A retrospective analysis of patients with compensated cirrhosis of any etiology under follow-up at our Liver Unit was performed. Patients with Child-Pugh score 5 or 6 (A), upper endoscopy indicated for evaluation of portal hypertension over the last 5 years, and blood analysis done ≤6 months before or after endoscopy, were included. Patients with previous variceal bleeding, history of endoscopic varical ligation, splenectomy, liver transplantation or esophageal or gastric surgery were excluded. High-risk varices were defined as large varices or varices with red spots. Results are shown as mean and percentages and analyzed by chi-square test and Student’s t test. Accuracy of MELD and platelets count for predicting high-risk varices was calculated.

Results: 115 patients were included (80.3% male), with a median age of 57 years (range 17–81). The main aetiology was alcohol (72.1%), followed by virus (12.1%) and steatohepatitis (6.8%). Upper GI endoscopy excluded the presence of varices in 60% of patients. 32 patients (27.8%) had small varices without red spots (low-risk), whereas high-risk varices were detected in 14 patients (12.1%). Patients with low-risk and high-risk varices were similar in terms of gender, age, aetiology and MELD score (7.57 vs 8.71; p = 0.063). Platelet count was significantly lower in patients with high-risk varices (86.071 vs 134.039/pL; p < 0.01). High-risk varices were never present in patients with a MELD score of 6 and a platelet count ≥100,000/pL (n = 36). Only one out of 62 patients (1.61%) with MELD ≤8 and platelets ≥100,000/pL had high-risk varices. A negative predictive value of 90.4% for high-risk varices was obtained in patients with MELD ≤8 and platelets >150,000/pL.

Conclusion: A MELD ≤8 together with a platelet count ≥150,000/pL allows avoiding upper GI endoscopy for esophageal varices screening in patients with liver cirrhosis.

Disclosure: Nothing to disclose
Introduction: Non-alcoholic fatty liver disease (NAFLD) is a growing disease worldwide and is an increasing cause of liver transplantation when progresses to non-alcoholic steatohepatitis (NASH) and cirrhosis. NAFLD may also complicates liver transplant recipients especially in patients who have undergone liver transplantation for NASH and cryptogenic cirrhosis.

Aims and Methods: This study aimed to investigate prevalence and risk factors of fatty liver disease after liver transplantation in patients with NASH and crypogenic cirrhosis. In a cross-sectional study liver transplant data of all patients who had undergone transplantation between June 2010 and 2017 at Shiraz Organ Transplant Center, Shiraz, Iran were reviewed. Fatty liver was diagnosed by ultrasound. Data regarding post-transplant diabetes mellitus (DM), hyperlipidemia, height, weight, body mass index (BMI), laboratory data and allograft steatosis were recorded. Patients were treated with tacrolimus based immunosuppressive regimen. Obesity was defined as BMI ≥ 30 kg/m². To investigate the impact of macrovesicular steatosis of graft on development of fatty liver after liver transplantation, recipients were grouped as those with ≤ 15% graft steatosis and those with >15% graft steatosis. Data were analyzed using the Student’s t-test, and Chi-square test. Logistic regression analysis was used to calculate the influence of independent variables on development of fatty liver.

Results: 267 patients were included in the study (72 patients with NASH and 195 with cryptogenic cirrhosis). In a mean follow up of 14.7 months, 56.9% of NASH patients and 26.9% of cryptogenic patients developed fatty liver after liver transplantation (OR = 3.59; 95% CI: 1.94–6.62; P < 0.001). There was no statistically significant difference in development of fatty liver between patients with ≤ 15% pre-transplant graft steatosis and those with >15% pre-transplant graft steatosis (OR = 1.07; 95% CI: 0.49–1.73; P = 0.817). In univariate analysis, post-transplant DM, hyperlipidemia, obesity, age, serum fasting blood sugar, triglyceride and cholesterol were associated with NASH after liver transplantation (P < 0.05). In regression analysis, post-transplant DM was an independent predictor of development of NASH after liver transplantation (OR = 2.29; 95% CI: 1.01–5.18, P = 0.045). Post-transplant DM (OR = 5.58; 95% CI: 3.03–10.29, P < 0.001; hyperlipidemia (OR = 4.17; 95% CI: 2.23–7.80, P < 0.001) and obesity (OR = 4.65; 95% CI: 2.17–9.94, P < 0.001) were more prevalent in patients with NASH compared to patients with cryptogenic liver cirrhosis. Conclusion: NAFLD and components of metabolic syndrome are prevalent after liver transplantation. Patients who underwent liver transplantation for NASH and cryptogenic cirrhosis.

Disclosure: Nothing to disclose.
P1294 HCV ERADICATION: A GAME-CHANGER IN THE RELATIONSHIP BETWEEN LIVER STIFFNESS AND PORTAL PRESSURE IN COMPENSATED ADVANCED LIVER DISEASE

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Introduction: Eradication of HCV infection with direct acting antiviral (DAA) therapy in patients with compensated advanced chronic liver disease (cACLD) is an important step further in the management of these patients, but brings new questions regarding the reliability and the accuracy of noninvasive tests in the post-HCV settings. Recent data reported that liver stiffness (LSM) rapidly decreased especially during first 4 weeks of DAA, with no notable changes at EOT or SVR12 (1). Data from the Peg-IFN era showed that baseline HVPG (hepatic-vein portal gradient), irrespective of achieving SVR, is the sole predictor of long-term uncompensation and mortality (2).

Aims and Methods: Knowing that LSM is a very good predictor of clinically significant portal hypertension (CSPH) (3,4), we aimed to investigate whether obtaining SVR diminishes the accuracy of LSM to estimate CSPH, and, as a consequence, if LSM could still be used to diagnose CSPH and to predict long-term outcome in cACLD patients that achieved HCV eradication.

Consecutive HCV cirrhotic patients evaluated for DAA therapy were included. Baseline LSM and HVPG measurement were performed in the same day, LSM was further assessed at EOT and when estimating SVR12, while HVPG was reassessed only at SVR12. Descriptive, correlation and accuracy statistic tests were performed using SPSS 21 software.

Results: Of the 69 HCV+cACLD patients (mean age 59.2±8.2 years; 63.8% males) treated with Sofosbuvir, 55 already finished the therapy and achieved SVR. LSM decreased from 23.16(6.4–62.7) kPa at baseline to 18.7(7.3–47.2) kPa at EOT (p<0.015) and remained unchanged at SVR12 [19.8(5.9–55.1) kPa; p=0.37]. HVPG dropped from 12.5(3–27) mmHg at baseline to 9(3–27) mmHg at SVR12 (p=0.001). The proportion of patients with CSPH decreased from 74.2% at baseline to 46.7% at SVR12 (chi-square =13.48; p<0.001).

Interestingly, the correlation between LSM and HVPG increased at SVR12 (r=0.839; p<0.001) as compared to baseline (r=0.698; p<0.001).

Furthermore, the performance of LSM to detect CSPH was better after obtaining viral clearance [AUROC of 0.88(95%CI: 0.82–1.00) vs. 0.82(95%CI: 0.70–0.94) for baseline and SVR12, respectively].

Conclusion: Eradication of recurrent HCV infection by DAA therapy has beneficial impact on glucose metabolism and renal profile and reverses the hypolipidemic effect of HCV in liver transplant recipients. These extrahepatic effects of DAA therapy need to be validated by larger prospective studies.

Disclosure: Nothing to disclose

References
RAS also had coexisting C125 RAS. In addition, no patients acquired these RAS. A significant multivariate analysis, coexisting NSSA RASs, NSSA P32 RAS, NSSB A218 and/or C316 RASs, and γ-glutamyltranspeptidase were associated with virologic failure. In the naive patients, all patients without NSSB A218 and/or C316 RASs achieved an SVR12. Notably, the SVR12 rates of patients with coexisting NSSA and NSSB RASs were significantly lower (83.3%).

Conclusion: Although SOF/LDV therapy resulted in a high SVR12 rate, coexisting NSSA and NSSB RASs were associated with virologic failure. These results might indicate that the coexisting baseline RASs influence the therapeutic effects of SOF/LDV.

Disclosure: Nothing to disclose.

P1297 SAFETY AND EFFICACY OF SOfosbuVIR-BASED REGIMENS IN TREATING HEPATITIS C VIRUS IN EGYPTIAN PATIENTS: REAL-WORLD STUDY: SINGLE-CENTER EXPERIENCE

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Introduction: Hepatitis C virus (HCV) is the main leading cause of liver disease in Egypt. A new era of HCV treatment has been started with the evolution of direct acting antiviral (DAA) treatments which are expected to change epidemiology of the disease. Sofosbuvir (SOF)-based therapy was introduced by the Egyptian ministry of health through a national HCV treatment program in 2014 in an attempt to decrease disease burden.

Aims and Methods: To evaluate efficacy and safety of Sofosbuvir-based regimens in HCV Egyptian patients with compensated liver disease. In the period between February 2015 and December 2016, 758 chronic HCV patients with compensated liver disease were randomized into 4 groups according to treatment regimen applied for each group: group 1 received SOF, PEG-IFN plus ribavirin (RBV) for 12 weeks, group 2 received SOF plus RBV for 24 weeks, group 3 received SOF and Simeprevir (SIM) with or without RBV for 12–24 weeks according to the state of fibrosis and treatment status, group 4 SOF and Dacatacsvir with or without RBV for 12–24 weeks according to the state of fibrosis and treatment status. Patients with Child-Pugh score more than 8, impaired kidney functions or hepatocellular carcinoma (HCC) whether active or recently treated with less than 4 weeks elapsed after successful treatment have been ruled out. SVR12 was the end point used to assess treatment efficacy. All adverse events have been reported in each group.

Results: Seven hundred out of 758 patients fulfilled the inclusion criteria; group 1 included 159 patients, group 2 included 138 patients, group 3 included 201 patients and group 4 included 202 patients. The mean age was 49.4 ± 9.2, 54.6 ± 9.3, 49.5 ± 11.4 and 50.3 ± 10.8 years in the 4 groups respectively. The overall SVR was 90.9% in group 1, 81.5% in group 2, 95% in group 3 and 98% in group 4. SVR in patients with liver cirrhosis was 90.56, 79.16, 95 and 98% respectively. In treatment experienced patients, SVR was 86.8% in group 1, 78.3% in group 2, 100% in group 3 and 86.7% in group 4. The overall SVR and SVR among patients with liver cirrhosis was significantly higher in patients who received SOF in treatment experienced patients was significantly higher in group 3 (p < 0.001). The rate of adverse events was 55.97, 59.42, 40.79 and 9.4% in the 4 groups respectively with significantly lower rate in group 4 (p < 0.001). The most reported adverse events were flu-like illness (15.1%) and anaemia (12.6%) in group 1, anaemia (18.5%) and hyperbilirubinemia (18.1%) in group 2, hyperbilirubinemia (11.9%) and fatigue (6.5%) in group 3, hyperbilirubinemia (5.9%) and anaemia (3.5%) in group 4.

Conclusion: Sofosbuvir plus daclatasvir with or without ribavirin is the safest and most effective SOF-based regimen in treatment of HCV Egyptian patients with compensated liver disease.

Disclosure: Nothing to disclose.
performed using biological tests, such as the FibroMax, or by using ultrasound based histologic methods, such as Transient Elastography (TE).

**Aims and Methods:** The aim of the present study was to evaluate the accuracy of these tests (FibroMax and Transient Elastography) for predicting HCV liver cirrhosis (LC), in viroscopic or treatment-experienced patients, with compensated liver disease.

The study prospectively included 460 consecutive patients previously diagnosed with compensated HCV LC based on clinical, biologic, ultrasonographic, endoscopic (esophageal varices), liver biopsy or/and laparoscopic criteria, who were considered for interferon-free treatment (Viekira, Obvi). Liver fibrosis was assessed during a two weeks period by means of TE (using M or XL probe) and by FibroMax. For TE, reliable measurements were defined as median value of 10 liver stiffness measurements, with a SR<±60% and an IQR <30%. For diagnosing cirrhosis by means of TE we used a cut-off value 12 kPa (1) and for FibroMax a value of 0.75.

**Results:** Out of the 460 patients, reliable measurements by TE were obtained in 453 (98.4%). According to the FibroMax cut-off, 77% (349/453) patients were classified as having significant fibrosis (F2) and 4.3% with severe fibrosis (F3). When we evaluated the performance of FibroMax, 8.1% of the 460 patients with LC were misclassified as having F1, 2.2% as having F2.10 (8/22), followed by radiofrequency ablation (RFA). One male patient from the DAA-TACE group had a viral relapse 12 weeks after EOT. **Conclusion:** SVR rate per protocol analysis in patients with treated HCC and compensated liver cirrhosis that received DAA with OBV/PTV+r+DSV + RBV was 86.4%. Although a recruitment bias may be involved, recurrence rate in patients with HCC treated by resection and RFA that received DAA therapy was 21% compared with 86% in the control group. In those with treated HCC by TACE on DAA therapy the recurrence rate was 37.5% vs 100% in the control group. This favorable impact of DAA therapy on the recurrence rate of HCC was reflected into an improved survival without recurrence in both groups.

**Disclosure:** Nothing to disclose

**Reference**

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**P1301 RECURRENT RATE OF HEPATOCELLULAR CARCINOMA (HCC) IN PATIENTS WITH HCV AND VIRUS C COMPLICATED CIRRHOSIS TREATED WITH OMBITASVIR, PARITAPREVIR/ RIBAVIRIN**

**Aims and Methods:** From a national prospective cohort enrolling 5861 Romanian patients with virus C compensated liver cirrhosis who received reimbursed DAA with Paritaprevir/Ombitasvir/r, Dasabuvir and Ribavirin (OBV/PTV+r+DSV + RBV) for 12 weeks during December 2013- August 2016, we analyzed 22 patients with a history of treated HCC. Most of them were treated by resection (8/22), followed by radiofrequency ablation (RFA) (6/22) and transarterial chemobolization (TACE) (8/22). DAA therapy was administered on the condition that the absence of tumor relapse was confirmed 6 months after the last session of therapy. A control group was defined including an equal number of HCC patients treated by surgery/RFA/TACE with matching age, gender and Barcelona Clinic Liver Cancer (BCLC) staging. All the patients were screened for tumor recurrence every 3-4 months with dynamic CT scan and/or MRI. They were divided in 4 groups: DAA- resection+ RFA (patients with HCC treated through resection or RFA who received DAA therapy), Control- resection+ RFA, DAA- TACE (patients with HCC treated through TACE who received DAA therapy), Control- TACE. Data were obtained from the Romanian National Health Agency. Ordinal and scale variables with non-normal distribution were summarized as mean (±standard deviation), and compared by t-student test, while categorical variables were summarized as number (%) and compared by Fisher exact test.

**Results:** Results are depicted in table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DAA-RESECTION</th>
<th>CONTROL-RESECTION</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex M</td>
<td>7/14 (50%)</td>
<td>6/14 (42.3%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Mean age (±SD)</td>
<td>62.8 ± 7</td>
<td>64.4 ± 8.2</td>
<td>0.59</td>
</tr>
<tr>
<td>Follow-up (mean ±SD)</td>
<td>46.7 ±/− 20.1</td>
<td>33.7+/− 27</td>
<td>0.16</td>
</tr>
<tr>
<td>SVR 12 (per protocol)</td>
<td>12/14 (85.7%)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Recurrence rate</td>
<td>3/14 (21.4%)</td>
<td>12/14 (85.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Survival without recurrence</td>
<td>45.1+/− 12.5</td>
<td>18.1+/− 16.2</td>
<td>0.005</td>
</tr>
<tr>
<td>Parameter</td>
<td>DAA-TACE (8) CONTROL-TACE (8)</td>
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<td></td>
</tr>
</tbody>
</table>

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**P1302 LONG-TERM FOLLOW-UP OF CHRONIC HEPATITIS C PATIENTS: WILL SUSTAINED ViroLOGICAL RESPONSE BE ENOUGH TO PREVENT CIRRHOSIS IN THE LONG TERM?**

**Aims and Methods:** To assess if sustained virological response (SVR) and some other predictive factors on development of cirrhosis secondary to chronic hepatitis C.

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**Introduction:** Cirrhosis development is an important stage in the natural history of chronic hepatitis C (CHC), because it heralds significant morbidity and mortality and higher health care costs related to complications of end-stage liver disease. Treatment response has been proven to be the determinant factor for the development of cirrhosis. It has also been shown that disease progression can be predicted by AST/ALT, Fibrosis-4 (FIB-4) and AST/Platelet ratio index (APRI) scores (1.23). In the present study, we aimed to evaluate the impact of sustained virological response (SVR) and some other predictive factors on development of cirrhosis in patients with CHC, who were followed for at least 1 year after the end of treatment in 2015 Uluabat, Kars, Turkey.

**Results:** The median follow-up period was 5.9 (1-14.4) years. The 10 year cumulative incidence of cirrhosis was significantly lower in the treated group compared to the untreated group (19.5% and 44.4%, p = 0.025). In the untreated group, cirrhosis wasn’t observed in the cases with SVR (p <0.001). Univariate analysis revealed that female gender (p = 0.041), age ≥ 40 (p = 0.05), platelet count >150,000 (p <0.001), low AST/ALT score (p <0.003), low FIB-4 score (p <0.003), low APRI score (p <0.001), SVR (p <0.001) resulted in statistically significant less cirrhosis. In Cox regression analysis, SVR was found to be the only independent factor affecting development of cirrhosis (Hazard ratio, HR = 0.279; p = 0.04).

**Conclusion:** Although there are useful parameters in predicting the development of cirrhosis in CHC patients, SVR is the only independent factor to prevent cirrhosis. Elimination of cirrhosis with higher SVR rates with currently used new direct-acting antiviral agents will be probably shown in the future long-term studies.

**Disclosure:** Nothing to disclose

**References**
P1301  DIAGNOSTIC PERFORMANCE EVALUATION OF RAPID DIAGNOSTIC ORIENTATION TEST IN THE DETECTION OF HEPATITIS C
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Introduction: Hepatitis C is an infectious disease of viral origin with primarily blood transmission. It is a real public health problem. Screening for hepatitis C is very interesting for preventing the spread of the infection, improving access to blood transmission. It is a real public health problem. Screening for hepatitis C is very interesting for preventing the spread of the infection, improving access to blood transmission. It is a real public health problem.
Methods: We aimed to prospectively evaluate the diagnostic performance of CE-marked RDTs (Toyo tests) which detects the anti-hepatitis C virus (HCV) antibodies in capillary whole blood and to study their sensitivity and specificity as well as their predictive values.
Results: One hundred and fifty patients were included. The average age of our patients was 47.74 years old with extremes: 17-98 years. There are 79 men and 71 women with a sex ratio H/F: 1.11. The risk factors for contamination by hepatotropic viruses were found in 71.33% (Non-medical care: 82.24%, tattooing: 32.71%, transfusion: 28.03%, cupping therapy: 18.70%, unprotected sex: 4.67%). The viral serology of hepatitis C (anti-HCV antibodies) was positive in 13 cases, or 8.66%. RDTs were positive in 10 cases (6.60%), as well as polymerase chain reaction (PCR). The sensitivity of the RDTs to viral serology was 76.92%, while its specificity was 100%. The positive predictive value was 100% and the negative predictive value was 97.8%. The same results were found by calculating the specificity, sensitivity and predictive values of PCR in relation to viral serology.
Conclusion: Based on the results obtained, we concluded that the positivity of RDTs allows the establishment of the hepatitis C diagnosis for 100 per cent. However, the use of a serological assay remains necessary when the test is negative. Within our study involved a small number of patients, it is a rough sketch for a work with a large sample size in the future to improve the efficiency of these RDTs and to estimate the real impact of their use in reducing the diagnosis of the infection at an advanced stage and facilitate access to rapid therapeutic management.
Disclosure: Nothing to disclose

Reference

P1305  COMBINATION THERAPY OF FENOFLIBRATE AND URSODEOXYCHOLIC ACID IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS WITH INCOMPLETE RESPONSE TO URSODEOXYCHOLIC ACID
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Introduction: Most patients with Primary Biliary Cholangitis (PBC) respond to ursodeoxycholic acid (UDCA) therapy. For those who do not respond to UDCA, therapeutic alternatives are scarce. Fibrates have been suggested as second-line agents in patients who do not achieve adequate biochemical response to UDCA monotherapy. The objective of this study is to evaluate the role of fibrates as second-line therapy in PBC.
Methods and Aims: PIC was diagnosed according to accepted criteria and staged according to the Ludwig classification. The absence of response to UDCA therapy was assessed using the GLOBE score. Liver function tests, renal function and the UK-PBC score were assessed at 6 and 12 months after fibrate onset and at the date of the last follow-up visit. Patients receiving fibrate were compared with a control group of patients not responding to UDCA who did not receive fibrates.
Results: Thirty-nine patients were included (fibrates group n = 13; control group n = 26). Patients in both groups did not differ in terms of age, gender or follow-up time. Side effects were observed in two patients (arthritis and myalgias). A statistically significant decrease in alkaline phosphatase levels at 6 and 12 months and at the end of the follow-up in the group that received fibrates compared to the control group (p < 0.05). Transaminase and IgM levels also decreased significantly, while bilirubin and albumin levels remained unchanged in the group receiving fibrates. A higher proportion of patients in the fibrate group achieved POISE response criteria compared to the control group at all time points studied (p < 0.05).
Conclusion: Combination therapy of fibrate and UDCA is safe and induces significant biochemical and progresive scores improvement in patients with PBC and incomplete response to UDCA.
Disclosure: Nothing to disclose

Introduction: Primary biliary cholangitis (PBC) is a cholestatic chronic liver disease characterized by a progressive destruction of small intrahepatic bile ducts. Ursodeoxycholic acid (UDCA) have benefit in slowing down the liver disease progression. However, some (30-40%) patients experience treatment failure. The aim of our study was to evaluate the prognostic factors of UDCA failure in patients with PBC.
Methods: We retrospectively collected the medical files of patients with PBC who received UDCA from January 2005 to December 2016. Non-response to treatment was evaluated with Paris criteria.
Results: Seventy-one patients were included in our study. There were 66 females and 5 males. Ages ranged from 23 to 81 years (median 55.23). All patients were treated with UDCA (13-15 mg/kg/day) associated with corticosteroids and azathioprine in overlap syndromes (28.1%). The average of follow-up time was 64 months (range 3-64 months).
Complete response was observed in 34 (48%) patients. Partial response or non-response were seen in 34 (52%) patients. Predictive factors of treatment failure were: high serum bilirubin level > 50 μmol/L (p = 0.039), advanced cirrhosis (p = 0.026), overlap syndrome (p = 0.046) and interface hepatitis (p = 0.006). Gender, age and association with other autoimmune diseases were not identified as prognostic factors. The evolution into an advanced cirrhosis was significantly observed in patients who failed UDCA (p = 0.038). Interestingly, 2 cases of hepatocellular carcinoma were diagnosed in patients with UDCA failure.
Conclusion: UDCA has a crucial role in PBC treatment. It may slow down the progression into advanced liver disease. However, high serum bilirubin level, positivity of AML, histological liver steatosis, Bile duct loss and ductular reaction according to accepted criteria, fibrosis, coexistence of other autoimmune diseases, and delay in starting UDCA therapy. However, biochemical response was inversely correlated o pretherapeutic level of total bilirubin (p = 0.023).

Conclusion: According to our study, an elevated pertherapeutic level of total bilirubin (superior to 2 ULN) is a predictive factor to the absence of a biochemical response to UDCA therapy in PBC.
Disclosure: Nothing to disclose
advanced cirrhosis, overlap syndrome and interface hepatitis predicted poor outcome.

Disclosure: Nothing to disclose

P3108 A STUDY ON PRURITUS IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS (PBC) BASED ON A SURVEY
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Introduction: Pruritus of the skin is a clinical symptom characteristic of primary biliary cholangitis (PBC), but the frequency and severity has not been studied enough in detail. The purpose of this study is to document the actual state of pruritus in PBC patients.

Aims and Methods: The subjects were 49 patients who were diagnosed with PBC at our department. By means of a questionnaire, we evaluated the patients regarding pruritus, and classified them into 5 stages (0: none, 1: slight; 2: mild, 3: moderate, 4: severe) by using disability caused by pruritus. Patients were asked about the severity of pruritus and compared them by age, duration from diagnosis, values of total bilirubin (mg/dl), albumin (g/ml), prothrombin time (%), platelet count, values of type 4 collagen (ng/ml), and hyaluronic acid (ng/ml).

Results: The patients were 3 men and 46 women, with an average age of 67.8. Pruritus evaluated in 5 stages (0/1/2/3/4) were present during the day in (12/13/11/10/9), during the night (11/12/11/10/9), and during 67% of the daytime. The patients feeling pruritus during the day was 75.5%, and during the night, 71.4%, accounting for a high percentage. There was no relation between pruritus and duration from diagnosis with PBC, for both daytime and nighttime. There was no correlation between pruritus and the value of total bilirubin/daytime: 0.6/0.7/0.7/0.8, nighttime: 0.6/0.6/0.5/1.4/0.5, the value of albumin: daytime: 4.1/3.9/4.0/4.1, nighttime: 4.2/4.0/4.0/3.4/1), the prothrombin time/daytime: 99.99/96/100/100, nighttime: 98.98/98.8/92/100, platelet count/daytime: 20.4/17.3/20.2/18.1/25.2, nighttime: 21.4/17.1/19.2/17.5/17.1, type 4 collagen 7S/daytime: 4.2/4.0/4.0/3.8/3.5, nighttime: 4.0/4.2/4.0/3.2/3.5, or hyaluronic acid/daytime: 109.3/100/98.8/162/30.1, nighttime: 98.3/107.5/ 80.1/106.3/44.9.

Conclusion: The liver lesions of the patients in this study were mostly not advanced, but the rate of those feeling pruritus was high. There was no significant correlation between pruritus and age, duration of disease, or indicators of liver reserve. It has become clear that in PBC, pruritus manifests in the early stage.

Among PBC patients there are many who have pruritus regardless of the degree of advancement, but at the present point, there is no other way to confirm it than by monitoring the symptoms. Identification of a useful biomarker for confirming pruritus will be needed.

Disclosure: Nothing to disclose

P3109 UGT2B28 GENOMIC VARIATION IS ASSOCIATED WITH THE ONSET OF ALCOHOLISM-ASSOCIATED HEPATOCELLULAR CARCINOMA
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Introduction: Early hepatocellular carcinoma (HCC) is often absent of pathognomonic symptoms, and thus many patients have untreatable disease when first diagnosed. Single-nucleotide-polymorphisms (SNPs) on the UDP glucuronosyltransferase family 2 member B28 (UGT2B28) gene have been proved associated with hepatitis B virus e-antigen clearance in response to peginterferon therapy, prostate cancer progression and colorectal cancer risk. The gene product, UGT2B28, is an enzyme associated with sex hormone metabolism, an important factor in HCC progression, whereas its clinical role in HCC has never been studied. Here, we aimed to investigate this issue and to explore the possible implication of UGT2B28 in the diagnosis of HCC.

Aims and Methods: A cohort of 382 patients with HCC having received curative resection was retrospectively recruited. We evaluated the correlation between UGT2B28 rs1336263-539023961 genotypes and clinicopathological characteristics.

Results: Among these patients, 52.0% patients had rs1336263-C/T genotype, and the others had rs1336263-C/C genotype. Intriguingly, none had rs1336263-G/G genotype. Univariate analysis revealed that “CT” genotype was associated with age (OR, 1.021; 95% CI, 1.006–1.036; P = 0.005), ascites (OR, 3.223; 95% CI, 1.130–8.995; P = 0.020), and hepatitis C (OR, 1.839; 95% CI, 1.148–2.845; P = 0.001). Multivariate analysis showed that these three factors were independent of each other. Subgroup analysis discovered that “CT” genotype was most significantly associated with age in alcoholism-related HCC patients (OR, 1.079; 95% CI, 1.035–1.125; P = 0.001). The average ages at diagnosis (onset ages) of alcoholism-related HCC were 59.3 ± 10.7 and 49.6 ± 12.2 years (a 10-year difference) for “CT” and “TT” genotypes, respectively.

Conclusion: Alcoholic patients with extensive lipid panel initially screened, this study was capable of detecting a set of 4 triglycerides as candidate serum biomarkers that allowed differentiating between persons affected with PBC or biliary dysplasia from the healthy controls. Importantly, 4 additional triglycerides allowed discriminating between PBC and biliary dysplasia patients.

Disclosure: Nothing to disclose

P3110 METHYLATION OF MULTIPLE TUMOR SUPPRESSOR GENES (RUNT-RELATED TRANSCRIPTION FACTOR 3 (RUNX3), RASSF1A, E-CADHERIN) IN HCV-RELATED LIVER CIRRHOSIS AND HEPATOCELLULAR CARCINOMA IN EGYPTIAN PATIENTS
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Introduction: Recognition of circulating DNA can be useful for the diagnosis of many cancers, including the hepatocellular carcinoma (HCC). The pathogenesis of HCC is both genetic and epigenetic alterations. HCV viral proteins may participate in epigenetic regulation of hepatic cancer and induce HCC-specific epigenetic changes. HCV infection was related to aberrant methylation on multiple genes. Runt-related transcription factor 3 (RUNX3), RASSF1A and E-Cadherin genes are tumor suppressor genes which could be inactivated by hypermethylation in many tumors including HCC, causing a decrease of gene expression.

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Disclosure: Nothing to disclose
Aims and Methods: In this study, the methylation of RUNX3, RASSF1A, and E-Cadherin genes were studied in the serum of patients with HCC as diagnostic biomarkers for HCC. DNA was extracted from the peripheral blood of 53 healthy volunteers, 207 HCC related liver cirrhosis (LC) patients and 193 HCC patients. Routine laboratory investigations, serum AFP and detection of circulating hypermethylated RASSF1A, RUNX3 and E-Cadherin genes by methylation-specific PCR were done for all participants.

Results: A significant hypermethylated RASSF1A gene was found in HCC group when compared to both LC and healthy groups (OR = 3.2380, (OR = 6.5732)) respectively. As regard E-Cadherin gene a significant hypermethylation was found in HCC group when compared to both LC and healthy groups (OR = 6.4459, (OR = 4.7850)) respectively with p-value <0.0005 whereas there was no significant hypermethylation was found between LC and healthy group as regard the 3 tumour suppressor genes (P= 0.05). No significant association was found between hypermethylation of RASSF1A, RUNX3 and E-Cadherin in serum may be useful biomarkers for HCC early prediction in patients of LC with HCV.

Disclosure: Nothing to disclose

References


P1312 THE ANTI-INFLAMMATORY RECEPTOR TREM2 HALTS THE GENERATION OF HCC IN MICE THROUGH THE INHIBITION OF LIVER INFLAMMATION AND HEPATOCYTE PROLIFERATIVE RESPONSES

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Aims and Methods: To study the role of TREM2 in the context of HCC development and progression, wild type (WT) and Trem2−/− mice were treated with the hepatocarcinogen diethylnitrosamine (DEN) and analysed at different time-points during disease development. The early molecular mechanisms triggered in response to DEN were analysed in WT and Trem2−/− mice in acute phases (6, 24, 72h). To evaluate the role of TREM2 in liver regeneration a ~70% partial hepatectomy (PHx) model was performed in WT and Trem2−/− mice, and animals were sacrificed at 1, 6, 36, 72 hours and 5 days post PHx.

Results: TREM2 mRNA expression is significantly upregulated in human HCC samples compared to controls and correlates with markers of inflammation. Similarly, Trem2 mRNA expression is also elevated in murine HCC and in a liver cancer xenograft model compared to controls. Trem2−/− mice showed augmented tumour number and bigger tumours after DEN. This was accompanied by an increase in the expression of liver damage and hepatocyte proliferation markers. Trem2−/− mice exhibited exacerbated liver damage and ROS in acute phases in response to DEN. Regarding liver regeneration following PHx, PCNA expression and BrDU incorporation indicated an increased hepatocyte proliferation in the Trem2−/− mice. The expression of pro-inflammatory genes was also elevated in these mice. Interestingly, the results observed in the HCC model could be rescued with an anti-inflammatory diet (BHA).

Conclusion: TREM2 is upregulated in human and murine HCC and in murine liver regeneration. This anti-inflammatory receptor inhibits proliferation and HCC tumour generation in mice through the inhibition of liver inflammation and ROS. TREM2 may represent a novel therapeutic strategy for HCC.

Disclosure: Nothing to disclose

References


P1313 MUSASHI 2 CONTRIBUTES TO THE MAINTENANCE OF STEMNESS OF CD44V6+ LIVER CANCER STEM CELLS VIA NOTCH SIGNALING PATHWAY

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Introduction: Liver cancer stem cells (LCSC) drive hepatocellular carcinoma (HCC) development and progression. Notch signaling pathway play crucial roles in the maintenance of stemness characteristics. Musashi 2 (Ms2), a member of conserved gene family of RNA binding protein, was highly expressed in HCC tissues correlating with poor prognosis of HCC patients. We hypothesize that Ms2 contributes to the maintenance of stemness of CD44v6+ liver cancer stem cells through activation of Notch signaling pathway via LFGN gene.

Aims and Methods: CD44v6+/− cells were isolated from human hepatoma cell lines (SNV398 and MHCC-97H) using microbeads sorting. Stem-like properties, such as self-renew and metastasis ability were analyzed in vitro and in vivo (spheroid tumor model in mice). In order to investigate the role of Ms2 gene in CD44v6+ LCSCs, we downregulated Ms2 with lentiviral particles (Lenti-Ms2, Lenti-Ms2+ and control virus) in CD44v6+ cells, and analyzed stem-like characteristic. Furthermore, we detected the mRNA and protein levels of Notch signaling pathway in the system above.

The roles of Notch signaling pathway in the CD44v6+ LCSCs was verified by inhibiting with lentivirus or γ-secretase inhibitor (RO492997). To explore the mechanism of Ms2 gene and Notch signaling pathway, RT2 Profiler PCR Array was carried out after Ms2 gene was downregulated in CD44v6+ liver cancer cells, and CO-IP was used to verify the direct binding of Ms2 and LFGN gene in Notch pathway.

Results: In our study, CD44v6+ could be one of the surface makers of liver cancer stem cells. CD44v6+ cells expressed more Ms2, compared with CD44v6- cells. We demonstrated that downregulating Ms2 in CD44v6+ LCSCs could decrease the ability of self-renewal, invasion and migration, proliferation, tumorigenicity and metastasis of stem cells. Meanwhile, upregulating Ms2 in CD44v6+ cells increased the ability of self-renewal, invasion and migration, chemotherapeutic resistance and tumorigenicity. In CD44v6+ cells, the key molecules downregulated after Ms2 gene was down-regulated, while in the CD44v6- cells the key molecules up-regulated after increasing Ms2 gene. Furthermore, the self-renewal ability and tumorigenicity of CD44v6+ cells was obviously decreased after inhibiting notch signaling pathway. Last but not the least, according to the result of RT2 Profiler PCR Array, Ms2 contributes to the maintenance of stemness of CD44v6+ liver cancer stem cells via activation of Notch signaling pathway via binding to LFGN gene.

Conclusion: Ms2 play an important role in the maintenance of stemness of CD44v6+ liver CSCs. Ms2 contributes to the maintenance of stemness of CD44v6+ liver cancer stem cells through activation of Notch signaling pathway via binding directly to LFGN. Our study provided a new insight to the recurrence and metastasis of HCC and potential molecular targets for targeted therapy for liver cancer.

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P1314 MICRORNA-195 INCREASES APOPTOSIS IN HEPATOCELULAR CARCINOMA BY TARGETING THE KEY CELL CYCLE REGULATOR WEE1

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Introduction: MicroRNA-195 (miR-195) plays an important role in many types of tumors. However, the roles of WEEl in cancer and miRNAs that directly regulate WEEl have not been elucidated. The purpose of this experiment is to assess
the effects of miR-195 on inhibiting WEE1 and to clarify the regulating mechanism of miR-195 in pancreatic cancer.

Aims and Methods: Real-time fluorescence quantitative PCR was used to detect the expression of miR-195 in HCC tissues and adjacent normal tissues from 36 cases. We also detected the expression level of miR-195 in eight human hepaticoma cell lines, including McA-RH7772, Hep2, Huh7, PLC/PRF/5, SMCC-7721, SK-HEP-1, MHC97-H, MHC97-L and Hep3B, as well as in human normal liver cell lines L02 and Chang liver. The effect of miR-195 and sNWE1 on cell viability was evaluated using cck-8 assays, apoptosis levels were determined using FACS analysis of Annexin V/PI stained cells, and target protein expression was determined using western blot. To investigate the potential anti-tumor activity of miR-195 in vivo, we constructed Tumorigenesis assay in nude mice. Results: We found that miR-195 was downregulated in HCC cell lines and tissue compared to normal liver tissue. Low expression of miR-195 could suppress the proliferation and increase the apoptosis of HCC cell line. Knockdown of WEE1 by RNAi in HCC cells, similar to miR-195 overexpression, decreased liver cancer cell growth and induced apoptosis. In a mouse model, therapeutic administration of miR-195 mimics could significantly suppress the growth of hepatoma xenografts in nude mice.

Conclusion: MicroRNA-195 increases apoptosis in hepatocellular carcinoma by targeting the key cell cycle regulator WEE1. This finding supports a potential novel strategy for therapeutic interventions of this disease.

Disclosure: Nothing to disclose.

P1315 THE RELATION BETWEEN MICRO-RNA GEN E POLYMORPHISMS AND DEVELOPMENT OF HEPATOCELLULAR CARCINOMA IN EGYPTIAN PATIENTS M. Abdel-Samie a, 1 M. A. Eljak y, 2 K. Diab c, 2 N. Sheb le 1, M. M. All am 2, 1 National Liver Institute, Menoufia University, Hepatology and Gastroenterology, Shebin El-Kom, Egypt, 2 National Liver Institute, Menoufia University, Clinical Pathology, Shebin El-Kom, Egypt, 3 National Liver Institute, Menoufia University, Microbiology and Immunology, Shebin El-Kom, Egypt, 4 National Liver Institute, Menoufia University, Biochemistry, Shebin El-Kom, Egypt

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Introduction: The development and progression of hepatocellular carcinoma (HCC) is a multistage process involving the deregulation of genes that are crucial to cellular processes. Multiple risk factors are correlated with HCC. MicroRNA is differentially expressed in development of different types of malignancies, including hepatic malignancy. Single nucleotide polymorphisms (SNPs) are the most common sequence variation in human genome. SNPs in miRNAs may affect transcription, processing or target recognition and result in malignant diseases.

Aims and Methods: We aimed to determine the association between micro-RNA gene polymorphisms and development of HCC in Egyptian Patients. This study included 200 individuals who were matched in age and sex. Tumor staging was done using BCLC staging system. Quantification and genotyping of Micro-RNA were performed.

Results: Among the 200 patients, 2 groups were described: group I included 90 HCC patients with a male majority (72.2%) and 110 controls in group II. Diabetes and hypertension were detected as risk factors. Three microRNA SNPs were assayed. There was a significant association between rs1006033 miR-499b and the risk of HCC. The genotypes GG or G allele were associated with the genotype of AA or AG or A allele.

Conclusion: There is an association between the mi-RNA SNPs and the susceptibility to HCC. This finding can help us to explore some roles and mechanisms of SNPs within miRNAs in the occurrence and development of HCC.

Disclosure: Nothing to disclose.

P1316 PERIOSTIN PROMOTES TUMORIGENESIS BY ACTIVATING EPITHELIAL-MESENCHYMAL TRANSITION IN LIVER CANCER

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Introduction: Hepatocellular carcinoma (HCC) mostly arises from underlying chronic inflammatory liver disease. Periostin is one of the matricellular proteins and the association of periostin with inflammation or tumor invasiveness and prognosis has been reported. We investigated a role and mechanism of periostin in the development of liver cancer.

Aims and Methods: Hep3B cells, a human hepatocellular carcinoma cell line, were used. Cell growth was assessed using the MTS assay and epithelial-mesenchymal transition signaling was explored by immunoblot analysis. Male wild type or periostin +/- mice (C57BL/6, 8 weeks old) were injected with diethyltinlsutoxide (DEN, 100mg/kg at week 8) and tetrachloride (CCl4, 1mg/kg biweekly from week 10-50) intraperitoneally to induce liver inflammation, fibrosis and tumor. Anti-tumor effects were evaluated by number of tumors and histopathological examination.

Results: Cell proliferation did not show significant change in Hep 3B cells treated with recombinant periostin or periostin siRNA. Recombinant periostin (50mM) promoted cell migration and invasion in Hep3B cells. E-cadherin expression was downregulated in Hep3B cells; however, periostin expression was increased in recombinant periostin treated Hep3B cells. Recombinant periostin also induced JNK expression and inhibition of JNK signaling restored N-caderin expression. Compared to wild type mice, the number of hepatic tumors was significantly lower in periostin +/- mice. Conclusion: Periostin may play a role in the tumorigenesis through epithelial-mesenchymal transition and is suggested as a potential target for the treatment of liver cancer.

Disclosure: Nothing to disclose.
P1319 ASSOCIATION BETWEEN XRCC1 GENE POLYMORPHISM AND HEPATOCELLULAR CARCINOMA IN EGYPTIAN PATIENTS

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Introduction: Several major risk factors for hepatocellular carcinoma (HCC) have been identified, including chronic infection of hepatitis B virus (HBV) and hepatitis C virus (HCV). Nevertheless, only a fraction of infected patients develops HCC during their lifetime suggesting that genetic factors might modulate HCC development. X-ray repair cross complementing group 1 (XRCC1) participates in the base excision repair pathway of DNA.

Aims and Methods: We aimed to investigate the association of X-ray repair cross complementing group 1 (XRCC1) gene polymorphism with HCC in Egyptian population. This study was assessed on 40 patients with HCC and 20 cirrhotic patients on top of HCV and 40 age and gender-matched healthy subjects as control group. After collection of relevant clinical data and basic laboratory tests, c.1517G[C SNP of XRCC1 gene polymorphism was performed by (PCR-RFLP) technique.

Results: Our study revealed statistical difference in XRCC1 (CC, GC) genotypes with increased (C) allele frequency in patients with HCC in comparison with cirrhotic patients as well as control group. In addition, patients with CC, GC genotypes showed significant higher number and larger size of tumor foci and significantly higher Child Pugh grades. The multivariate analysis showed that the presence of c.1517G[C SNP of XRCC1 is an independent risk factor for the development of HCC in chronic HCV patients with 3.742 fold increased risk of HCC development.

Conclusion: The XRCC1 gene polymorphism could be associated with increased risk of HCC development in chronic HCV-infected Egyptian patients.

Disclosure: Nothing to disclose

P1320 PD-HYDROXY PYRENE IN URINE AS A BIOLOGICAL MONITORING OF EXPOSURE TO POLYCYCLIC AROMATIC HYDROCARBONS MIGHT EXPLAIN WHY HEPATOCELLULAR CARCINOMA DEVELOPED AMONG SOME CASES OF CHRONIC ACTIVE VIRAL HEPATITIS

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Introduction: Polycyclic aromatic hydrocarbons (PAHs) are among the most carcinogenic, mutagenic and toxic contaminants. Their exposure and metabolism via the cytochrome P450 (CYP) family in different cancer entities is considered to contribute to the etiology of many types of the human cancers.

We aimed to find out if exposure to polycyclic aromatic hydrocarbons is a risk factor for development of hepatocellular carcinoma among the exposed cases of chronic active hepatitis B and C.

Aims and Methods: A case-control study was conducted between the periods from the first of March 2015 to end of August 2017. The study was conducted in the outpatient clinic of the Department of Hepatology and Gastroenterology at Theodor Bilharz Research Institute (TBDI), Cairo, Egypt. The minimum sample size required for the present study was calculated using Epi info program, considering the following data: two sided Confidence level=95%, Power of test = 80%. Ratio of control: cases = 1:1. Percent of control exposed=21%. Percent of cases exposed=42% and Odds ratio=2.8. Estimated number of cases was (77 cases with HCC on top of chronic active hepatitis B and C) and (77 controls without HCC but suffering chronic active hepatitis B and C). All subjects of both groups were subjected to the selected interview medical sheet and to biological monitoring of urinary 1-hydroxy pyrene as a biomarker for PAHs exposure.

Results: 75% of cases of HCC have been found with increased level of 1-hydroxy pyrene in urine compared to the controls, there was significant positive association between exposure to PAHs and development of HCC among cases group (OR = 4.9). There was significant association among the case groups between smoking and abnormal high level of 1-hydroxy pyrene in urine (Chi square=0.001). There was significant positive association between exposure to PAHs and development of HCC among males (OR = 1.6). There was a highly positive correlation between 1-hydroxy pyrene and Alfa Feto Protein (AFP) among positive cases of 1-hydroxy pyrene in case group.

Conclusion: PAHs might be a factor for developing HCC among cases of chronic active hepatitis B and C. 1-hydroxy pyrene in urine could be an early indicator of HCC among cases of chronic active hepatitis B and C.

Disclosure: Nothing to disclose

P1321 DIAGNOSTIC PERFORMANCE OF ALPHA-FETOPROTEIN, ALPHA-FETOPROTEIN-L3, PROTEIN INDUCED BY VITAMIN K ABSENCE, GLYPICAN 3 AND ITS COMBINATIONS FOR HEPATOCELLULAR CARCINOMA IN PATIENTS ADMITTED IN A LARGE TRANSPLANT CENTER IN ROMANIA

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Introduction: Alpha-fetoprotein (AFP) is the most widely used serum biomarker for hepatocellular carcinoma (HCC), despite its limitations. Alpha-fetoprotein-L3 (AFP-L3), protein induced by vitamin K absence (PIVKA-II) and Glypican-3 (GPC-3) are other supplementary biomarkers.

Aims and Methods: This study aimed to investigate the diagnostic performance of AFP, AFP-L3 PIVKA-II, and GPC-3 as single or in combination to seek the best biomarker or panel, and to investigate the clinical factors affecting their performance for hepatocellular carcinoma (HCC) diagnosis in patients admitted to a transplant center from Romania.

From March 2016 to October 2017 we prospectively included a number of 153 patients, 101 were with HCC and 52 controls patients with liver cirrhosis. Serum levels of AFP, AFP-L3, PIVKA-II and GPC-3 were measured by ELISA and cDNA microarray (Affymetrix) and clinicopathological features were determined for all subjects. To compare the diagnostic value in distinguishing HCC from nonmalignant chronic liver disease, receiver operating characteristic (ROC) curves were performed for each biomarker and for every combination of four to markers.

Results: Of the four biomarkers, AFP-L3 showed the highest area under the curve (0.85). The sensitivity and specificity for each single biomarker was 55.6% and 99% (AFP >18.9ng/mL), 86.1% and 58.3% (PIVKA-II >63 mg/L), 86.1% and 72.2% (AFP-L3 >13.5 ng/ml) and 77.8% (GPC-3 >466ng/mL), respectively. The area under the curve was 0.75 for PIVKA-II, 0.79 for AFP and 0.77 for GPC-3 for HCC diagnosis.

Among the combinations of two biomarkers, AFP >18.9ng/mL and AFP-L3 >13.5ng/mL showed the best diagnostic performance with an area under the curve of 0.93. Triple or quadruple combination did not improve the diagnostic performance further. The patient’s age, etiology and tumor invasiveness of HCC affected the performance of each marker.

Disclosure: Nothing to disclose

Comprises also p63 and p73 with their different splice variants. Although p63 and p73 share a variety of tasks with p53, such as regulating cellular stress responses, they can also exert independent functions. Depending on their splice variants – with transactivation domain (TA)domainant negative (DN) – and the characteristics of the particular binding site p53 proteins activate or inhibit specific target genes by direct or indirect binding of the DNA. e.g. via regulation of microRNAs. microRNAs are small, non-coding RNA molecules with a length of about 22 nucleotides, which play an important role in gene regulation. They can exert tumor suppressive or oncogenic functions and many of them are known to be induced or repressed by the p53-family in different cancer entities. For instance, microRNA 34a can be induced by p53 and in turn – exerts its tumor suppressive functions by stabilizing the robustness of p53 responses to genotoxic stress.

Aims and Methods: So far, little is known about p73-controlled microRNAs in HCC. The aim of this study was therefore to analyze regulation of microRNAs in HCC therapy.

Results: In non-transfected cells tivantinib treatment induced an increase of all mentioned tumor suppressive microRNAs by up to 3.6-fold compared to DMSO-treated controls after 48h. Overexpression of DNP73 did not substantially alter microRNA expression profiles in the presence or absence of tivantinib. In contrast, overexpression of TAP73 in the absence of tivantinib had strong inductive effects on the expression of miR-34a (5.0-fold) and miR-149 (8.1-fold) after 72 hours compared to GFP-transfected cells, whereas the expression levels of miR-192 and miR-194 remained unchanged. Notably, a combination of TAP73 overexpression and tivantinib treatment was most effective, resulting in further enhanced microRNA expression rates of miR-34a (9.4-fold) and miR-149 (14.9-fold) compared to Ad-GFP-transfected and DMSO-treated cells after 72h.

Conclusion: TAP73 is an important regulator of tumor suppressive microRNA expression in Hep3B cells. Combined effects of TAP73 overexpression and tivantinib treatment result in a strong induction of miR-34a and miR-149. In contrast, DNP73 did not influence these targets, highlighting the differential target gene regulation by TA and DN-isomorphs.

HCC systemic therapies are rare and characteristics and pathways of most of the used drugs are not well understood. In this study we now provide evidence for regulation of tumorsuppressive microRNAs by a combination of tivantinib and TAP73 overexpression, suggesting novel therapeutic and prognostic options for HCC therapy.

Disclosure: Nothing to disclose
There was a moderate significant correlation between initial PIVKA-II value and maximum diameter of the tumoral nodule (r = 0.50, p = 0.001), but no correlation between AFP value and tumoral diameter.

**Conclusion:** AFP-L3 was the most useful single biomarker for HCC diagnosis, and the combined measurement of AFP and AFP-L3 could maximize the diagnostic yield. PIVKA-II has a better correlation with tumor size compared to AFP. Clinical decision should be based on the consideration of different factors affecting the diagnostic performance of each biomarker. Efforts to seek novel HCC biomarkers should be continued.

**Disclosure:** Nothing to disclose.

P1322 TALIN-1, OTHER THAN A POTENTIAL MARKER FOR HEPATOCELLULAR CARCINOMA DIAGNOSIS

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**Introduction:** Hepatocellular carcinoma (HCC) is a major cause of cancer mortality worldwide. The outcome of HCC depends mainly on its early detection. Alpha-fetoprotein (AFP) is the currently available marker for HCC diagnosis. Talin-1 was previously proposed as a potential novel biomarker for HCC diagnosis but with a limited and inconsistent data.

**Aims and Methods:** We aimed to study the possible role of Talin-1 in diagnosis and prognostic stratification of patients with hepatocellular carcinoma. In this prospective study, we recruited 96 patients from Ain Shams University hospitals’ clinics and inpatient department, then classified them into three groups; 1) Cirrhosis group: 40 patients with liver cirrhosis without HCC; 2) HCC group: 40 patients with liver cirrhosis and HCC as diagnosed by triphasic CT; 3) Control group: 16 healthy volunteers, with matched age and gender. Talin-1 was detected using enzyme linked immunosorbent assay (ELISA).

**Results:** The highest level of Talin-1 was observed among HCC group followed by cirrhosis then control groups (25 vs. 12 vs. 1.9 ng/ml; p = 0.001). In cirrhosis and HCC groups; we found a significant positive correlation between Talin-1 and ALT, AST, ALP, Bilirubin, INR, urea and AFP (p = 0.001), and a significant negative correlation between Talin-1 and albumin, creatinine, hemo-globin, WBCs and platelets (p = 0.001), and no significant differences were found regarding Talin-1 and HBsAg (p = 0.05). In HCC group; significant correlation was found between Talin-1 and each of multifocal HCC (29.5 vs. 23 ng/ml; p = 0.001), portal vein invasion (27 vs. 21 ng/ml; p = 0.022), and presence of ascites (27 vs. 20 ng/ml; p = 0.001). No significant correlation was detected with tumor size (p = 0.065). ROC curve analysis was used to test the performance of Talin-1 and AFP for cirrhosis diagnosis; Talin-1 at 6.2 ng/ml cutoff level had 90% sensitivity, 93.75% specificity and AUC = 0.980, while AFP at 2.5 ng/ml cutoff level had 92.50% sensitivity, 87.50% specificity and AUC = 0.969. By combining both markers, sensitivity was 95% with 96% specificity and AUC = 0.967. As regard discrimination between HCC and cirrhosis groups; Talin-1 at 14 ng/ml cutoff level had 100% sensitivity, 100% specificity and AUC = 1.000. After combining both markers, sensitivity was 95% with 100% specificity.

**Conclusion:** Talin-1 is a potential marker for diagnosis and prognostic assessment of both cirrhosis and HCC. Measuring both serum Talin-1 and AFP levels enhanced the diagnostic sensitivity in early detection of HCC. Further studies are needed to investigate the ultimate diagnostic and prognostic utility of serum Talin-1.

**Disclosure:** Nothing to disclose.

P1324 RISK OF AGGRESSIVE/ADVANCED HEPATOCELLULAR CARCINOMA DEVELOPMENT AFTER DIRECT ACTING ANTIVIRAL TREATMENT IN PATIENTS WITH HCV-RELATED CIRRHOSIS

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**Introduction:** Hepatocellular carcinoma (HCC) represents a serious complication of HCV-related cirrhosis. Introduction of direct acting antiviral (DAA) agents achieved high sustained viral response (SVR) rates of 90–95%, however, various risks regarding risk of HCC development after DAA treatment, moreover data on the risk of developing aggressive or advanced HCC in DAA-treated patients is still unknown and needs to be assessed.

**Aims and Methods:** Our aim was to compare the patterns of HCC development after DAA treatment to HCC patients who did not receive DAA. Moreover, we conducted a retrospective study on 137 patients presented to the HCC clinic at our institute over the period of 2 years. 88 patients were included in the study and 49 were excluded due to insufficient DAA treatment details. The patients were divided into 2 groups according to receiving DAA including “DAA-treated” group with patients who received DAA and “DAA-non-treated” group with those who didn’t receive DAA. Dynamic contrast enhanced CT/MRI were used to classify HCCs according to their size, number and presence of tumor vascular invasion (TIV) into: I) Early/less-aggressive (NA-HCC) defined as either single lesion < 5 cm or < 3 lesions all of which ≤ 5 cm in diameter and absence of tumor vascular invasion, and II) Advanced/aggressive patterns (A-HCC) defined as either single lesion ≥ 5 cm, ≤ 3 lesions with any ≥ 5 cm, or > 3 coexisting lesions (multicentric), or infiltrative HCC pattern ≥ presence of TIV. Results: Our study included 69 males and 19 females, with a mean (±SD) age of 60.2 (±8.48). The onset of HCC presentation in DAA-treated group had a median (IQR) value of (12.6) months after end of treatment. The DAA-treated group showed significantly higher frequencies of A-HCC patterns on presentation as compared to the DAA-non-treated group (x² = 8.17, p = 0.004), with a higher risk of presence of A-HCC patterns after DAA therapy (RR = 0.67, CI 95%: 0.46–0.95; p = 0.021). The treated group also showed higher frequencies of presence of TIV as compared to the DAA-non-treated group (x² = 7.016, p = 0.008) with a significantly higher risk of presence of TIV after DAA therapy (RR = 3.18, CI 95%: 0.26–12.80). Among the DAA-non-treated group the treated SVR and 16 were DAA responders, yet no significant correlation was found between DAA relapse and absence of presence of HCC patterns (p = 0.948).
P1326 FAVORITORES DE FACTORES PARA COMPLEJO RÉSPONS Y RECURRENCIA DESPUÉS DE CÁNCER CARCINOMATOUS: UNA EXPERIENCIA DE 5 AÑOS

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Introduction: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide, with most of the patients being diagnosed at intermediate to advanced tumour stages, at which therapy options are limited. TACE is the most used palliative treatment modality in this setting.

Aims and Methods: To investigate the predictive factors for complete response (CR) and recurrence after CR in patients with hepatocellular carcinoma (HCC) treated with transarterial chemoembolization (TACE).

From January 2013 to December 2017 we enrolled 168 newly diagnosed patients with HCC who were treated with TACE as a first therapy. We analyzed the predictive factors for CR and the risk factors for local and distant recurrence after CR using Cox proportional hazard model.

Results: The mean age of the patients was 62.2 ± 7.9 years. There were 115 male patients (68.4%) and 53 females (31.5%). Eighty-eight patients had an α-fetoprotein (AFP) level > 20 ng/mL. The median maximal diameter of the tumors was 3.5 cm. The median follow up period was 27.6 months. Sixty-three patients (37.5%) achieved CR after TACE, and recurrence after CR was detected in 37 patients (58.7%). In univariate analysis elevated serum AFP (≥ 20 ng/mL) level (hazard ratio [HR], 1.985; 95% confidence interval [CI], 1.047 to 3.839; p = 0.0355); tumor size (≥ 5 cm) (HR, 3.558; 95% CI, 1.347 to 9.389; p = 0.0104); multistage disease (HR, 5.0682; 95% CI, 2.2703 to 11.3144; p < 0.0001) were correlated with CR after TACE. In multivariate analyses, tumor size (≥ 5 cm) and single nodularity were predictive factors for CR with hazard ratios (HRs) of 2.56 (p = 0.0330) and 2.87 (p = 0.02). The recurrence rate of patients with tumor size (≥ 5 cm) and single nodularity was 3.5 cm. The median follow up period was 27.6 months. Sixty-three patients (37.5%) achieved CR after TACE, and recurrence after CR was detected in 37 patients (58.7%). In univariate analysis elevated serum AFP (≥ 20 ng/mL) level (hazard ratio [HR], 1.985; 95% confidence interval [CI], 1.047 to 3.839; p = 0.0355); tumor size (≥ 5 cm) (HR, 3.558; 95% CI, 1.347 to 9.389; p = 0.0104); multistage disease (HR, 5.0682; 95% CI, 2.2703 to 11.3144; p < 0.0001) were correlated with CR after TACE. In multivariate analyses, tumor size (≥ 5 cm) and single nodularity were predictive factors for CR with hazard ratios (HRs) of 2.56 (p = 0.0330) and 2.87 (p = 0.02), respectively. From the total 63 patients with CR, 55 patients had tumor size ≤ 5 cm, and only 8 patients (12.6%) had a tumor size > 5 cm. Fifty-one patients (80.9%) had a single nodule and 12 patients (19%) showed multiple nodules. In patients with recurrence after CR, in univariate analysis, multistage disease (HR, 8.226; 95% CI, 0.9535 to 72.3505; p = 0.473) and elevated serum AFP (≥ 20 ng/mL) level (HR, 2.995; 95% CI, 0.4557 to 14.9057; p = 0.0541) were associated with HCC recurrence. In multivariable analysis only multistage disease (HR, 3.835; 95% CI, 1.452 to 12.961; p = 0.0325) was associated with HCC recurrence after TACE-induced CR. Of the 63 patients with CR, 11 patients (17.4%) had multinodularity and 22 patients (34.9%) had elevated serum AFP (≥ 20 ng/mL) level. The recurrence rate of multinodularity (11/12 patients) was higher than that of single nodularity (26/51 patients) (91.6% vs 50.9%; p = 0.02). The recurrence rate of patients with elevated serum AFP (≥ 20 ng/mL) level (18/23 patients) was higher than that of patients with normal serum AFP (≤ 20 ng/mL level) (19/40 patients) (78.2% vs 47.5%; p = 0.03).

Conclusion: In patients treated with TACE as a initial therapy, tumor size (≤ 5 cm) and single nodularity were predictive factors for CR. Multinodularity was a predictive factor for recurrence after CR. After achieving CR the median time period to recurrence was 12 months.

Disclosure: Nothing to disclose.

P1328 ANALYSIS OF THE BILIARY BACTERIAL COMMUNITIES IN CHOLEDOCHOLITHIASIS PATIENTS WITHOUT RECENT ANTIBIOTICS TREATMENT BASED ON 16S RNA AMPLIFICATION SEQUENCING

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Introduction: Biliary bacteria play an important role in the pathogenesis of choledocholithiasis, but at present there are very few studies about the biliary microbiota. Our previous studies observed great bacterial community heterogeneity among patients and provided evidence for the potential source of biliary bacteria. However, the sample numbers of both studies were small due to the difficulty of sample collection. Besides, the medication history (i.e. the recent antibiotics treatment) might also lead to bias in the composition of bacterial communities. Thus, the biliary microbiota of a larger scale of choledocholithiasis patients, especially those with no recent antibiotics treatment, still needs further investigations.

Aims and Methods: This study aimed at the biliary microbiota of a larger scale of patients diagnosed with common bile duct stones. Bile samples from the common bile duct of primary choledocholithiasis patients were collected by ERCP. These patients had no other infections and did not receive antibiotics for at least one month before ERCP. They were divided into two groups: group NN, the first treatment ones, no recent antibiotics use with no endoscopic sphincterotomy history. Eventually, group NN contained 33 patients and group NE contained 19 ones. 16S amplicon sequencing was employed to analyze the biliary bacterial communities. At the phylum level, Proteobacteria, Firmicutes, Bacteroidetes, Fusobacteria and Actinobacteria were identified in both groups with a total relative abundance ≥ 87. At the genus level, the abundance of Escherichia/Shigella was the highest in both groups (NN = 0.27 and NE = 0.17). The average relative abundances of Pseudomonas, Streptococcus, Enterococcus, Prevotella, Neisseria, Klebsiella, Fusobacterium, Granulicatella, Veillonella, Aeromonas, Bacteroides and Pyramibacter were greater than 0.01, which was consistent with our previous studies.

2) Analysis of similarity using Bray-curtis distance showed that the microbiota dissimilarity of intra-group was significantly lower than that of inter-group. The similarity of the bacterial communities between samples within group NN was
significantly higher than that within group NE (P = 0.003). Principal coordinate analysis indicated that there were microbial composition differences between the two groups. Compared with group NN, the relative abundances of Pseudomonas, Neisseria, Ochrobactrum, Actinomyces and Rothia in NE group were decreased, while the abundances of Pyramidobacter, Akkermansia and Porphyromonas were increased (all P < 0.05). These bacteria were also confirmed by our previous studies.

3) The relative abundances of KEGG pathways in the biliary microbiota of group NN were predicted by PICRUSt. Compared with group NN, the abundances of pathways such as Peptidases, Energy metabolism and Lipopolysaccharide biosynthesis were increased in group NE, while that of the Glutathione metabolism pathway was decreased (all P < 0.05).

Conclusion: 1) Both groups had common kinds of bacterial taxonomic units, which indicates the shared pathogenesis of them. 2) EST may affect the composition of the biliary microbiota. 3) Pyramidobacter, Akkermansia and Porphyromonas may play key roles in the recurrence of cholecodolithiasis. 4) The Peptidases, Energy metabolism and Lipopolysaccharide biosynthesis pathways might be involved in the recurrence of cholecodolithiasis.

Disclosure: Nothing to disclose.

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INTRODUCTION: OJ is a condition that might lead to acute cholangitis and sepsis and multiorgan dysfunction, especially after surgical procedures. Intestinal mucosal barrier dysfunction and intestinal immune function decline might result in endotoxemia and bacterial translocation, which are important contributors to disease progression or death in patients. Toll-like receptors (TLRs) is a class of transmembrane receptors widely existed in mammalian cells. TLRs can recognize a number of conservative pathogen associated molecular patterns of pathogenic microorganism, initiate signal transduction, eventually stimulate the activation of NF-κB and induce inflammatory mediators expression. TLRs may thus play a key role in innate immune system.

Aims and Methods: We aimed to investigate the role of TLR4 in intestinal mucosa barrier damage and bacterial translocation in mice with obstructive jaundice (OJ). A total of 100 male C57BL/6J mice were randomly assigned to two groups: (I) sham operation (SH); (II) bile duct ligation (BDL). Mice were sacrificed at different time points (Before operation, as well as 1, 3, 5, 7 and 7 after operation). The blood, terminal ileum, liver, spleen and mesenteric lymph node ((MLNs)) were collected after the anesthetized condition simultaneously for further usage. The aminotransferase (ALT), total bilirubin (TB), alkaline phosphatase (ALP) and diamine oxidase (DAO) in blood were detected. The morphological changes of distal ileum tissue were observed using haematoxylin-eosin (HE) staining. The expression of Nuclear factor xB (NF-xB), TLR4 in different stage of OJ were observed by Western blot and Real-time PCR. The liver, spleen and MLNs were harvested for the detection of bacterial translocation.

RESULTS: In the SH group, TLR4 protein and mRNA were rarely expressed in the intestinal mucosa of mice and there were no significant differences at different time points (p > 0.05). By contrast, TLR4 protein (0.12 ± 0.06, 0.16 ± 0.08, 0.35 ± 0.12 and 0.41 ± 0.13 respectively) and mRNA (0.49 ± 0.19, 0.62 ± 0.23, 0.98 ± 0.32, 1.42 ± 0.41 and 1.72 ± 0.49 respectively) were increased gradually with the extension of OJ time in the BDL group (p < 0.05). The grade of mucosal injury, the level of plasma DAO and the expression of NF-κB were also increased with the extension of OJ time (p < 0.05). In addition, the rate of bacterial translocation was also increasing in the liver, spleen and MLNs in the BDL group. There were positive correlations between the grade of mucosal injury and expression of TLR4 (r = 0.781, p < 0.05) and NF-κB (r = 0.828, p < 0.05) in BDL group. In addition, there were positive correlations between the level of plasma DAO and expression of TLR4 (r = 0.775, p < 0.05) and NF-κB (r = 0.783, p < 0.05) in BDL group. NF-κB expression was positively correlated with TLR4 expression (r = 0.744, p < 0.05).

Conclusion: The expression of TLR4 was significantly up-regulated in the distal ileum of mice with obstructive jaundice. Overexpression and activation of TLR4 were involved in the occurrence and development of intestinal mucosa barrier damage and bacterial translocation in mice with OJ.

Disclosure: Nothing to disclose.
P1332 EVALUATION OF THE POTENTIAL USE OF A SET OF miRNA IN DIFFERENT BILIARY TRACTS FOR EARLY DIAGNOSIS OF CHOLANGIOCARCINOMA

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Introduction: Early diagnosis of malignancy in biliary tracts can be challen-
ging given the low rate of diagnostic accuracy of current modalities. Biliary
tracts in Endoscopic Retrograde Cholangiopancreatography (ERCP) with
nondiagnostic and/or biopsies, serum markers and imaging tests are con-
didered indeterminant. MicroRNAs (miRNA or miRs) are small
non-coding RNA molecules that have been associated with pathophysiological
processes in different organs and cell types, and are postulated as potential
targets for diagnosis and therapy.

Aims and Methods: The aim of the study was to evaluate the potential diagnostic
accuracy of a set of 3 miRNAs related to cholangiocarcinoma in indeterminate
biliary tracts. We performed a prospective case-control observational study of 18
patients, diagnosed with cholangiocarcinoma, indeterminate stenosis or
normal bile duct, who underwent ERCP and cholangioscopy. Biopsies under
direct visualization and/or brush cytology were obtained. Specimens were eval-
uated histologically and miR-21, miR-675 expression was quantified using Reverse Transcription Polymerase Chain Reaction (RT-PCR, relative
quantification).

Results: 18 patients underwent cholangioscopy (male 50%, mean age: 67.8). 8
patients had cholangiocarcinoma (mean age: 77.1), 6 had indeterminate bile
tracts (mean age: 63.3) and 4 had normal bile duct (mean age: 56). Normal
bile duct cohort results were used as control. MiR-21 expression was upregulated in both cholangiocarcinoma [4.20 times \(\pm 2.32\), \(2.32–9.09\)] and indeterminate
cohorts [1.92 times \(\pm 1.20\), \(1.12–1.92\)]. MiR-675 expression was upregulated in both cholangiocarcinoma [5.59 times \(\pm 2.09\), \(2.78–7.19\)] and downregulated in indeter-
minate cohort [3.34 times \(\pm 3.24\), \(2.32–9.09\)]. Similarly, miR-675 expression
was upregulated in cholangiocarcinoma [4.4 times \(\pm 2.45\), \(2.19–9.21\)] and down-
regulated in indeterminate cohort [\(3.16 times \pm 0.98\), \(2.08–4.54\)]. Surprisingly, all cases in cholangiocarcinoma and indeterminate cohorts upregulated or down-
regulated as above mentioned miR-483 and miR-675 expression, respectively.

Conclusion: Our limited data suggest that there may be a role for miRNAs in
differentiating between malignancy in indeterminate biliary tracts. MiRNAs
may represent a new research area. More trials are required for confirmation of the
above results and establishment of cut-off values.

Disclosure: Nothing to disclose

P1334 SURVIVAL OF PATIENTS WITH DISTAL
CHOLANGIOCARCINOMA: A POPULATION-BASED DUTCH
COHORT


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Introduction: Real-life treatment and outcomes of distal cholangiocarcinoma in
the Western world are largely unknown. This study investigated treatment, out-
comes, time trends and predictors for survival in a nationwide cohort of patients
with distal cholangiocarcinoma.

Aims and Methods: A population-based cohort derived from the Netherlands
Cancer Registry was studied. All patients (resected and unresected) registered
to have distal cholangiocarcinoma between 2009–2015 were included. Missing
data were handled using multiple imputation. Survival and predictors for survi-
val were analyzed using Kaplan Meier and Cox regression analysis (backward
selection).

Results: During the study period, 1152 patients were registered; 537 (46.6%)
underwent resection, 376 (32.6%) had unresected non-metastasized disease
(M0) and 239 (20.7%) had metastasized disease (M1). In the resected group, 36-
day mortality was 5.4% (n=29) and adjuvant chemotherapy was rarely used
(8.4%, n=45). Palliative chemotherapy was administered in 19 (5.1%) of the
patients with non-resected M0 and in 74 (31.0%) of the M1 patients. Median
global survival for patients with resected, unresected M0, and M1 patients was 23
months (95% CI 20.25–7.10 months) (95% CI 1.43–7.06) and 4 months (95% CI 3.5–3)
(p < 0.001), respectively. Over time, survival did not improve in any of the sub-
groups. Negative independent prognostic factors for survival in resected patients
were increasing age (p < 0.01), T3/T4 stage (p < 0.02), higher lymph node ratio
(p < 0.001), poor differentiation (p < 0.001), and age (p < 0.001) and microscop-
ic (p < 0.03) residual disease.

Conclusion: This largest nationwide Western study on distal cholangiocarcinoma
demonstrates a 47% resection rate with acceptable survival despite limited use
of adjuvant chemotherapy, and poor survival and limited use of chemotherapy in
unresected patients. The study identified predictors for survival which can be
useful to stratify future clinical trials with (neo-) adjuvant or palliative treatment.

Disclosure: Nothing to disclose

P1333 A STUDY OF CORRELATION BETWEEN NEUTROPHIL-TO-
LYMPHOCYTE RATIO AS A PROGNOSTIC FACTOR IN
CHOLANGIOCARCINOMA

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Introduction: Neutrophil-to-lymphocyte ratio (NLR) is an indicator of the sys-
temic inflammatory response, which has been proposed to be used as a prognos-
tic marker in various types of cancers. Cholangiocarcinoma is a common cancer
in Thailand. However, data regarding NLR in this cancer is still limited.

Aims and Methods: We would like to verify if NLR could be used as another
predictor of survival which can be utilized to predict prognosis of cholangiocar-
cinoma.

Results: 536 consecutive patients met the inclusion criteria, after considering the
exclusion criteria, 171 patients were eligible for the final analysis. The mean age
of patients was 59.26 ± 10.88 years. Eligible patients were categorized into 3
groups according to treatment modalities; palliative chemotherapy (N = 77,
45%), adjuvant therapy (N = 37, 21.6%) and surgery group (N = 57, 33%). The NLR value of the palliative chemotherapy (N = 77)
was 2.76 with sensitivity of 74% and specificity of 53%. Patients who had NLR < 2 across the study
time (before, during and after treatment) had the best survival (Median
OS = 34.8 and 37.1 months). Patients with initial NLR < 2 had median overall
survival (OS) and progression-free survival (DFS) (Median OS = 34.8 and 50.6 months respectively compared to median OS of 21.6 months
(P = 0.001) and median DFS/DFS of 16.6 months (P = 0.004) in patients with
NLR ≥ 2. Multivariate analysis demonstrated that high level of CEA and CA19-
9 were significant predictors for DFS/DFS (HR 2.29 and 2.03, P = 0.016 and 0.043, respectively). Worse OS were predicted by NLR ≥ 2 (HR 1.76, P = 0.021, CA 19-1 > 300 (HR 1.79, P = 0.009), and ECOG ≥ 2 (HR 6.24, P = 0.016). Only patients in surgical group had significantly survival difference
according to the change of NLR.

Conclusion: NLR can be considered as another independent prognostic factor to
predict survival in patient with cholangiocarcinoma. As NLR is a cheap and
simple, already available test, we proposed to use NLR as a useful biomarker to
predict prognosis of cholangiocarcinoma.

Disclosure: Nothing to disclose

P1335 ENDOCOSPIC SNARE PAPILLOLECTOMY (ESP) FOR
AMPULLARY TUMOURS – SINGLE-CENTER EXPERIENCE

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Introduction: Ampullary tumors may be adenoma, adenocarcinoma or other rare
lesions. Although it carries high morbidity, Whipple’s pancreatico-duodenecto-
yomy is the recommended treatment modality in most. There is an increasing
interest in endoscopic snare papillotomy (ESP) as an alternative minimally inva-
sive treatment option. We report long-term results of ESP in a retrospective
patient cohort from a single center.
Aims and Methods: Patients with localised ampullary tumors treated by ESP during 2007–2017 were included. Only a small proportion of patients with perihilar cholangiocarcinoma (hCCC) can be delivered to curative surgical resection. If surgery is impossible, the treatment consists of palliative chemotherapy and biliary drainage. In addition, local ablative therapy such as photodynamic therapy (PDT) can be obtained. In previous studies, PDT showed ambiguous results regarding overall survival and clinical profit. Aim of this investigation is to analyse the therapeutic benefit of PDT in a clinical retrospective setting without restriction to combination of PDT with stent or concomitant chemotherapy.

Methods: We retrospectively analysed the data of 65 patients with histologically confirmed hCCC that were treated from 2003 until 2013. 30 patients received only stent therapy (group A), 35 patients received stent therapy with PDT (group B). PDT was performed with the photosensitizer porfimer sodium. The photosensitization (wavelength: 680 nm, light dose: 180 J/cm²). Survival time, numbers of needed ERCP and complication rate were statically evaluated. Subgroup analyses were done for patients with concomitant chemotherapy.

Results: PDT did slightly improve the survival time (A: 9.2 ± 6.2 months, B: 11.7 ± 8.8 months; p = 0.348) and reduced the numbers of needed ERCP within 3 months (A: 1.8 ± 1.2, B: 1.5 ± 0.49; p = 0.115). The complication rate per person was equal in both groups (A: 3.17 ± 2.86, B: 2.69 ± 2.12%). Photostation skin reactions occurred in 17.4% of patients with PDT. 32.3% of the patients were able to receive additional chemotherapy which only minimally increased the survival time in both groups (A: 10.7 ± 4.5 months, B: 16.1 ± 10.7 months; p = 0.348).

Conclusion: The impact of PDT on survival time in unselicted patients with hCCC is low. The attributed advantages of PDT were not statistically significant and independent of additional chemotherapy.

Disclosure: Nothing to disclose

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P1340 MAST CELL STABILIZERS AMELIORATE PAIN IN EXPERIMENTAL CHRONIC PANCREATITIS

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Introduction: In both chronic and acute pancreatitis (AP), pain is the cardinal symptom and notoriously difficult to manage. In recent studies, we detected a significant enrichment of mast cells around islet tissue of pancreatitis patients with painful chronic pancreatitis (CP).

Aims and Methods: In the present study, we analyzed whether administration of mast cell stabilizers can improve the pain due to CP. For this purpose, AP and CP were induced in 8-week-old C57BL/6J mice via repeated i.p. injections of the cholecystokinin octapeptide (CCK8) or saline. Mice were either prophylactically, 15 min before CCK8 injection or 1h after (AP) or 1 week (CP) prior to disease induction, or therapeutically, i.e. beginning in the third hour (AP) or at week 2 (CP) after disease induction, with one of the mast cell stabilizers ketotifen or cromoglicate. Metamizol was applied as a positive control, and solvent was applied as control. The mast cell stabilizers were applied i.p. during AP, and combined orally and s.c. during CP. The pain-associated behavior of mice was assessed via the von Frey mechanical sensibility test, and via the open-field locomotion test.

Results: In dose-finding experiments, the effective analgesic doses for each drug were identified (metamizol: 500mg/kg BW, ketotifen: 10mg/kg BW, cromoglicate 500mg/kg BW). In the final therapy experiment, in AP, the mast cell stabilizers ketotifen and cromoglicate were as effective as single therapeutics to the mice. However, in CP, we observed a significant reduction in the von Frey pain scores and improvement in the locomotion scores of the mice treated with ketotifen or cromoglicate.

Conclusion: The present study showed for the first time a potential analgesic effect of mast cell stabilizers in pancreatic pain. Further preclinical studies analysing mast cell stabilizers as adjunct analgesics are currently underway. This novel concept also needs testing in early phase clinical trials.

Disclosure: This abstract was also presented at the DGVS 2017 congress.

References

P1342 FUNCTIONAL GENOMIC SCREENING DURING SOMATIC CELL REPROGRAMMING IDENTIFIES DKK3 AS A ROADBLOCK OF PANCREATIC REGENERATION

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Introduction: The reprogramming process partly eliminates disease- and aging-associated phenotypes, inducing a “partial cure” or “rejuvenation” in pluripotent cells as shown in studies using somatic cells from centenarians or patients with cellular reprogramming therapies and aged-matched controls. The reprogramming process partly eliminates disease- and aging-associated phenotypes, inducing a “partial cure” or “rejuvenation” in pluripotent cells as shown in studies using somatic cells from centenarians or patients with disease. The reprogramming process partly eliminates disease- and aging-associated phenotypes, inducing a “partial cure” or “rejuvenation” in pluripotent cells as shown in studies using somatic cells from centenarians or patients with disease.

Aims and Methods: We propose that studying somatic cell reprogramming could serve as a tool to gain valuable insights into adult stem cell fitness in organ regeneration. As logical consequence we have successfully applied a straightforward functional genomics approach using RNA-interference techniques during iPSC formation.

Results: We identified a set of factors limiting both cellular reprogramming and stem cell fitness in the hematopoietic system. Dkk3 (Dickkopf 3) was found to be a factor limiting these two features. Consequently we aimed to investigate the role of Dkk3 during liver and pancreas regeneration upon injury. To do so, we used Dkk3 null mice to examine its role in a cerulein-induced acute pancreatitis context. First, there was no effect on the acute injury but Dkk3 loss appeared to increase pancreatic regeneration. To do so, we used Dkk3 null mice to examine its role in a cerulein-induced acute pancreatitis context. First, there was no effect on the acute injury but Dkk3 loss appeared to increase pancreatic regeneration. To do so, we used Dkk3 null mice to examine its role in a cerulein-induced acute pancreatitis context. First, there was no effect on the acute injury but Dkk3 loss appeared to increase pancreatic regeneration. To do so, we used Dkk3 null mice to examine its role in a cerulein-induced acute pancreatitis context. First, there was no effect on the acute injury but Dkk3 loss appeared to increase pancreatic regeneration. To do so, we used Dkk3 null mice to examine its role in a cerulein-induced acute pancreatitis context. First, there was no effect on the acute injury but Dkk3 loss appeared to increase pancreatic regeneration.

Disclosure: Nothing to disclose

References
edema and inflammation scores, and a diminished fibrotic content. Additional mechanistical insights are given by organoid cultures derived from wild type and Dkk3 null pancreata. In contrast, partial hepatectomy in Dkk3 null mice revealed just a trend toward better regeneration.

Conclusion: DKK3 appears to act as a brake of acinar regeneration after pancreatitis insult in a tissue-specific manner.

Disclosure: Nothing to disclose

P1343 SMALLER PORTAL SYSTEM VEIN DIAMETERS PREDICT COMPLICATIONS AND OUTCOME IN ACUTE PANCREATITIS


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Introduction: Acute pancreatitis (AP) progresses to necrotizing pancreatitis in 15% of cases [1]. An important pathophysiological mechanism in AP is third spacing of fluids, which leads to intravascular volume depletion that may progress to hypovolemic shock [2, 3]. This compromises the splanchnic circulation to the portal, splenic and SMV compared to those with predicted severe AP. Radiological scoring systems to predict the severity of pancreatitis.

Methods: We explored the use and yield of additional diagnostic tests (i.e. endosonography, MRI/MRCP, CT, diagnostic ERCP and IgG4). Between 2008 and 2015, patients presenting with acute pancreatitis were registered. This initial work-up included: personal history (signs of a biliary etiology), clinical examination, diagnostic work-up with regard to the etiology of their pancreatitis, laboratory data and imaging. Computed tomography (CT) scan identified the diameters of the vein of interest. Analysis of association between vein diameter and mortality (RR 0.75 (0.59–0.97)), a smaller diameter was a risk factor for mortality. The secondary endpoints were (infected) necrotizing pancreatitis and (persistent) organ failure.

Results: The total sample consisted of 177 patients. Multivariate regression analysis corrected for possible confounders. Additionally, we performed an analysis in which we compared the mean vein diameters in patients with predicted mild and severe AP by Student’s t-test. The primary endpoint was AP-related mortality. The secondary endpoints were (infected) necrotizing pancreatitis and (persistent) organ failure.

Conclusion: We observed that a smaller diameter of the splenic vein is a risk factor for mortality and a smaller diameter of all portal system veins is a risk factor for mortality. The results of the univariate and multivariate analysis are displayed in the table. Patients with predicted mild AP had significantly larger diameters of the portal, splenic and SMV compared to those with predicted severe AP.

Disclosure: Nothing to disclose

References

P1344 DIAGNOSTIC WORK-UP IN IDIOPATHIC ACUTE PANCREATITIS, A POST-HOC ANALYSIS OF A PROSPECTIVE MULTICENTER OBSERVATIONAL COHORT

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Introduction: After standard diagnostic work-up, the etiology of acute pancreatitis remains unknown in up to 25% of cases, a condition referred to as idiopathic acute pancreatitis (IAP). Determining the etiology of pancreatitis is essential, as it may direct treatment in the acute phase of the disease and guide interventions to prevent recurrent pancreatitis.

Methods: We explored the use and yield of additional diagnostic tests (i.e. endosonography, MRI/MRCP, CT, diagnostic ERCP and IgG4). Furthermore, we analyzed the recurrence rate of acute pancreatitis after a first episode of IAP and assessed what the impact was of establishing an etiological diagnosis on recurrence rates.

Results: Out of the 1632 patients that were registered, 191 patients were diagnosed with at least one episode of IAP. Of these 191 patients, 176 (92%) underwent one or more additional diagnostic test: CT (n = 124, yield 8%), EUS (n = 62 patients, yield 35%), MRI/MRCP (n = 56, yield 33%), repeat ultrasound

Disclosure: Nothing to disclose

References
Aims and Methods: Consecutive patients of AP with symptomatic ANC or WON undergoing PCD were evaluated in a tertiary care centre in North India between January 2011 and December 2017. The two were compared for indications and outcome (mortality and surgical necrosectomy). The need for up-grading of first PCD, need for additional drain, total duration of PCD and length of hospital stay). Complications related to PCD were also compared.

Results: Of the 650 patients (mean age was 38.58 ± 12.28 years; 71.56%; males; 97.3% biliary etiology), 128 patients underwent PCD for ANC and 522 for WON. The commonest indication for PCD was, in both ANC (n = 135, 52.3%) and WON (n = 79, 67.5%) was suspected infection of pancreatic necrosis. Persistent organ failure as an indication for PCD was significantly more common in patients with ANC than WON (38% vs 16.2%, p = 0.001). Pressure symptoms formed the indication for PCD in 9.7% patients with ANC and 16.2% with WON (p > 0.05). Infection of pancreatic necrosis was proven with culture of drain fluid in 146 (56.6%) patients with ANC and 75 (61.5%) patients with WON (p = 0.104). One PCD was placed in 152 (58.9%) patients with ANC and 72 (61.5%) patients with WON with a mean of 1.50 ± 0.66 and 1.50 ± 0.72 PCDs per patient respectively (p = 0.915). The total duration of PCD in ANC was 28.38 ± 20.72 days versus 30.16 ± 26.20 days in WON (p = 0.479). Surgical necrosectomy was needed in 14% patients with ANC versus 12% patients with WON (p = 0.364). Mortality was 19% in patients with ANC as compared to 13.7% in those with WON (p = 0.132). Complications of PCD included external pancreatic fistula (27.5%), blockade of PCD catheter (12.3%), slippage of PCD catheter (10.9%), and bleed through PCD catheter. External pancreatic fistula which occurred more often in WON than in ANC (24.4% versus 34.2%, p = 0.034).

Conclusion: Outcome of PCD is similar in patients with ANC and WON. However, persistent organ failure formed an indication for PCD in greater number of patients with ANC than WON. External pancreatic fistula occurred more often in WON than ANC.

Disclosure: Nothing to disclose

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Introduction: Percutaneous catheter drainage (PCD) is the initial step of step-up approach for management of acute pancreatitis (AP). Currently no reliable criteria are available to predict which patients may benefit from PCD.

Aims and Methods: The aim of this study was to identify factors that lead to surgical intervention or mortality after initial management with PCD. In a prospective observational study, 101 consecutive AP were managed by step up approach of PCD when indicated. Primary outcome measures were need for surgical necrosectomy and mortality.

Results: Out of 101 patients of AP, 50 patients were treated conservatively and 51 required PCD. A total 87 PCD catheters were placed. The success rate of PCD in our study was 66.66% (34/51) and 4 patients required additional surgical necrosectomy after PCD. Overall mortality rate in our study was 29.4% (13.51, including 2 after surgery). PCD alone improved organ failure in 72.54% patients. Patients were divided into two groups, PCD success group (i.e survival without necrosectomy) and failure group. Size of first PCD was significantly larger in PCD success group (13.94 ± 2.48 vs 12.58 ± 1.17 F, p = 0.011). There was a
significant percent volume reduction in PCD success group than in failure group (96.3% ± 31.02% vs 54.5% ± 30.0%). Non-specific scores on predicting intra-hospital mortality, need for surgery and complications in SAP were also observed in the non-survivor group (p = 0.005) and percentage of volume reduction after PCD insertion (7.96 vs 13.23, p = 0.006) were similar between groups. ICU stay was significantly longer in PCD failure group (6.35 ± 7.96 vs 13.23 ± 12.21, p = 0.046). Higher number of patients had volume of collection more 750 CC before PCD (p = 0.005) in PCD failure group.

Conclusion: Larger size of the first PCD and more than 50% reduction of collection after PCD were positive predictors of PCD success. Total volume of collection more than 750 CC before PCD was a negative predictor of PCD outcome.

Disclosure: Nothing to disclose

P1348 COMPARISON OF PROGNOSTIC SCORES IN THE CRITICALLY ILL PATIENT WITH SEVERE ACUTE PANCREATITIS

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Introduction: A large number of studies have focused on identifying severe forms of acute pancreatitis (SAP) within heterogeneous groups of patients mostly of whom exhibit non-severe forms. However, the value of such predictors in the identification of patients with the worst prognosis in pre-selected groups, such as the critically ill patient with SAP, has been less studied.

Aims and Methods: We aimed to compare the accuracy of non-specific and specific scores in the prediction of hospital mortality, need for surgery and complications in SAP. We have also evaluated the accuracy of individual clinical and laboratory parameters.

Single-center retrospective cohort including all adult patients with severe acute pancreatitis admitted between January 2007 and February 2017 at a general intensive care unit (ICU). Severity and local complications were defined according to the 2012 Atlanta classification. Clinical, age, body mass index, vasopressor use, mechanical ventilation, hemodialysis and blood transfusions, laboratory parameters (C-reactive protein, CRP, serum creatinine, albumin levels) data and Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA) Simplified Acute Physiology Score (SAPS), Systemic Inflammatory Response Syndrome (SIRS), Ramsay’s criteria, Bedside Index for Severity in Acute Pancreatitis (BISAP), Pancreatitis Outcome Prediction (POPC) were collected on admission. Laboratory parameters were also recorded at 48 hours from admission. Statistical analysis was performed with SPSS v.24 and STATA v.14.

Result: 57 consecutive patients were included in the study (59.6% male, median age 71 ± 13 years). 49.1% had cardiovascular comorbidity. 42.1% of the SAP cases were biliary and 43.9% had necrotizing pancreatitis. 49.1% had SAP complications mostly intra-abdominal ischemia. 19 patients required surgery after admission with ICU mortality 6.3%.

APACHE II, SAPS, POP and SOFA scores were significantly higher in the non-survivor group when compared to the survivor group (p < 0.0001, < 0.0001, p = 0.004, respectively). Significantly higher serum levels of creatinine (Cr) and CRP were also observed in the non-survivor group (p = 0.048 and p = 0.001 respectively). Other scoring systems and laboratory parameters did not differ significantly. ICU related variables associated with increased mortality included need of hemodialysis (p = 0.001) and vasopressor requirement (p = 0.002).

POPC score had the highest prediction accuracy for mortality without statistical significance (p = 0.5). None of the scoring systems were able to predict with high accuracy the need for surgery or SAP complications. Necrotic pancreatitis correlated significantly with need for surgery during ICU stay and complications is expected (p < 0.0001 and p = 0.047 respectively) but not with mortality (p = 0.057). Age, Body Mass Index, and comorbidities had no statistical correlation with any of the outcomes.

Conclusion: Severe acute pancreatitis is associated with high intensive care unit mortality rates. POP, APACHE II, SAPS and CRP, were able, in this group of patients, to predict mortality with high accuracy. We believe that an early risk stratification of the critical patient influences subsequent management and outcomes positively and should be used in everyday clinical practice.

Disclosure: Nothing to disclose

P1349 ACUTE PANCREATITIS AS A RARE COMPLICATION OF HYDATID LIVER CYST. REPORTS FROM MOROCCO

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Introduction: Acute pancreatitis (AP) due to hydatid liver cyst (HLC) is an exceptional complication of hydatid liver cyst (HLC). Its pathogenesis is probably due to pancreatic duct obstruction secondary to fistulization of the HLC in the biliary duct. It combines the measures of AP and endoscopic retrograde cholangiopancreatography (ERCP) to unblock the biliary duct and the cystic duct of the HLC and bili cystic fistula in order to prevent recurrence. We report a first case of 16 patients diagnosed and treated at the University Hospital Hassan II in the western part of Morocco.

Aims and Methods: This retrospective study was conducted between January 2013 and April 2018. Sixteen patients were hospitalized in our center for acute pancreatitis associated with biliary fistulization HLC assessed by ultrasound and computed tomography (CT) and ERCP showed: age, sex, severity of pancreatitis, imaging data, modalities and outcomes of endoscopic and surgical treatment.

Results: The average age of our patients was 44.33 years (20–66). We observed a female predominance with a sex ratio F/H of 1.3. All patients had acute pancreatitis associated with angiocholitis. Only 12.5% (n = 2) of the patients had past history of surgical cure of HLC. Nine patients (56.25%) had systemic inflammatory response syndrome (SIRS) at admission. In CT, Baltazar’s APACT scores A, B, and C accounted for 87.5% (n = 14) and the E stage for 12.5% (n = 2). The hydatid liver cyst was classified stage II according to G哈RBII classification in 62.5% of patients (n = 10). The size of the cyst varied between 4 and 12 cm. In the 15 patients who underwent ERCP (N = 15) for visualization of cystic fistula, all patients had surgical cure of their HLC the biopsy of resection of the biliary and cystic fistula. After treatment, one patient had anaphylactic shock following intraoperative rupture of the cyst, and another patient had a perforation of the residual cavity, he benefited from percutaneous drainage afterwards.

Conclusion: Acute pancreatitis is an exceptional complication of hydatid liver cyst. It is often associated with angiocholitis. Imaging allows diagnosis and visualization of cystic fistula in 2/3 of cases. The ERCP combined to surgery of HLC remain the key treatment.

Disclosure: nothing to disclose

P1350 whole-exome sequencing to identify genetic risk factors for multiple-organ failure in severe acute pancreatitis

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Introduction: Acute pancreatitis has a severe disease course in 20% of the patients, often characterized by persistent (multiple) organ failure. It is largely unknown what factors contribute to this severe complication. Genetic risk factors are thought to enhance severity in complex traits like acute pancreatitis, and this could be an explanation for observed difference in phenotype. However, discovery and validation of novel genetic associations often requires large sample sizes. One strategy to maximize power is to select and compare patients with extreme phenotypes.1 One strategy to maximize power is to select and compare patients with extreme phenotypes.

Aims and Methods: A case-control study with an extreme phenotype approach was performed to identify genetic risk factors for multiple organ failure in patients with acute pancreatitis. The study population was a Dutch cohort of 30 patients that were potentially eligible for inclusion in a randomized clinical trial that investigated the efficacy of prophylactic probiotics in patients with predicted severe acute pancreatitis (PROPATRIA).2 Consent was given for the use of stored blood for genetic studies in acute pancreatitis. Nine patients with early multiple-organ failure were matched with mild to moderate acute pancreatitis. After DNA isolation and exome capture, the samples were sequenced on an Ion-Proton platform. Candidate variants that are associated with multiple-organ failure were identified using bio-informatics approaches.

Results: Exome sequencing resulted in 161,690 variants that passed quality control, of which 38,333 were synonymous and subsequently selected for downstream analyses. Of these, 153 variants were overrepresented in patients with multiple-organ failure. Gene-set enrichment analyses showed that one gene-set, KEGG (regulation of processing, harbors more variants than can be expected by chance. Among the highest ranking candidate variants were in the caspase gene family, CASP9 and CASP10, which are key regulators of apoptosis. Other promising variants are in genes involved in the innate immunity, such as HLA-DQB1, KIR2DS4 and FCGRI4. Finally, a candidate list of 52 variants was constructed for the validation process.

Conclusion: This is the first study that identifies genetic risk factors of multiple-organ failure in acute pancreatitis using Next-Gen sequencing. Whole-exome...
P3151 PULMONARY FUNCTION IN THE EARLY PHASE OF ACUTE PANCREATITIS: A PROSPECTIVE COHORT STUDY


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Introduction: During the early phase of acute pancreatitis (AP), which lasts about one to two weeks, about two-thirds of the patients develop respiratory complications. This might be due to the pathological complexity. Activated pancreatic enzymes are important mediators of severe pancreatic inflammation and systemic toxicity including activation of the complement system, over activation of the leucocyte system, and the involvement of the inflammatory mediators, which in turn can cause endothelial and epithelial barrier dysfunction [2]. Pulmonary complications based on gas exchange, chest x-rays and computerized tomography scans have been evaluated [3,4]. Only few studies have attempted to evaluate the pulmonary function in the early phase of AP and with conflicting results have been reported [5,6].

Aims and Methods: To evaluate the changes in pulmonary function tests during the early phase of acute pancreatitis (AP), We included patients with their first attack of AP regardless of aetiology or disease severity admitted to our department in the period February 2016 to June 2017. The diagnosis of AP was based on revised Atlanta criteria [7].

Severe AP was defined as C-reactive protein (CRP) > 150 mg/l. Patients were evaluated on day 1, 2, 3, 6, and 10, and one month after hospital discharge in our outpatient clinic. We measured plasma values of CRP, white blood count (WBC), amylase and albumin, and performed chest x-rays. Pulmonary function tests included the % predicted: forced expiratory volume during the first second (FEV1), forced vital capacity (FVC), total lung capacity (TLC), diffusion lung capacity (DLCO) and the ratio between DLCO and alveolar volume (Dl/VA). Patient characteristics were summarized using means with standard errors (SD) or proportions. Groups were compared using t-test or one-way analysis of variance (ANOVA) with Bonferroni’s correction for multiple comparisons.

Results: A total of 44 patients (52% men; mean age 52 years; gallstone pancreatitis 66% and alcohol related pancreatitis 20%) admitted with their first attack of AP and 22 healthy controls were included. Eighteen patients (41%) developed severe AP. Six patients were treated at the intensive or semi-intensive care unit. Three patients died (7%) during admission. Twenty-eight percent developed pulmonary complications with pneumonia, atelectasis and/or pleural effusion. Thirty-four percent required oxygen therapy, and 34% required continuous airway pressure. None required mechanical ventilation or pleural drainage. From day one, patients had impaired FEV1, FVC, DLCO, and TLC compared with controls (p < 0.0001 in all analyses). The pulmonary dysfunction was greater for patients with lung complications compared with controls (p < 0.0001). Patients without lung complications (p < 0.0001). Evidence of pulmonary dysfunction, especially DLCO, was also seen after discharge.

Conclusion: This study suggests that patients with AP develop pulmonary dysfunction, probably due to combination of extra-pulmonary causes and alveolar damage, from the first day after hospital admission and that the dysfunction may last for several weeks after hospital discharge.

Disclosure: L.L.G. acted as investigator in clinical trials funded by Merck, Abbvie, Intercept, and Norgine, got travel expenses covered by Novo Nordisk, and have gave lectures funded by Eli Lilly and NovoNordisk. The remaining authors declare no conflicts of interest.

References

P3152 DEVELOPMENT OF A SCORE TO DETERMINE THE RISK OF ACUTE BILIARY PANCREATITIS RELAPSE BEFORE CHOLECYSTECTOMY

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Introduction: International guidelines for Acute Pancreatitis (AP) recommend that patients with Acute Biliary Pancreatitis (ABP) should undergo cholecystectomy during index admission or in 4 weeks’ time after discharge. However, this recommendation is not consistently followed and the disease recurs in a proportion of patients. A system is needed to determine the risk of recurrence after ABP to prioritize patients for cholecystectomy in the surgical waiting list.

Aims and Methods: We developed a model to determine the recurrence of ABP, based on demographic data, endoscopic procedures and laboratory tests at admission for a first episode of ABP.

A retrospective cohort study of patients admitted at our Department from 2010 to 2015 with a first episode AP was carried out. All patients were prospectively enrolled in a central electronic medical record (EMR), which is shared by all the hospitals and health centres around the north-west of Spain. Biliary aetiology was defined by the presence of stones, or sludge/microthiasis in the CBD or gallbladder at abdominal ultrasound, EUS or MRCP, together with the absence of AP relapse over at least 2-year follow-up after cholecystectomy. Liver laboratory tests at admission were recorded. Primary outcome was ABP recurrence during the first six-month period after admission for ABP. Survival analysis was performed using the Kaplan–Meier method. Factors associated with ABP recurrence were scored and patients were classified as low, intermediate and high risk of relapse according to the total score. A Cox regression to compute hazard ratios (HR) and 95% CIs to determine associations between risk of progression and scores were used.

Results: 353 patients with a first episode of ABP were included. The median time for cholecystectomy was 135 days (range 72–199). After exclusion of patients who waited longer than 6 months for cholecystectomy, 221 patients were finally included; 135 (60.5%) were female, mean age 67.6 years (range 51.2 to 77.7). ABP relapsed in 56 patients (25.1%). Serum levels of alkaline phosphatase, endoscopic sphincterotomy (EE) and severity of AP were significantly associated with the risk of ABP relapse. Scores assigned (Table) identified patients at risk of ABP relapse with a c-statistic of 0.63 (95% CI 0.57–0.68), (p < 0.001). HR 3.33 (95% CI 1.73–6.40). Patients in the high, intermediate and low-risk group had a rate of ABP relapse of 21.5%, 3.6% and 0.0%, respectively.

Conclusion: A score system (named Recurrence Acute Biliary Pancreatitis (RABP) score) was developed based on admission serum levels of alkaline phosphatase, EE and severity of AP. The RABP score identified patients with ABP at low, intermediate and high risk of recurrence, allowing patients in the cholecystectomy waiting list to be prioritized.

Serum alkaline phosphatase Score
0 to 263 (Normal limit) 5
264 to 526 (1–2 ULN) 4
527 to 789 (2–3 ULN) 3
790 to 1052 (3–4 ULN) 2 >1052 (>4 ULN) 0

Severity of AP
Mild AP 4
Moderate AP 3
Severe AP 2

ERCP + EE
No 0
Yes 4

ULN, upper limit of normal.
Low risk: 4 to 8 points; intermediate risk: 9 to 11 points; high risk: 12 to 13 points

[Relieving Acute Biliary Pancreatitis Score.]
Introduction: The timing of, and indication for ERCP in acute biliary pancreatitis (ABP) is an unresolved issue. Whilst expert opinion suggests early ERCP (<72 hours) should be performed in the setting of cholangitis and ongoing obstruction, lack of consensus guidelines means that practise is variable. Data suggests that often ERCP is not necessary as most ductal gallstones pass spontaneously.

Aims and Methods: The purpose of this study was to assess the use of ERCP in the setting of ABP, specifically evaluating timing and findings at ERCP. We retrospectively reviewed the case notes of all patients admitted to Brighton and Sussex University Hospitals NHS Trust with a diagnosis of ABP between 1st January 2013 and 31st December 2017. Data recorded included age, sex, LFTs on admission, hospital course, and imaging obtained. If ERCP was performed, the timing and ERCP findings were analysed, and details of any subsequent cholecystectomy were recorded.

Results: One hundred and fifty seven patients (64 male, 93 female) were admitted with acute biliary pancreatitis during the three-year period with a median age of 63 (Range 14–101), 69 patients (44%) underwent ERCP, 16 patients (23%) had ERCP within 72 hours. The median time to ERCP from admission was 10 days (range 1–48 days). ERCP was unsuccessful in 4 cases (5.7%). Stones were found in less than half the cases (32.65; 49%). Compared with definite imaging findings, equivocal imaging findings (eg possible stone and biliary dilatation only) was associated with no stone being found at ERCP (66% in equivocal, vs 42% in definite imaging findings). A trend towards lower chance of finding a stone at ERCP in those who had the procedure 3–14 days from admission compared with those ERCP’d within 72 hours (46% vs 75%, p = 0.09). 26 patients proceeded to cholecystectomy and median number of days before cholecystectomy is 33.5 days (range 4–663 days)

Conclusion: In ABP, ERCP is not always indicated even when stones are seen in the CBD on imaging. Our data suggests that stones often pass spontaneously after the imaging and that unnecessary ERCPs are performed. We suggest that in selected cases (eg with equivocal imaging), repeat imaging/critical evaluation is performed at 10–14 days to reassess the need/indication for ERCP.

Disclosure: Nothing to disclose

References
6. Acute pancreatitis: recent advances through randomized trials.

P3135 CLINICAL AND NUTRITIONAL FEATURES ARE PREDICTABLE FOR HOSPITALIZATION IN PATIENTS WITH CHRONIC PANCREATITIS: A COHORT STUDY

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Introduction: Hospitalization-free survival was evaluated with Kaplan-Meier and Cox regression analysis.

Results: 110 patients (64% male; mean age 57) enrolled with a median FU of 36 months. 52% had a toxic aetiology and 35% had EPI; 10% of patients had severe CP and 29% had a MUST score ≥2 at diagnosis. During the FU, 2% of patients died, 2% had cardiovascular events, 8% had infections and 16.4% needed endoscopic/surgery treatment. 34% needed hospitalization, in 49% for extra-pancreatic events. There was no association between EPI and extra pancreatic events. A BMI <20 and a MUST score ≥2 were borderline significant for being associated with an increased risk of hospitalization (HR 2.1 95% CI 0.7–6 p 0.07; HR 2.9 95% CI 0.8–3.9 p 0.09). Toxic aetiology had a two-fold risk of new hospitalization (HR 2.9 95% CI 0.9–5.7 p 0.001). Patients with severe disease had a higher risk of hospitalization (HR 4.5 95% CI 0.9–22 p 0.0002) and more often needed endoscopic/surgery treatment (55% vs 13% p 0.006).

Conclusion: About 30% of patients were at high risk of malnutrition at diagnosis, and 34% of them were hospitalized during the FU, often for extra-pancreatic events that caused death in 2%. Toxic aetiology and severe disease are associated with hospitalization and MUST score seems to be less useful in predicting these events.
Disclosures: Nothing to disclose

P1358 THERAPEUTIC EFFICACY OF ENZYMATIC SUPPLEMENT AND CLINICAL CHARACTERISTICS IN EARLY CHRONIC PANCREATITIS

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Introduction: Chronic pancreatitis (CP) is a progressive and permanent destruction of the pancreas resulting in exocrine and endocrine insufficiency and often causing chronic disabling pain. Recently, early CP has been recognized by typical abdominal symptoms and serum pancreatic enzyme levels.

Aims and Methods: Thirty-four patients with early CP were treated with protease inhibitor and pancreatic enzyme for at least two years. They showed typical EUS findings for early CP, presented with repetitive abdominal pain and elevated serum pancreatic enzyme levels. The outcomes measured were changes in abdominal symptoms, serum pancreatic enzyme levels, pancreatic exocrine functions, and EUS findings.

Results: The median treatment duration was 66.5 months, during which 80% of the patients showed decreased pain intensity. The face rating scale significantly improved after treatment (p=0.01). Serum pancreatic enzyme levels (amylase, lipase, and elastase-1) significantly decreased compared to before treatment (p<0.05). Although EUS findings revealed some differences compared to before treatment in 4 of the 24 patients, the changed EUS findings were not related to the possible recurrence of improvement in abdominal symptoms and serum pancreatic enzyme levels.

Conclusion: Our results indicate that therapeutic intervention for early CP should have clinical significance. However, the changes of early CP may be irreversible because there was no correlation between time-dependent changes in EUS findings and the improvement of clinical parameters.

Disclosure: Nothing to disclose

P1359 CLINICAL OUTCOME OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY COMBINED WITH ENDOSCOPIC TREATMENT FOR CHRONIC PANCREATITIS WITH Pancreatic STONE

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Introduction: In ESGE guidelines, also in Japanese guidelines, endoscopic treatment and extracorporeal shock wave lithotripsy (ESWL) for symptomatic chronic pancreatitis with/without pancreatic stone is recommended, however, the selection of treatment methods and procedures are not established yet.

Aims and Methods: Evaluating the clinical outcome of the chronic pancreatitis with pancreatic stone patients underwent ESWL in our center.

59 consecutive patients underwent ESWL for pancreatic stone with chronic pancreatitis between January 2010 and December 2014 at our tertiary referral center in Japan. ESWL was performed under X-ray fluoroscopy using a device of MODULITH SLX (Storz Medical, Switzerland). If it was difficult to recognize stone by X-ray, ENPD tube was indwelled and it was performed under the contrast.

In patients with pancreatic duct stricture, pancreatic stent insertion for 2 to 3 months was applied in addition to ESWL. After the initial treatment, we deployed ENPD tube and clinical success was evaluated by pancreatography and ERCP was well confirmed. The patients were observed without additional procedure. If clinical success was not obtained, the patients underwent additional ESWL and/or upgraded the size of the stent or placing of multiple stents.

Primary endpoints were the results of the treatment and the asymptomatic period, and secondary endpoints were the complications of the procedures, and the risk factors for the recurrence.

Results: Of the 59 patients, the median age was 60 years old, 46 males and 13 females. The etiologies of pancreatitis were alcohol (n=40), idiopathic (n=12), autoimmune pancreatitis (n=5) and pancreas divisum (n=2). The region of the stones were pancreas head (n=41), body (n=9), tail (n=3) and multiple regions (n=6). 31 patients (52.9%) needed pancreatic stenting for the main pancreatic duct structures.

In all patients the treatments were successful. The median period of the treatment was 62 days (2-637). The median number of all procedures were four (1-10), ESWL were two (1-6). During the median observation period of 412 days (4-2794), one year asymptomatic duration rate was 76.7%, and three years rate was 55.9% using Kaplan-Meier method.

The risk of recurrence was high in the patients with non-alcoholic pancreatitis and the obstruction/stricture of body-tail. Seven patients (12%) had the complications after ERCP: pancreatitis (n=3), incompetence of basket catheter (n=2), guidewire penetration (n=1), cholangitis (n=1). They had improvement with conservative or endoscopic therapy.

In order to detect the risk factors for the recurrence of the symptoms we performed univariate analyses, non-alcoholic patients (p=0.02) and the obstruction/stricture of body-tail (p=0.009) resulted as significantly correlated with the recurrence.

We also performed a multivariate logistic regression analysis, non-alcoholic patients (OR = 3.71, 95% C.I.: 1.09–12.6, p=0.036) and the obstruction/stricture of body-tail (OR = 4.42, 95% C.I.: 1.28–15.3, p=0.019) also resulted as significantly correlated with the recurrence.

Conclusion: ESWL combined with endoscopic treatment for chronic pancreatitis with pancreatic stone is the safe and effective treatment. The risk of recurrence was high in the patients with non-alcoholic pancreatitis and the obstruction/stricture of body-tail.

Disclosure: Nothing to disclose

P1360 CHRONIC PANCREATITIS AND ENDOCRINE INSUFFICIENCY AND CARDIOVASCULAR RISK IN PATIENTS WITH Pancreatic ENDOCRINE INSUFFICIENCY (PEI), A PROSPECTIVE, LONGITUDINAL COHORT STUDY

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Introduction: Previous studies have suggested that chronic pancreatitis (CP) is associated with increased risk of cardiovascular (CV) disease independently of other major risk factors.

Aims and Methods: We evaluated the risk of CV events in a well-phenotyped cohort of patients with CP and its association with pancreatic exocrine insufficiency (PEI) and pancreatic endocrine insufficiency (pancreatogenic diabetes) among other CV risk factors.

Prospective, longitudinal cohort study of patients with CP, followed-up at the Pancreas Unit of the University Hospital of Santiago de Compostela, Spain. Results: 430 patients were included (mean 47.8 ± 14.4 years of age, 79.1% male). Mean follow-up was 8.6 ± 4.6 years. CV etiology was toxic (alcohol and/or smoking) in 290 patients (67.4%). PEI and pancreatogenic diabetes mellitus (DM) were present in 29.3% and 29.5% of the patients, respectively. A total of 45 cardiovascular events was prospectively recorded (10.5%); 21 patients had a major cardiovascular event (stroke or myocardial infarction) and 27 developed coronary artery disease. A higher incidence of cardiovascular events was prospectively recorded (10.5%); 21 patients had a major cardiovascular event (stroke or myocardial infarction) and 27 developed coronary artery disease. A higher incidence of cardiovascular (CV) disease independently of other major risk factors.

Conclusion: PEI without DM (OR = 3.40; IC95%: 1.05–10.81), arterial hypertension (OR 3.40; IC95%: 1.02–10.76; p=0.001) and diabetes mellitus (OR 6.54; IC95%: 2.71 to 15.77) were associated with increased risk of cardiovascular (CV) disease independently of other major risk factors.

Aims and Methods: The etiologies of pancreatitis were alcohol (n=40), idiopathic (n=12), autoimmune pancreatitis (n=5) and pancreas divisum (n=2). The region of the stones were pancreas head (n=41), body (n=9), tail (n=3) and multiple regions (n=6). 31 patients (52.9%) needed pancreatic stenting for the main pancreatic duct structures.

In all patients the treatments were successful. The median period of the treatment was 62 days (2-637). The median number of all procedures were four (1-10), ESWL were two (1-6). During the median observation period of 412 days (4-2794), one year asymptomatic duration rate was 76.7%, and three years rate was 55.9% using Kaplan-Meier method.

The risk of recurrence was high in the patients with non-alcoholic pancreatitis and the obstruction/stricture of body-tail. Seven patients (12%) had the complications after ERCP: pancreatitis (n=3), incompetence of basket catheter (n=2), guidewire penetration (n=1), cholangitis (n=1). They had improvement with conservative or endoscopic therapy.

In order to detect the risk factors for the recurrence of the symptoms we performed univariate analyses, non-alcoholic patients (p=0.02) and the obstruction/stricture of body-tail (p=0.009) resulted as significantly correlated with the recurrence.

We also performed a multivariate logistic regression analysis, non-alcoholic patients (OR = 3.71, 95% C.I.: 1.09–12.6, p=0.036) and the obstruction/stricture of body-tail (OR = 4.42, 95% C.I.: 1.28–15.3, p=0.019) also resulted as significantly correlated with the recurrence.

Conclusion: ESWL combined with endoscopic treatment for chronic pancreatitis with pancreatic stone is the safe and effective treatment. The risk of recurrence was high in the patients with non-alcoholic pancreatitis and the obstruction/stricture of body-tail.

Disclosure: Nothing to disclose
events in patients with CP. Coexistence of pancreaticobiliary diabetes increases the CV risk associated with PEI in CP.

### Univariate and Multivariate Analysis

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<th>P value</th>
<th>OR (95% CI)</th>
<th>P value</th>
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CI, confidence interval; CP, chronic pancreatitis; CV, cardiovascular; EUS, endoscopic ultrasound; OR, odds ratio PEI, pancreatic exocrine insufficiency; SD, standard deviation.

[Analysis of variables associated with CV events (logistic regression model)]

Disclosure: Nothing to disclose.

### P1361 OVERALL CARDIOVASCULAR RISK ASSESSMENT IN PATIENTS WITH CHRONIC PANCREATITIS AND EXOCRINE INSUFFICIENCY RECEIVING ENZYME REPLACEMENT THERAPY

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Introduction: Patients with chronic pancreatitis (CP) and pancreatic exocrine insufficiency (PEI) are at increased risk of cardiovascular events. Cardiovascular risk (CVR) assessment leads to proper primary and secondary prevention and may improve the quality of life.

Aims and Methods: To investigate CVR in patients with CP and PEI. Study enrolled 82 patients (48 males, mean age 49.46 years), receiving pancreatic enzyme replacement therapy due to PEI. CVR was assessed by Framingham risk score (FRS) used to predict an individual chance of developing cardiovascular disease in the next 10 years; by routine lipid profile and apolipoproteins (apo A-I and apo B) (protective against CV events, HDL-associated), apo A-I (proatherogenic), Apo B/Apo A-I ratio (associated with myocardial infarction and coronary disease in the next 10 years; by routine lipid profile and apolipoproteins (apo A-I and apo B) (protective against CV events, HDL-associated), apo A-I (proatherogenic), Apo B/Apo A-I ratio (associated with myocardial infarction and coronary disease in the next 10 years).

Results: According to FRS 25.61% of the patients were with high CVR, 20.73% – with moderate and 53.66% – with low. We observed a tendency to increase CVR (FRS) as the severity of both morphological changes and CP by M-ANNHEIM worsened. Vitamin D levels were significantly lower in patients with moderate CVR by FRS versus those at low risk, p = 0.05. Statistically significant correlations occur between CVR by FRS and HDL (p = 0.0002), total cholesterol (p = 0.002), non-HDL (p = 0.003), VLDL (p = 0.0002), total cholesterol/HDL ratio (p = 0.0001). In patients with high CVR by FRS we found significantly higher apo B (p = 0.0003) and apo B/Apo A-I (p = 0.007) levels, as well as an increased risk of myocardial infarction using Apo B/Apo A-I ratio (p = 0.04). Dyslipidemia with borderline high and high levels of the atherogenic total cholesterol, triglycerides and/or LDL was evaluated in 50.68% of patients with CP. There was no significant difference in the incidence of dyslipidemia compared to both CP severity and structural changes. Low HDL levels were found in 35 of the studied patients (21 men) and high non-HDL levels in 71.23% of patients. There was a statistically significant difference in HDL levels between mild and moderate CP, p = 0.04. High total cholesterol/HDL ratio (above 5), which is associated with higher CVR, was observed in 41.1% of the patients. A progressive increase in the total cholesterol/HDL ratio was observed as the CP severity increased. Significant lower apo A-I and vitamin D levels were found with malnutrition risk and lipid malabsorption worsening (p = 0.047, p = 0.032). A significant difference was found in apo A-I levels between mild and moderate CP (p = 0.007) and between mild and advanced CP (p = 0.04) and in Apo C-II between mild and advanced CP (p = 0.047). With morphological changes worsening significantly lower apo A-I levels were found between Cambridge grade I and Cambridge grade III (p = 0.03) and between Cambridge grade I and Cambridge grade IV (p = 0.005). Similar observation was made for apo A-I between Cambridge grade I, II and Cambridge grade III, IV (p = 0.000). Conclusion: Overall CVR assessment using FRS, lipid profile and apolipoproteins could identify patients at high risk of cardiovascular events and allows the proper control of the risk factors.

Disclosure: Nothing to disclose.

### P1364 SERUM ALBUMIN LEVEL, PROGNOSTIC NUTRITIONAL INDEX, AND CA19–9 ARE TREATMENT-PREDICTIVE MARKERS FOR DISEASE CONTROL RATE IN PATIENTS WITH UNRESECTABLE PANCREATIC CANCER


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Introduction: Pancreatic Lipase-Related Protein 2 (PNLIPRP2) is a less lipase isoform which can digest long chain triglycerides, diglycerides and monoglycerides. This study aimed to investigate the correlation of PNLIPRP2 with chronic pancreatitis. Expression of the truncated protein is inhibited at the mRNA level likely by “nonsense-mediated mRNA decay”, therefore, this variant causes the formation of a shorter misfolded protein that is not secreted well but induces endoplasmic reticulum (ER) stress. ER stress is a known susceptibility factor for chronic pancreatitis, suggesting that the p.W358X mutation of the PNLIPRP2 gene might contribute the development of pancreatitis.

Aims and Methods: Our aim was to investigate whether the p.W358X mutation of the PNLIPRP2 gene is associated with idiopathic and alcoholic chronic pancreatitis. In our study we enrolled 15 patients with idiopathic and alcoholic chronic pancreatitis and 200 controls recruited by the Hungarian Pancreatic Study Group (HPSG – www.pancreas.hu). Exon 11 and its flanking intronic regions were analyzed by Sangersequencing. The p.W358X mutation of the PNLIPRP2 gene was studied by RT PCR using human donor pancreas cDNA samples.

Results: When allele frequencies were considered, the p.W358X mutation was not overrepresented either in the idiopathic or the alcoholic chronic pancreatitis groups compared to the controls (13% vs. 5% and 50% vs. 56%, respectively). RT-PCR on a homozgyous cDNA sample indicated drastically reduced PNLIPRP2 expression at the mRNA level. Additionally, we identified 5 more PNLIPRP2 variants (c.1071–379delG, c.1071–321C>T, c.1084A>C p.G1362C, c.1161A>G p.S387R and c.1181+55C>A) but none were associated with chronic pancreatitis.

Conclusion: The p.W358X mutation of the PNLIPRP2 gene is not associated with chronic pancreatitis. Expression of the truncated protein is inhibited at the mRNA level likely by “nonsense-mediated mRNA decay”, therefore, this variant does not cause ER stress in the human pancreas.

Disclosure: Nothing to disclose.
Introduction: Pancreatic cancer is a deadly disease that is often detected in late stages due to the unobtrusive nature of its evolution. Various centers around the world are currently investigating the feasibility and yield of surveillance for pancreatic cancer in high-risk individuals. Evidence is beginning to accumulate that surveillance may lead to the early detection of precursor lesions and asymptomatic pancreatic cancer. Proper screening methods and identification of such precursor lesions can allow early therapeutic measures and interventions to be administered in order to prevent further fatalities. The primary objective of this project was to check feasibility of identifying precursor lesions in high-risk individuals by endoscopic ultrasound surveillance in attempt to prevent the development of pancreatic cancer or at least detect early cancer.

Aims and Methods: Between 2008 and 2018, a cohort of 123 high-risk individuals came for annual/biannual endoscopic ultrasound screening for pancreatic cancer. Referrals were from both physicians and self-referrals. Inclusion criteria included at least one first-degree relative or otherwise within the consensus guidelines recommended criteria. Retrospective and prospectively collected data was obtained, analyzed, and compared on several variables. These variables included age at beginning of screening, gender, smoking, obesity, diabetes and presence of tumor markers. Genetic mutations were taken into account as well as the patients personal and family history of cancer. Each screen date and their respective result and plan were recorded. Pancreatic cancer screening guidelines, based on consensus opinions, have been applied in various centers around the world; however, evidence for effectiveness is lacking. At Rambealth Health Care Campus, we have established a cohort of high-risk individuals and herein report our results from this cohort.

Results: Detection of precursor pancreatic lesions is feasible with endoscopic ultrasound screenings, however adherence remains an important challenge to surveillance of findings. Patients may best be categorized based on specific risk factors, including genetics and family history, as an indication of when to initiate screening.

Average age at first screening was 57. 210 EUS exams have been performed. 22% also submitted to genetic consultations. Overall two patients underwent pancreatic surgery, and both have survived long-term. 40% of patients showed any EUS abnormalities.

Conclusion: International Collaborations, such as the International Cancer of Pancreas Screening (CAPS) consortium, are needed to collate evidence for screening to prevent pancreatic cancer morbidity and mortality, and are essential to achieve proof of concept. Pancreatic cancer is a challenging field and endoscopic ultrasounds alone cannot prevent all cases of pancreatic adenocarcinoma. Screening programs, however, within research protocols may yield actionable results to restrict some pancreatic cancers at an early stage.

Different countries with varying healthcare systems and budgets may find that variance of screening procedures may be appropriate.

Disclosure: Nothing to disclose.
Introduction: Pancreatic ductal adenocarcinoma (PDA) is the fourth leading cause of cancer-related death with a 5-year survival rate of approximately 7%. While surgery is currently the only potentially curative therapy, only 15–20% of the patients are considered for resection. However, in some 25% of patients the tumor cannot be resected due to unexpected liver or peritoneal metastases. As of now, it is not possible to accurately determine whether PDA patients are suitable for resection and they have to undergo invasive surgery in order to determine the resectability status. Therefore, applying image analysis techniques to routine abdominal CT scans, i.e. quantitative radiomics, could be helpful to predict local resectability of PDA and aid in treatment planning.

Aims and Methods: The aim of our study was to compare the performance of an expert radiologist to that of quantitative radiomics for prediction of local resectability of pancreatic ductal adenocarcinoma on routine abdominal contrast-enhanced CT. We included 50 patients (m:f = 28:22, range 48–79 yrs) with histologically proven pancreatic ductal adenocarcinoma who were operated within 4 weeks of an initial routine portal-venous phase multidetector-row CT examination. An expert abdominal radiologists scored CT data for tumor resectability. Another expert abdominal radiologist drew tumor contours to obtain a volume of interest, from which we computed 90 intensity, shape and texture features. During training the number of features was reduced with a feature selection algorithm and combined with several classifiers to predict local resectability using radiomics.

Results: There were 33 hypo- and 17 iso-attenuating tumors, of which 29 were resectable and 21 non-resectable. The best classification result was obtained with a support vector machine classifier with the feature vector reduced by regularized discriminative feature selection. Accuracy for predicting resectability was 68% for the radiologist, and 74% for radiomics. Sensitivity, specificity, positive and negative predictive value for resectability were 90%, 38%, 67% and 73%, respectively, for the radiologist and 97%, 42%, 70%, and 90%, respectively, for radiomics.

Conclusion: Quantitative CT-based radiomics for prediction of local resectability of pancreatic ductal adenocarcinoma on routine CT, may outperform expert radiology for clinical routine.

Disclosure: Nothing to disclose.
**P1372** **HETES IN PATIENTS WITH Pancreatic CANCER: A PRELIMINARY REPORT**

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2Pomeranian Medical University, Szczecin, Poland

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**Introduction:** Lipoxigenase (LOX)-derived bioactive lipids represent a family of important biological molecules that can be of great importance in the pathogenesis of various conditions. We hypothesised that LOX-derived Hydroxyeicosatetraenoic acids (HETEs) may be associated with clinical presentation of pancreatic neoplasms in humans, as well as with previously reported phenomenon of intensified circulation of various populations of bone marrow-derived stem cells in these patients.

**Aims and Methods:** In the current study, we comprehensively evaluated the systemic levels of selected HETEs such as 5-, 12-, and 15-HETE in patients with pancreatic adenocarcinoma (n=36), chronic pancreatitis (n=39), and in healthy individuals (n=35).

**Results:** Compared to healthy individuals, patients with pancreatic adenocarcinoma showed 3-8-fold higher levels of 5-, 12-, and 15-HETE (at least p <0.003). Similar results were observed in patients with chronic pancreatitis, who had elevated concentrations of all examined HETE acids compared to healthy volunteers (in all cases at least p < 0.03). Interestingly, the levels of the examined HETEs were not significantly associated with the TNM stage of pancreatic cancer in our patients. However, 12-HETE and 15-HETE concentrations were correlated with progression of pancreatic intraepithelial neoplasia PanIN and early cancer. Family history of pancreatic cancer and several genetic syndromes must be taken into account for early detection of pancreatic cancer.

**Conclusion:** Our study provides first clinical evidence for the significance of the examined HETEs in the clinical pathogenesis of pancreatic cancer and other pathological conditions. Moreover, due to its initiation and progression of cancer, LOX/HETEs may be used for the design of new therapeutic approaches.

**Disclosure:** Nothing to disclose

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**P1373** **Sarcopenia as a Predictor of Complications After Pancreatic Resection in Patients with Pancreatic Adenocarcinoma**

L. Pererva, V. V. Kopchak, I. Khomyak, A. Duvalko, N. Davydenko, K. Kopchak

1State Institution «A.A. Shabolov National Institute of Surgery and Transplantology, Pancreatic Surgery, Kyiv, Ukraine
2Institution «A.A. Shabolov National Institute of Surgery and Transplantology, Kyiv, Ukraine
3National Cancer Institute, Kyiv, Ukraine

Contact E-Mail Address: perervalina@bigmir.net

**Introduction:** Sarcopenia can be a predictor of complications after pancreatic resection.

**Aims and Methods:** We performed a retrospective analysis of treatment of 104 patients with pancreatic adenocarcinoma, who underwent pancreaticoduodenectomy in our institution in the period 2012-2017. Preoperative computed tomodensitometry (CT) was performed for all patients. Sarcopenia was quantified using Hounsfield Unit Average Calculation (HUAC). They were measured at the level of the third lumbar vertebral body (L3).

**Results:** Sarcopenia was diagnosed in 44 (42.3%) patients vs 60 (57.7%) patients in the group with sarcopenia and in 17 (28.3%) patients in the group without sarcopenia (c2 = 9.9, p = 0.0017). Mortality was 2 (4.5%) and 1 (1.6%) respectively (c2 = 0.75, p = 0.38). In patients with sarcopenia infectious complications occurred in 5 patients, pancreatic fistula Grade B or C in – 14 patients, delayed gastric emptying – in 2, haemorrhage- in 5.

**Disclosure:** Nothing to disclose

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**P1374** **ANALYSIS OF VOLUME ADJUSTMENT IMPACT, RESULTS AND COMPLICATIONS USING THE SPATZ BALLOON FOR EXCESS WEIGHT TREATMENT: A LARGE BRAZILIAN EXPERIENCE IN FOUR HUGE CENTERS**

R.J. Fittipaldi-Fernandes1,2, A.C. Hoff1,2

1Endogastro Rio, GI Endoscopy, Rio de Janeiro, Brazil
2Angiokope, GI Endoscopy, São José dos Campos, Brazil

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**Introduction:** Intragastric Balloons (IGB) are used for decades worldwide in excess weight treatment with well-established success. SPATZ adjustable IGB (Bariatric Solutions, Inc.) proved for 12-month major clinical and systemic weight loss due to surgical intervention by HUAC is a reliable indicator of the surgical outcome and significantly influences on total level of postoperative complications. It is also a strong predictor of clinically relevant postoperative pancreatic fistula occurrence. The assessment of sarcopenia downregulates MHCII co-stimulatory molecules CD80/CD60, reducing clonal expansion of T-lymphocytes. Recently several showed that IL-17 have an important role in progression of pancreatic intraepithelial neoplasia PanIN and early cancer. Family history of pancreatic cancer and several genetic syndromes must be taken into account for early detection of pancreatic cancer.

**Aims and Methods:** We aimed to evaluate weight loss and complications in 04 private Brazilian clinics with a high volume of patients; To report whereas downward adjustments can be used to improve the selection of patients with pancreatic cancer prior resection.

**Disclosure:** Nothing to disclose

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**WEDNESDAY, OCTOBER 24, 2018**

**09:00-14:00 Endoscopy and Imaging III – Hall X1**

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**Disclosure:** Nothing to disclose
P1376 FEASIBILITY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL NEOPLASMS IN ELDERLY PATIENTS: A SINGLE-CENTER, LARGE-SCALE, RETROSPECTIVE STUDY
1University of Ulsan College of Medicine, Asan Medical Center, Internal Medicine, Seoul, Korea (Republic of)
2University of Ulsan College of Medicine, Asan Medical Center, Gastroenterology, Seoul, Korea (Republic of)
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Introduction: Although the number of elderly patients with superficial esophageal neoplasms (SENs) has been steadily increasing, there is still an evident lack of studies focused on the clinical outcome of esophageal submucosal dissection (ESD) in the elderly. We investigated the feasibility and safety of ESD for SENs in elderly patients.

Aims and Methods: Patients who underwent ESD for SENs between December 2005 to December 2017 were eligible. Clinical features and treatment outcomes according to the three age groups (not-old, <65 years; young-old, 65–74 years; middle and oldest-old, >74 years) were retrospectively reviewed using medical records.

Results: ESD was performed in 426 patients with 79 lesions, including 97 cases (20.4%) of dysplasia, 364 cases (76.6%) of squamous cell carcinoma and 14 cases (3%) of adenocarcinoma. The age was divided into three groups, the not-old (n = 200), young-old (n = 179) and middle & oldest-old (n = 47). Gender, Smoking and characteristics of tumor (circumference, location, lesion size, resected specimen size, histology and depth of invasion) did not differ. Underlying disease such as hypertension (not-old vs. young-old vs. middle & oldest-old; 30.0% vs. 41.9% vs. 40.4%, p = 0.045), chronic kidney disease (0.5% vs. 0.0% vs. 4.3%, p = 0.033) and cardiovascular disease (2.0% vs. 7.8% vs. 4.5%, p = 0.028) significantly differed between the three groups. En bloc resection (96.8% vs. 95.5% vs. 100.0%, p = 0.075), perforation (4.5% vs. 3.0% vs. 5.6%, p = 0.601) and submucosal dissection (88.2% vs. 87.5% vs. 83.3%, p = 0.622) and curative resection rates (77.2% vs. 77.0% vs. 81.5%, p = 0.768) were no significant differences between the three groups. Complications of procedure such as bleeding (2.3% vs. 0.0% vs. 1.9%, p = 0.075), perforation (4.5% vs. 3.0% vs. 5.6%, p = 0.601) and stricture (5.4% vs. 6.0% vs. 11.1%, p = 0.297) also occurred similar in the three groups. During the follow-up period (median, 27.4 months; interquartile range, 7 to 40), among the patients with curative resection, cumulative recurrence rate did not differ significantly between the three groups (local recurrence, 0.7% vs. 0.0%; synchronous recurrence, 4.0% vs. 3.7% vs. 2.6%; metachronous recurrence, 5.4% vs. 6.0% vs. 10.3%).

Conclusion: ESD is a feasible and effective procedure for the treatment of SENs in elderly patients as well as non-elderly patients which showed favorable outcomes.

Disclosure: Nothing to disclose

P1377 ENDOSCOPIC HAND-SUTURING FOR MUCOSAL DEFECTS AFTER GASTRIC ESD IN CASES WITH ANTITHROMBOTIC AGENTS: A CASE SERIES STUDY IN 8 PATIENTS
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Introduction: Endoscopic submucosal dissection (ESD) for gastric neoplasms is gaining an acceptance as one of curative treatment options. The major post-operative adverse event of gastric ESD is delayed bleeding. Although effective countermeasures for post-ESD bleeding are proton pump inhibitors and

Abstract No: P1375
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<td>2 min 50s</td>
<td>10</td>
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<td>2 min 58s</td>
<td>2 min 21s</td>
<td>11</td>
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<td>3 min 25s</td>
<td></td>
<td>30.3 x 27.2 x 11.5</td>
<td>3 min 12s</td>
<td>4 min 38s</td>
</tr>
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</table>

F = frontal approach ** from begin injection to end of flushing lesion with warm water
T = tangential approach  ** from begin positioning snare to extracting resection specimen

Aims and Methods: Development of a technique (EMR+) which allows endoscopic en bloc resection of lesions up to 30 mm.

Results: En bloc resection of lesions up to 20 mm. The technique was associated with a higher rate of recurrence and R0 resection is difficult or impossible to determine after piecemeal resection. Endoscopic submucosal dissection (ESD) allows en bloc resection for lesions >20 mm but the technique is difficult, time-consuming and associated with a higher risk for complications. Submucosal injection is well investigated and essential for both resection techniques. The standard solution used for injection is saline solution, but the created submucosal cushion disappears quickly as saline is absorbed by the adjacent mucosa. Frequent re-injections and prolonged procedure times are the consequences.

Aims and Methods: Development of a technique (EMR+) which allows endoscopic en bloc resection of lesions up to 30 mm. The technique was developed and evaluated in an explanted pig stomach. The stomach was adjusted in a special simulation model to be accessible to endoscopy. An additional working channel was mounted on a standard gastroscope and used for a resection snare. The conventional working channel of the scope was used for an anchor device. For submucosal injection a new developed agent was used for an anchor device. For submucosal injection a new developed agent was used simultaneously with the snare to facilitate resection. After the resection technique was established 22 resections (11 with a frontal and 11 with a tangential approach) were performed and evaluated.

Conclusion: The technique (EMR+) allows fast en bloc resection and obtains resection specimens of 30 mm. The technique needs to be evaluated in vivo.

Disclosure: Nothing to disclose
proliferative coagulation of visible vessels on mucosal defect after ESD, the incidence of post-ESD bleeding is not negligible. Furthermore, patients receiving antithrombotic agents are increasing because of population ageing and progress of treatment for cardio-cerebrovascular disease, which may increase the risk of post-ESD bleeding.

Aims and Methods: To prevent postoperative bleeding after gastric ESD of the patients receiving antithrombotic agents, we conducted endoscopic hand suturing (EHS), which was a suturing technique using a through-the-scope needle holder and an absorbable barbed suture attached to a curved needle; for mucosal defects after ESD (Goto O, et al. Endoscopy 2017). Eight patients who were receiving antithrombotic agents and underwent EGD for gastric neoplasms (less than 3 cm in size) were recruited. The details of antithrombotic agents were as follows: aspirin in 2 patients, aspirin and clopidogrel in 2 patients, triple antithromboplast agents in 1 patient, warfarin in 1 patient, apixaban in 1 patient, and aspirin and warfarin in 1 patient. In all cases, aspirin were continued and warfarin were replaced to heparin during perioperative period. Other antithrombotic agents were interrupted before ESD and resumed immediately after ESD. We performed EHS for the mucosal defects after successful lesion resection by ESD. Success rate, adverse events, and suture maintenance of EHS and the incidence of delayed bleeding were subsequently investigated.

Results: EHS was successfully completed in 9 lesions in 8 patients without severe adverse events. The tumor locations, the mean size of mucosal defects and the mean procedure time of EHS were U/M/L: 1/4/4, 26.0 ± 12.6 min, respectively. The mean number of stitches for a lesion and the mean time per one stitch was 6.3 ± 1.4 stitches and 6.9 ± 3.0 min, respectively. The sures of 8 lesions in 7 patients were completely maintained in second endoscopy on third day after ESD. In one patient who had acute myocardial infarction on 2 days after ESD under aspirin underwent second endoscopy on 7th day after ESD, which showed that the defect remained closed. In all cases, there was no post-ESD bleeding.

Conclusion: This small-numbered case series showed that the mucosal defects after ESD were successfully closed and no post-ESD bleeding occurred. EHS appears to be feasible and useful for prevention for gastric post-ESD bleeding.

Disclosure: Research funds and supply of devices: Olympus Co., Ltd., Tokyo, Japan

Reference

P1378 ENDOSCOPIC SUBMUCOSAL DISECTION FOR GASTRIC INDEFINITE FOR NEOPLASIA: WHICH SHOULD BE RESECTED?
S.-J. Kim1, D.-H. Kang2, H.W. Kim3, C.W. Choi4, S.B. Park1, H.S. Nam1, D.G. Ryu1, J.W. Lee1, J.P. Lee1, K.H. Lee1
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Introduction: The management plan for gastric indefinite for neoplasia is yet to be determined and endoscopic forceps biopsy might be inconclusive to decide to resect or not. The aim of this study was to evaluate the clinical outcomes of endoscopic mucosal resection (EMR)/endoscopic submucosal dissection (ESD) of true neoplasm and to know the highly suspicious factors associated with true neoplasia.

Aims and Methods: Between November 2008 and December 2015, a retrospective study was conducted in a single, tertiary, referral hospital. A total of 109 gastric indefinite for neoplasia (G-EN) biopsies composed of 99 patients who underwent EMR and 10 patients who underwent ESD were enrolled. The outcomes and endoscopic factors for prediction of true neoplasia were analyzed.

Results: A total of 99 patients (90.8%) were diagnosed as definite neoplasia after ESD; category 3 (n = 42), category 4 (n = 50) and category 5 (n = 7) according to the revised Vienna classification. The patients’ mean age was 65.8 ± 9.8 years. The mean lesion size was 10.7 ± 6.1 mm. The patient population was male predominant (70.6%). The en-bloc and complete endoscopic resection rate were 98.2% and 94.5%, respectively. Associated factors with true neoplastic lesions were male sex (OR 8.596, p = 0.008) and lesion size ≥ 5 mm (OR 11.355, p = 0.003). Associated factors with category 4-5 were male sex (OR 3.165, p = 0.021) and erosive change (OR 2.841, p = 0.031).

Conclusion: Endoscopic resection for indefinite for neoplasia with larger lesions size with erosive changes especially in male sex should be considered when possible.

Disclosure: Nothing to disclose

Reference

P1381 NEOANGIOGENESIS IN LOCALLY ADVANCED GASTRIC CANCER TREATED BY NEOADJUVANT CHEMOTHERAPY EVALUATED BY PROBE CONFOCAL LASER ENDOMICROSCOPY (PCLE)
R. Cannizzaro1, R. Magri2, M. Fornasarig3, E. Pittavina4, S. Maiero4, M. Meng1, V. De Re3, V. Canzonieri4, A. De Paoli4, A. Buonadonna4, F. Di Mario1, D. Serraino5, C. Bellucio5, E. Cantoni5, P. Spessotto5
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3 Centro di Riferimento Oncologico di Aviano S.O.C. di Gastroenterologia, Aviano, Italy
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5 Centro di Riferimento Oncologico di Aviano S.O.C. di Gastroenterologia, Aviano, Italy

Introduction: Symptomatic epiphrenic diverticula are mostly treated with laparoscopic diverticulectomy. Recently, submucosal tunneling endoscopic septum division (STESD) has been used for the treatment of esophageal diverticulum. Our study aimed to demonstrate the safety and efficacy of STESD for treatment of symptomatic epiphrenic diverticula and elucidate the possible of STESD combined with POEM for treating patients with epiphrenic diverticula and achalasia.

Aims and Methods: Data of patients with symptomatic epiphrenic diverticula who underwent STESD between October 2016 and January 2018 at Jiangsu Province Hospital (Jiangsu, China). Endoscopy database was retrospectively reviewed. The para meters analyzed were the modified Eckardt score, total procedure time, hospital stay, the number of clips used, the incidence of complications and patient satisfaction.

Results: A total of 7 patients were enrolled in our study. There were 4 men and 3 women with the mean age of 66.42 ± 6.8 years. The most common symptoms were dysphagia, heartburn and regurgitation. The mean size of epiphrenic diverticula was 3.70 ± 1.95cm. One patient had Zenker’s diverticula while the others had epiphrenic diverticula. One patient had multiple diverticula and four patients had co-existent achalasia, peroral endoscopic myotomy (POEM) was simultaneously performed by the same tunnel. The mean procedure time was 56.42 ± 24.0 minutes. The median number of clips applied was 6 (range: 3–16). The modified Eckardt score significantly decreased after STESD (P = 0.002). The mean hospital stay was 5.57 ± 0.79 days. No complications were observed during the median follow-up of 7.83 months.

Conclusion: STESD is an effective and safe procedure for the treatment of epiphrenic diverticula. STESD can be combined with POEM for treating patients with epiphrenic diverticula and achalasia.

Disclosure: Nothing to disclose

Reference
Our Immunohistochemistry (IHC) and flow cytometry (FACS) data video-rate simultaneous color and near-infrared (NIR) fluorescence endoscopy.

Disclosure: This work was supported by the following grant Ministry of Health RF-2016–

dual patients. The analyses performed on gastric cancer patients suggest that

ing the efficacy of treatments and for achieving tailored interventions for indivi-

dation of angiogenic status was given in real time by the endoscopist during the

Results: 5 out of 12 (41.6%) GC patients showed an improvement of angiogenesis index, while in the remaining GC (59.4%) no substantial changes were docu-

Conclusion: In GC patients median angiogenesis index remained unmodified, without positive changes in vascular morphology, probably due to the presence of fibrosis.

The evaluation of tumor vasculature may provide vital information for predict-


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Introduction: Per Oral Endoscopic Myotomy (POEM) is becoming standardized for treatment of Achalasia. Recently, the new Triangle tip (TT) knife is equipped with water-jet function which could hasten the opera-

time. We retrospectively compared the use of TT knife with and without water-jet function on the clinical outcomes of POEM for treatment of Achalasia

Aims and Methods: This is a retrospective cohort study comparing use of TT knife against TT knife with water jet function (TJ) for performance of POEM. All patients who received POEM using TT knife for treatment of Achalasia at our institution were recruited. The POEM procedures were all performed under general anesthesia by single endoscopist. The outcomes including baseline demo-

Disclosure: Nothing to disclose

References: 1. P.W. Chu1, Y.W. Wong1, J.C. Wu2, E. Ng1, J. Lau1

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Introduction: Anastomotic leak is one of the most common complications of esophagectomy. The endoscopic vacuum-assisted closure (EVAC) which is based on continuous negative pressure applied to the wound with a sponge, has advantages of effective drain of infected fluid and accelerating wound healing by inducing formation of granulation tissue over fully covered self-expanding metal stent (SEMS) treatment.

Aims and Methods: We aimed to evaluate the efficacy and to identify factors associated with longer (> 21 days) treatment duration of EVAC for esophageal anastomotic leak following esophagectomy for cancer. We retrospectively ana-

ized 20 esophageal cancer patients who had undergone EVAC for esophageal leak after esophagectomy between October 2016 and December 2017 at the Samsung Medical Center.

Results: All 20 patients were male. Of these, 10 (50.0%) received neoadjuvant treatment and 6 (30.0%) had one or more comorbidities. The median size of fistula opening was 1.75 cm. During a median of 14.5 days of EVAC treatment, a median of 5 interventions were performed. Treatment success was achieved in 19 patients (95.0%). Neoadjuvant treatment was significantly associated with longer EVAC treatment. There was a non-significant trend toward the need for longer treatment duration for a larger fistula opening size.

Conclusion: EVAC treatment is a good non-surgical option for anastomotic leak following esophagectomy. Long duration of treatment is associated with neoad-

junctive treatment and a large leakage opening.

Disclosure: Nothing to disclose

References: 1. H.-Y. Fang,...
**Results:** From 2010 to 2017, 91 patients received POEM performed by using TT capsule (81 patients with conventional TT and 10 patients with TTJ). There was no difference between two groups in the age, gender and baseline demographics. The preoperative Eckhardt score was 5 (1–11) for TTJ group and 6 (1–12) for TT group (p = 0.875). The mean motility length was 9.8 ± 0.9cm for TTJ group and 10.0 ± 1.3 cm for TT group (p = 0.223). The examination time was significantly shorter for the TTJ group as compared to the conventional TT group (79.3 ± 21.6 vs 101.6 ± 34.3 mins; p = 0.05). There was no difference in the hospital stay between the two groups (2.7 ± 0.5 (TTJ) vs 3.1 ± 1.1 (TT); p = 0.409). There was no peri-operative morbidity, and no difference in the mortalities between two groups (1 (TTJ) vs 6 (TT); p = 1.0). The postoperative Eckhardt score was 0 (0–1) for TTJ group and 0 (0–6) for TT group (n.s.).

**Conclusion:** In this retrospective cohort study, we showed that the use of TT capsule with wait start function significantly reduced operative time of POEM while achieving similar length of motility, clinical efficacy as well as safety for treatment of Achalasia.

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<td>Mean Hospital stay (days)</td>
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<td>Complications (%)</td>
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<td>13.7 ± 15.4</td>
<td>37.8 ± 21.4</td>
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**References**


**POEM**

**Contact E-Mail Address:** driztt1202@gmail.com

**Introduction:** Conventional oesophagogastroduodenoscopy (OGD) is uncomfor-
table, unpopular with patients and may result in non-attendance. When mean examination time using this invasive modality exceeds 7 mins, the chance of detecting neoplasia increases by 3-fold compared to mean examination times for variceal hemorrhage. No additional findings were seen on OGD. Mean procedural distress, discomfort and pain were excellent (scores from best to worst 0–10; 0, 0, 0) despite patients expecting more discomfort and pain prior to investigation (2.9 and 2.3 respectively). Overall, 96.6% of patients with successful UGIC would have a repeat examination. UGIC changed patient management in 25.8% (n = 8). In patients with liver disease, 2 were placed on variceal surveillance (with UGIC), 2 patients had beta blockers started or increased and in one omeprazole initiated for incidental erosive gastritis. In 9 patients with dyspepsia and/or reflux, a third had their PPIS prescribed or doses altered.

**Conclusion:** UGIC is extremely well tolerated and highly acceptable to patients, almost all of whom would agree to having repeat procedures. A range of oeso-
phageal and diffuse gastric pathologies were identified. No focal gastric lesions were identified in this small study, but the longer examination duration suggest that a blinded comparison with OGD is warranted.

**Disclosure:** Nothing to disclose

**References**


**P1386 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR NON-AMPULLARY DUODENAL LESIONS**


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**Introduction:** Because of thin anatomical structure and high risk of complication including perforation, endoscopic resection (ER) for non-ampullary duodenal lesions (NADLs) is technically more difficult than lesions of stomach. High incidence with development of duodenal cancer, endoscopic treatment of duodenal lesions has been performed recently.

**Aims and Methods:** The aim of this study was to evaluate the efficacy and safety of endoscopic resection for NADLs. Retrospectively, patients who underwent ER for NADLs between December 2004 and June 2017 were included. We analyzed clinical and pathologic features of the lesions including the clinical outcomes and adverse events.

**Results:** The study included sixty-two patients (57.7% male) with NADLs. The median age of patients was 55.5 years (range 22 to 80 years). The mean NADL size was 10.19 ± 7.72 mm and the mean procedure time was 14.55 ± 12.08 min. After resection, final histological data showed 39 adenomas (61.5%), 10 Brunner’s gland tumors (19.2%) and 3 pyloric gland tumors (5.8%). The en-
bloc resection rate was 99.3% (48/52), and the complete resection rate with clear margins was 86.5% (45/52). According to the location of NADLs, half (26/52) of the lesions were located in duodenal bulb including superior duodenal angle. Endoscopic micro-perforation occurred from 2 out of 52 patients, it was treated only with conservative treatment.

**Conclusion:** ER for NADLs might be an effective treatment method with favorable long-term outcomes. However, it should always be performed with the possibility of perforation complication in mind.

**Disclosure:** Nothing to disclose

**References**

Introduction: The risk of treatment failure as well as short-term recurrence of bleeding is high with endoscopic therapy for risk-polyps. In patients with risk-polyps, endoscopic ulcer bleeding (HRUB) is high even after successful primary control of bleeding. We evaluated the use of OTSC in patients with HRUB.

Aims and Methods: Between 04/2014 and 03/2018, N= 100 patients (pts) with primary HRUB (Forrest Ia – Ib) who received primary treatment with OTSC or secondary treatment after unsuccessful standard endoscopic therapy, were recorded in a database. The primary endpoint of the study was either uncontrolled bleeding or recurrence after primary control (within 30 days). Furthermore, we examined factors that influenced the clinical success of OTSC treatment.

Results: OTSC as a single procedure for bleeding control was possible in N= 76 (76%) of all cases. OTSC as the primary and only treatment was performed in 64 pts (76%), 29 pts had medical success (78.5%). Another 36 pts received the OTSC as a rescue treatment after failed initial standard endoscopic treatment. In 26 pts (72.2%) the treatment by OTSC alone was successful. In 8 pts the bleeding could not be controlled by OTSC. 5 pts received a successful endoscopic treatment, one pt underwent surgery and two pts died during active bleeding.

In 16 pts the bleeding was initially controlled by OTSC but recurrent bleeding occurred after 1–12 days. 11 pts received subsequent endoscopic retreatment, 5 pts received surgery, one pt underwent surgery and one pt died.

OTSC failure occurred more often in large ulcers (> 3 cm p=0.03), in the duodenal bulb (p=0.03) and in ulcers with negative helicobacter test (p=0.045). The patients with OTSC failure received more blood transfusions (p=0.002). We found no statistically significant difference for the Rockall Score (median 7.5), the Glasgow Blatchford score (median 15.5), NSAID use or anticoagulation.

Conclusion: OTSC has a good clinical success rate in primary and secondary bleeding control in peptic ulcers with high-risk stigmata of bleeding. Potential risk factors for treatment failure are large ulcer size, location in the duodenal bulb and a negative helicobacter status.

Disclosure: Nothing to disclose.

Conclusion: Endoscopic resection of gastric supépithelial tumours after application of full-thickness sutures with a device originally designed for endoscopic anti-reflux therapy was proven to be feasible and efficient in a recent study on 31 patients (Schmidt A, et al. Endoscopy, 2015)

Aims and Methods: The aim of this study was to extend the above-mentioned study and further analyze safety of endoscopy full-thickness resection of gastric supépithelial tumours in a larger cohort. The above-mentioned study was extended until January 2018 and patients were identified retrospectively. The tumours were resected as following: after prior full-thickness suturing underneath the tumour with either the Plicator device or the GERDX device, the tumour was then resected with a snare. Besides basic demographic and health characteristics we as well included information on peri- and post-interventional complications.

Results: 50 patients were finally included in the study. The tumour was located in the gastric antrum in 12, the corpus in 26, the fundus in 7 and the cardia in 5 patients. Median tumour size as measured by endoscopic ultrasonography prior to resection was 20 mm (range: 7–60). In 27 patients the resection was done with the Plicator and in 22 with the GERDX device. A median of 3 (range: 1–12) sutures was applied in total, of which a median of 2 were applied before resection; in 23 patients at least one further suture was applied after snare resection. Endoscopic resection was feasible in all patients. Bleeding during resection occurred in 29 patients and was successfully managed endoscopically in all patients; peri-interventional transfusion of red blood cells was necessary in only 1 patient. A perforation or dehiscence of the gastric wall after resection occurred in 14 patients and could be closed by application of further sutures or clips in all cases. A control endoscopy the following day was routinely performed.

Conclusion: Treatment of bleeding was necessary in 7 patients during control endoscopy and in 3 patients treatment of perforation was performed. An episode of further bleeding after control endoscopy occurred in 7 patients and could again be managed endoscopically. During follow-up the most severe complication was noted in one patient who died 8 days after resection due to delayed perforation and peritonitis. One patient experienced oesophageal perforation and pleural empyema, who finally could be discharged 36 days after resection. Median hospital stay in all patients was 4 days (range: 2–36).

Disclosure: Nothing to disclose.

Reference

Introduction: Foreign bodies (FBs) ingestion is a common medical emergency accounting for 4% of all emergency endoscopies, secondary only to the GI bleeding.[3] 70–75% of FBs are located in the esophagus[3]. The need of endoscopic management reached up to 63–76%[2,3] with 3%–20% of incidence of complications[3]. According to the latest guidelines from ESGE, emergent endoscopy is recommended for the impaction of sharp-pointed objects within 24 hours[3]. However, there were still different opinions on the endoscopic methods with different FBs.

Aims and Methods: The study was performed from October 2015 to August 2016 among 595 patients with clinical suspicion of foreign body ingestion from 18 general hospitals in China. The patient data including age, gender, clinical features, and data about endoscopic management including types and locations of complications were recorded.
foreign bodies, retrieval devices, outcomes and complications were collected and analyzed.

**Results:** 1) The most common types of foreign bodies were sharp ones (75.9%), including fish bones (34.0%), chicken bones (22.1%), and fruit nucleus (17.1%). A few were non-sharp ones (24.1%), such as food bolus (14.6%). The majority of them were short objects (<2.5cm, 74.0%), subsequently followed by middle objects (2.5–6.0cm, 24.5%) and long objects (>6cm, 1.5%). Most objects were lodged in the proximal esophagus (75.9%), followed by the middle segment (15.2%) and the distal segment (8.9%) of esophagus. 2) Complication rate was as high as 6.0% which was increased with long retention time and sharp objects (P < 0.001). The rate was increased by 2.2- and 6.1- folds after impacted for over 24 hours or 48 hours as compared to in 12 hours. Logistic regression analysis indicated that sharp objects had obviously more complications than non-sharp ones (OR 3.36, 95% CI: 1.97–5.74). In particular, the incidence of perforation was 5.6%, which was strongly related with long retention time and sharp objects (P < 0.001), but not with locations or lengths of the objects (P>0.05). For sharp objects (75.9%), complication rate was increased by increased retention time (P < 0.001).

**Conclusion:** Foreign bodies, especially sharp ones, should be removed as soon as possible within 24 hours, to further decrease severe complications.

**Disclosure:** Nothing to disclose

**References**


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**Introduction:** Esophageal caustic stricture is the stubborn disease and postoperative medical management limits clinical efficacy for esophageal dilation. Some refractory cases with frequent recurrence or anatomic abnormality may require surgical intervention. Autologous mucosa graft has been successfully applied for treating urethral stricture and preventing stricture after extensive mucosal resection. We aimed to use mucosal autograft endoscopically to treat the refractory esophageal stricture.

**Aims and Methods:** Three patients with intractable corrosive esophageal stricture were treated endoscopically via combining dilation with autologous mucosal transplantation. For donor graft, the autologous normal esophageal mucosa was firstly chosen considering with tissue homology. The standard ESD was successfully performed as described. The isolated normal mucosal patch was spread in 37 °C 0.9% saline, then rapidly delivered to the defect region endoscopically following gastric intubation. The basolateral side of mucosal patch should orient towards the defect surface. The graft was fixed by clips (Olympus, Japan). All patients received postoperative anti-acute and anti-infection intervention, and were fasted for 5-7 days.

**Results:** All procedures were successful without severe complications. Mucosa regeneration were shown at the transplanted segments. One patient maintained normal diet with complete remission after one-year follow-up. Intraluminal stenosis and dysphagia were significantly improved in another two cases.

**Conclusion:** Our preliminary human experience achieved the amazing success for refractory caustic stricture. The findings need to be verified in more controlled trials. The standard modality of operation and post-operative care are urgently required for clinical practice. If effective and reproducible, this strategy might substantially benefit patients suffering from corrosive esophageal stricture.

**Disclosure:** Nothing to disclose

**References**


treated with proton pump inhibitor. The patient without motility disorder had an Eckard score of 2 at 1 month follow up.

**Conclusion:** Mid-esophageal and epiphrenic diverticula may be associated with esophageal motility disorders. In this case, POEM performed contralateral to the diverticulum allows to treat the cause underlying the diverticulum and seems to achieve good early clinical outcomes. In the absence of a motility disorder, endoscopic diverticulotomy appears feasible in experienced hands with promising early clinical outcomes, and might be offered as an alternative to surgical diverticulectomy in selected patients.

**Disclosure:** Nothing to disclose

**References**


### P1394 PERORAL ENDOSCOPIC MYOTOMY (POEM) IS EFFECTIVE IN TREATMENT OF NON CARDIAC CHEST PAIN CAUSED BY HYPERCONTRACTILE ESOPHAGEAL MOTILITY DISORDERS

**D. Albers**

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**Introduction:** Non cardiac chest pain (NCCP) is recurrent angina pectoris like pain without evidence of coronary heart disease in conventional diagnostic evaluation. The treatment options and therapeutic results for patients with hypercontractile esophageal motility disorders are disappointing so far. Recently, peroral endoscopic myotomy (POEM) was established as treatment option in achalasia. However, limited data exist on the effectiveness of POEM in NCCP with hypercontractile esophageal motility disorders.

**Aims and Methods:** In this prospective study 18 patients (female = 8, mean age 63.2 ± 13.2 years) with NCCP and hypercontractile esophageal motility disorders (type III achalasia = 8, Jackhammer esophagus = 9, distal esophageal spasm n = 1) were included. All patients underwent standardized diagnostic work-up including esophagogastroduodenoscopy with esophageal biopsies, high-resolution esophageal manometry and combined intraluminal impedance and pH testing before and 3 weeks after procedure. The POEM procedure was executed standardized (Hybridknife®, t-type, electric generator VIO 300D®, Erbe, Tuebingen, Germany) with myotomy of the lower esophageal sphincter and the manometrically identified hypercontractile segments in the esophageal body. A standardized symptom questionnaire was disposed before POEM, 3 weeks after and every 6 months after the intervention.

**Results:** 15 patients (clinical success rate 83.3%) showed significant symptom relief after POEM (pre-Eckardt-score: 7.9 ± 1.4, 3 weeks post: 1.8 ± 1.6, 6 months post: 2.3 ± 2.9 and 1.9 ± 2 after a mean follow-up of 10.5 ± 10.0 months). Endoscopy-related morbidity showed significant reduction in IRP (pre-POEM: 22.8 ± 17.8 mm Hg, post-POEM: 12.9 ± 14.7 mm Hg and DCI (pre-POEM: 4208 ± 3334 mmHg*s*cm, post-POEM: 1133 ± 1017 mmHg*s*cm). Two moderate adverse events classified with ASGE lexicon severity grading were handled endoscopically. One case of gastroesophageal reflux disease (Type B, LA-Classification) occurred after intervention and was handled successfully with PPI. Two patients required secondary intervention because of persisting hypercontractile segments in HR-manometry.

**Conclusion:** The results suggest that POEM is an effective and safe therapeutic option for patients with NCCP and hypercontractile esophageal motility disorders.

**Disclosure:** Nothing to disclose
P1397 EFFECT OF VONOPRAZAN ON THE TREATMENT OF POST-ENDOSCOPIC SUBMUCOSAL DISSECTION ARTIFICIAL GASTRIC ULTER
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Introduction: Proton pump inhibitors (PPI) are effective for the treatment of gastric ulcers (GU) after endoscopic submucosal dissection (ESD). Vonoprazan, a potassium-competitive acid blocker, has a strong inhibitory effect for gastric acid secretion. However, the efficacy of Vonoprazan is unclear in this field.
Aims and Methods: The aim of this study is to clarify which factors are more important for healing of GU after ESD procedure. We compare the healing status of ESD-induced GU and incidence of post-ESD bleeding between subjects treated with Vonoprazan and Rabeprazole.
Two hundred twenty-two patients who were performed ESD for the treatment of gastric neoplasms between April 2014 and April 2017 at our hospital were enrolled in this study. Twenty mg per day Vonoprazan (V group) or 10mg per day Rabeprazole (R group) for 4 weeks after ESD. Endoscopic images on 30 days after ESD were used for the evaluation of the shrinking rate of GU ulcers. For the assessment of healing effect, age, sex, past history, smoking, drinking, drugs, the status of Helicobacter pylori (HP) infection, tumor location (Upper/Middle/Lower), tumor size, tumor depth, and tumor histopathology were analyzed by multivariate analysis.
Results: The ulcer healing was only related to the tumor size (P < 0.01) and drugs. The ratio of treated lesions with scar-stage was significantly higher in the V group than in the R group (30.1% vs 40.3% P = 0.027). In the V group, patients got good healing regardless of HP infection. 50% of patients with HP infection had the low rate of ulcer scar-stage as compared with patients without HP infection in the R group (P = 0.015).
Conclusion: Vonoprazan was significantly superior to Rabeprazole for the healing of post-ESD GU ulcer. This study demonstrated that Vonoprazan may supersede PPI in treating post-ESD artificial GU ulcer.
Disclosure: Nothing to disclose

P1398 FLEXIBLE ENDOSCOPIC MYOTOMY IN ZENKER’S DIVERTICULA: NO CORRELATION BETWEEN OUTCOME AND DIVERTICULUM SIZE OR PRETREATMENT AFTER COMPLETE SEPTOTOMY
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Introduction: Flexible endoscopic myotomy offers several advantages over competing techniques like surgery or rigid endoscopic myotomy because of less invasiveness. Nevertheless different studies displayed a declining success rate with rising diverticulum size or in pretreated patients.
Aims and Methods: This is a single-center retrospective study including 42 patients with symptomatic Zenker’s diverticulum between 4/2014 and 12/2016. Patient characteristics showed a male-female ratio of 3:2, mean age 73 years (range 43–94). 26% of patients were pretreated (flexible endoscopic myotomy (5), open surgery (2), rigid endoscopic diverticulotomy (4)). Mean size of diverticulum was 3.3 cm (range 1.5–6.5 cm). The intervention was performed following a standardized protocol. On first day routine endoscopy and barium esophagogram was performed. On day 2 mucomyotomy under conscious sedation took place using a needleknife (Zimmon knife, Cook medical, Winston-Salem, NC) with a diverticuloscope (Cook medical, Winston-Salem, NC) or a standard transparent cap. The complete incision of the septum was intended in one session. On first postinterventional day water-soluble contrast-esophagogram excluded perforation and oral intake was started. Clinical success was defined as complete resolution of clinical symptoms and disappearance of diverticulum in esophagogram.
Clinical success rate was interpreted in relation to the variables diverticulum size after pre-treatment. Level of significance was evaluated with fishers exact test.
Results: Overall clinical success rate was 88%. Adverse events occurred in 3 patients: bleeding (2), microperforation (1), all treated conservatively (complication rate 7.1%).
Mean follow-up was 19±10 months, 6 patients developed recurrence of disease (14%), 4 of them were treated successfully with second endoscopic intervention. Mean time until recurrence was 8.4±5 months. There were no significant changes in outcome in relation to the variables diverticulum size or pretreatment.
Conclusion: Flexible endoscopic myotomy is a safe and effective treatment in Zenker’s diverticulum.
Our retrospective data suggest that clinical success rate is independent of diverticulum size or state of pretreatment when complete septotomy is performed.
Disclosure: Nothing to disclose

P1399 TRANSORAL OUTLET REDUCTION FOR WEIGHT REGAIN AFTER GASTRIC BYPASS: ONE-YEAR FOLLOW-UP
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Introduction: Enlargement of gastrojejunal anastomosis is associated with weight regain in patients with Roux-en-Y gastric bypass (RYGB). Endoscopic transoral outlet reduction (TORe) has proven safe and effective for treatment of weight regain. The objective of this study was to evaluate the safety and the efficacy in weight loss and quality of life after TORe.
Aims and Methods: Patients with at least 50% of weight regain and enlarged gastric outlet after RYGB treated at our centre were retrospectively identified from a prospectively collected database. Endoscopic outlet reduction was performed with Overstitch (Apollo Endosurgery), a full-thickness endoscopic suturing device. Before suturing the outlet rims were cauterized with pulsed Argon Plasma Coagulation on 40 Watts, 1/min (VIO 300D, ERBE Elektromedizin GmbH). Telephonic follow-up was done at 1, 3, 6 and 12 months. The quality of life was evaluated according to the Quality Of Life Scale (QOLS).
Results: Thirty-three patients (29 female, mean age 43.7) underwent TORe from January 2015 to April 2017. Baseline mean BMI was 37.9 (range 31–50) and weight was 107.9 kg (range 77–132). Mean procedure time was 34 minutes (range 15–60) and a mean number of 2.3 stitches per patient were placed (range 2–4) on the level of the gastric outlet. After suturing the patency of the redone outlet was tested with a standard gastroscope. There were 2 (6%) complications: one patient developed fever due to a small retrogastric collection and weight was 107.9 kg (range 77–132). Mean procedure time was 34 minutes (range 15–60) and a mean number of 2.3 stitches per patient were placed (range 2–4) on the level of the gastric outlet. After suturing the patency of the redone outlet was tested with a standard gastroscope. There were 2 (6%) complications: one patient developed fever due to a small retrogastric collection and was treated with antibiotics, while one patient had a gastric perforation that required urgent surgery. Mean hospital stay was 2.4 days (range 1–10). Thirty patients completed the follow up at 1, 3, 6 and 12 months. These patients were lost during the follow-up. Mean weight loss at 1-month was 8.7 kg, at 3 months was 11.7 kg, at 6 months was 14.1 kg while at 12 months was 14.8 kg. Mean BMI was 32 and the %EWL was 34.5 at 1 year. Only two patients regained weight compared to baseline during the follow up. All the patients reported satiety after 1 month, which was confirmed by 50% of patients after 6 months and by 37.5% after 12 months of follow-up. In addition, over 50% of the study population had an improvement quality of life in terms of physical activity, relationships and dietary habits at 1 year follow-up.
Conclusion: In our experience TORe was a safe and effective procedure in patients with weight regain after RYGB, with stable promising results even in the long-term follow-up. Moreover, our study showed an improvement in patients’ quality of life, in terms of satiety, relationships, dietary habits and aerobic physical exercise.
Further clinical trials are needed to confirm these results and to establish the role and correct timing of TORe after RYGB in the multidisciplinary strategy.
Disclosure: Nothing to disclose
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**P1400** LONG-TERM OUTCOMES OF ENDOCUTIVE SUBMUCOSAL DISSECTION FOR UNDIFFERENTIATED EARLY GASTRIC CANCER, BEYOND EXPANDED CRITERIA

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Introduction: Expanded indication of endoscopic submucosal dissection (ESD) for intramuscular undifferentiated early gastric cancer (EGC) up to 2 cm without lymphovascular invasion have been accepted because of negligible lymph node metastasis.

However, preoperative measurement of the tumor was completely not as same as postoperative one and if the postoperative tumor size would be a little more than 2 cm with R0 resection, additional surgery recommended.

Aims and Methods: The aim of this retrospective study was to analyze the long-term outcomes of ESD carried out to treat undifferentiated EGC in two groups (group A: up to 2 cm, group B: 2-3 cm). Between January 2001 and March 2015, 104 patients with undifferentiated early gastric cancer (EGC) including poorly differentiated adenocarcinoma (PD, n = 65), signet ring cell carcinoma (SG, n = 38) on preoperative biopsy underwent ESD (group A: 71 cases, group B: 33 cases). Total ESD specimens were evaluated on bloc resection, R0 resection, and curative resection (CR) and to evaluate long-term outcome, annual endoscopic surveillance with biopsy and CT scan were done.

Results: M/F was 40/31 and 17/16. Mean follow-up period in group A and B were 61.10 ± 38.12, 60.79 ± 47.75. Mean age in group A and B were 55.90 ± 13.62, 57.00 ± 12.25. En bloc in group A and B were achieved in 92.9%, 90.9% of patients, respectively (NS). R0 resection in were achieved in 87.3%, 51.5% of patients, respectively (p < 0.05). Curative resection was 83.0% in group A and group B was not include this definition. Postoperative bleeding, perforation during the procedure, and delayed perforation were no significantly different in both groups, respectively. Recurrence rate in group A and B were 3.6% (n = 4), 18.1% (n = 6), retrospectively (NS). Recurrence rate with R0 resection in group A and B were 1.7% (1/59), 6.25% (1/16) (NS). All cases with lateral margin positive required additional ESD (n = 2), destructive therapy (n = 3), or surgery (n = 4) and no recurrence happened. No patient died of gastric cancer.

Conclusion: In group B, R0 resection rate was lower than group A. However, long term follow up showed en bloc resection, recurrence rate, and with R0 resection in both group were not different. Carefully, undifferentiated EGC with 2 to 3 cm in size recommended ESD and long-term close follow-up.

Disclosure: Nothing to disclose

**P1401** EFFICACY OF G-POEM IN REFRACTORY GASTROPARESIS: A SYSTEMATIC REVIEW

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Introduction: Gastric peroral endoscopic myotomy (G-POEM) of the pylorus has emerged as a novel endoscopic technique for refractory gastroparesis (GP). However, limited data on the efficacy and safety of G-POEM are available. Therefore, a systematic review was conducted to evaluate the efficacy of G-POEM in refractory GP.

Aims and Methods: We performed a thorough literature search using PubMed, EMBASE, Cochrane library, Medline, Google scholar and Science citation index for G-POEM between January 2010 to January 2018. Search terms included MeSH and non-MeSH terms relating to gastroparesis, refractory gastroparesis, gastric peroral endoscopic myotomy, endoscopic techniques in gastroparesis and delayed gastric emptying. Additional case-reports, case series, and abstracts were retrieved by searching from references of relevant studies. Pooled technical success, clinical success, and adverse events were calculated.

Results: Based on our search criteria 23 studies were identified and 7 were excluded after careful review. 16 studies which included 189 patients were analyzed. The overall technical success rate, clinical success rate, and frequency of adverse events were 88.5, 83.2, and 10.8%, respectively. The common adverse events associated with G-POEM were pneumoperitoneum (4.7%), ulcer (1.6%), bleeding (1.5%) and stricture (1.0%). Overall mean procedure duration was 61.2 ± 11.4 minutes.

Conclusion: G-POEM is a technically feasible and effective therapeutic option for gastroparesis with good clinical responses. However, larger data is still required to determined the subgroup of patients who would benefit from this novel procedure.

Disclosure: Nothing to disclose

References

**P1402** FLEXIBLE ENDOSCOPY VESSEL-TISSUE SEALER ASSISTED TREATMENT OF ZENKER DIVERTICULUM: AN EFFECTIVE AND SAFE PROCEDURE

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Introduction: Zenker’s diverticulum (ZD) is an uncommon disease. Therapy of symptomatic ZD has evolved from an open surgical approach to less invasive transoral endoscopic techniques. Flexible endoscopy allows to use vessel-tissue sealer to perform diverticulotomy. An overtube protects both diverticulum and esophageal wall with a well-view of the septum. This procedure has demonstrated to be safe for high-risk surgical patients in small previous case series with a lower morbidity rates and quick patient’s recovery. Very little has been published with this approach in ZD treatment.

Aims and Methods: 1. To evaluate the effectiveness and safety of flexible endoscopy treatment assisted by vessel-tissue sealer technique. 2. Describe epidemiology data of ZD patients. 3. To describe the treatment technique. 4. To describe our experience with flexible endoscopy, using vessel-tissue sealer technique for the resection of ZD.

Patients were included consecutively from March 2009 to April 2018. Patients were censored until the end of the follow-up or death. We analysed complications, symptoms before treatment, sex, age, type of sedation and number of interventions needed for resolve ZD. Bleeding complication was considered when cases required a second endoscopy.

Results: 46 symptomatic ZD patients were included in the final analysis. Women were 41.3%, median-age of 73.7 ± 11 years. Median follow-up period was 37.21 ± 28 months. 38.7% ZD were considered small (<3 cm). Solid or semi-solid food related dysphagia were present in 55.6% of patients, whereas liquid-food and total dysphagia were observed in 34.8% and, 6.7% respectively. There were 4.3% complications with this technique. Bleeding was the most frequent adverse event in relation to endoscopy procedure (2.2%). This technique was successful in 76.1% in one single procedure. However, it increased until 89.1% with a second procedure. No statistically significant differences were found between complications rates according to diverticulum length, or number of interventions needed. Likewise, we did not find differences between the need of re-intervention and diverticulum length or symptoms. The majority of patients (80.7%), were managed as out-patient or short admission less than 24 hours.

Conclusion: In this large case series study, ZD treatment based on flexible endoscopy assisted by vessel-tissue sealer is an effective and safe procedure with a high successful rate in a few endoscopy sessions and low complications rate. This procedure can be recommended as a solid alternative in ZD endoscopic treatment.

Disclosure: Nothing to disclose
**P1403 PRIMARY ENDOCOSCOPIC MANAGEMENT OF POST-SURGICAL FISTULAE IN THE UPPER GI TRACT IS AN EFFECTIVE AND SAFE THERAPEUTIC OPTION**

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**Introduction:** Post-surgical fistulae involving the upper digestive tract (UDT) are associated with significant morbidity and mortality. Endoscopic management is a minimally invasive alternative option to surgical repair in this situation.

**Aims and Methods:** We aimed to access efficacy and safety of a primarily endoscopic management of post-surgical fistulae involving the UDT. Retrospective multi-centric study, involving 71 consecutive patients that were managed endoscopically for post-surgical fistula of the UDT, between March 2012 and December 2017, in 3 endoscopic centers. Factors associated with fistula closure, fistula recurrence and mortality including age, indication for surgery, fistula orifice size and time to fistula diagnosis/treatment were evaluated. Complications related to endoscopic therapy were classified as early (<1 week) or late (>1 week).

**Statistical Analysis:** Statistical analysis was performed with IBM SPSS®/22 and a p value <0.05 was considered significant.

**Results:** The mean age was 52.3±16.2 years and 63.4% (45) were women.

**Indications for surgery:** For: obesity 57.7% (41); neoplasia 32.4% (23); others 9.9% (7). A total of 92% were between surgery and endoscopy assessment in 60 days. The average size of fistula orifice was 7.7±4.0mm. Endoscopic interventions included: Metallin stents in 86% (61) patients (totally covered 29; partially covered 32), clips in 21.1% (15) patients (OTSC 7, TTS 8) and intraluminal drainage with stent in 2% (2) patients.

**Early complications (<1 week):** Occurred in 7.0% (5) patients: stenosis (n=3); mucosal dissection (n=1); anastomotic dehiscence (n=1) and late complications (>1 week) in 29.6% (21) patients: dysphagia related to mucosal ingrowth/overgrowth (n=8), stent fracture (n=4), stenosis after stent removal (n=3), migration (n=3), other (n=3).

**Overall clinical success (fistula closure):** Documented in 76.1% (54) patients. Fistula closure was obtained with a single endoscopic intervention in only 38% (27) patients. The median number of endoscopies until fistula closure was 21–8. Median time until confirmation of fistula closure was 84(6-83) days. Surgical re-intervention was performed in 21.9% (13) patients. The main reasons for surgical re-intervention were: Abdominal fluid collection drainage and peri-anastomotic lavage (n=2), esophageal exclusion (n=3), fistula suture (n=2), fistula jejunostomy (n=1).

**Conclusion:** Endoscopic treatment of post-surgical fistulae involving the upper digestive tract is associated with high clinical success with an acceptable safety profile.

**Disclosure:** Nothing to disclose

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**P1405 “DIAGNOSE-AND-LEAVE” STRATEGY FOR DIMINUTIVE LEFT COLORECTAL POLyps**


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**Introduction:** The “diagnose-and-leave” strategy is based on the decision of leaving in situ diminutive (<5 mm) rectosigmoid hyperplastic polyps, based on optical chromoendoscopy. ASGE recommends this strategy only if endoscopic diagnosis provides a 90% or higher negative predictive value for adenomatous histology when used with high confidence.

**Aims and Methods:** Our aim was to assess the feasibility of this strategy in our centre. We performed a prospective observational study of patients submitted to colonoscopy with optic chromoendoscopy (narrow-band imaging – NBI) during 2017. Pathological and endoscopic characteristics of diminutive left colorectal polyps (location, size, NICE classification and degree of confidence in this assessment) were collected. We compared NICE classification using optic chromoendoscopy and histology for each polyp.

**Results:** 107 colonscopies and 199 diminutive left colorectal polyps were included: 48% from the descending/sigmoid colon and 52% from the rectum. Mean size was 3.4±1.3mm. According to the NICE classification, 74% of polyps were type I and 26% type II. Pathology revealed that 58% were hyperplastic polyps, 33% were adenomas, 1% were sessile serrated polyps and 8% were inflammatory changes. The endoscopic diagnosis using NICE classification for adenomatous histology had sensitivity 51%, specificity 95%, positive predictive value 80% and negative predictive value 82%.

**Conclusion:** Optic chromoendoscopy assessment of diminutive left colorectal polyps did not reach the ASGE recommended cut-off. We will need to improve our optic chromoendoscopy performance, for instance trough the implementation of NBI training programs, before the “diagnose-and-leave” strategy can be used in our centre.

**Disclosure:** Nothing to disclose
localization in 30% of cases. However, there was no endoscopic aspect of UC. The more serious endoscopic description was congealed with erythematous, aphthous ulcerations, and erosions. The histological results in this group of patients were in favor of IBD in 31% of cases (N = 19) including 18 cases of CD and 1 case of UC, adal and/or colic lesions were non-specific in 30 patients.

- Revealed the presence of colonics the presence of colonic polyposis in 4 patients without lesions of the mucosa and the histological study was in favor of tubular adenoma in low-grade dysplasia in 2 cases and normal in the 2 others. Colonomoscopy was associated with a single case of complication represented by colon perforation.

Of the patients in whom endoscopy was in favor of IBD, 49% were asymptomatic in the digestive tract.

Conclusion: In our study, systematic ileocolonoscopy performed in patients with ACD and microscopic evidence in favor of IBD in 36.4%. This systematic screening is therefore recommended for early management of IBD.

Disclosure: Nothing to disclose

P1408 ROBOTIC FLEXIBLE ENDOSCOPY ALLOWING INTRALUMINAL SURGICAL TRIANGULATION FOR COMPLEX ENDOSCOPIC PROCEDURES: PRECLINICAL EXPERIENCE WITH 20 COLONIC ENDOSCOPIC MUCOSAL SECTIONS

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Introduction: Interventional procedures performed by means of flexible endoscopy have been considerably increasing thanks to recent technical and technological advances. Endoscopic submucosal dissection (ESD) is as effective as technically demanding. Robotic assistance and endoscopic translation of surgical principles could shorten the learning curve of existing endoluminal interventions and help establish innovative procedures. Our group previously described a master-slave robotic flexible endoscopic platform allowing for intraluminal surgical triangulation1.

Aims and Methods: The aim of this study was to evaluate preclinical feasibility of robotic colonic ESD in a porcine model. A mobile robotic cart and a detachable flexible endoscope compose the slave unit. The endoscope has 2 working channels for telemanipulated flexible instruments (graspers, a hook, and an isolated tip knife) and a third working channel for conventional endoscopic instruments. The jaw-like opening of the tip of the scope allows for the spacing of operative instruments offering surgical triangulation. The whole system has 10 degrees of freedom. The ergonomic master unit allows a single operator to control all movements of the endoscope and instruments through two control handles.

A surgeon without prior exposure to ESD had to perform 20 robotic colonic mucosal sections with coagulation marks on the bottom, lateral, and upper walls of the colon at a distance from the anal verge ranging between 15 and 35 cm. The assistant at the patient’s side performed a lifting submucosal injection when required by the operator. Total time (from starting to complete excision), ESD time (from the first incision to complete excision), “en bloc” resection of the marked area, specimen size, excision speed (specimen size/ESD time) and complications were recorded.

Results: All 20 pseudotumors, with the mean size of 15.18 ± 6.86 cm², were resected “en bloc”. One perforation (5%) occurred during the first experimental session and was managed intraoperatively, without interference with the planned procedure. Mean total time, ESD time, and excision speed accounted for 35.36 ± 14.20 min, 29.42 ± 14.29 min and 57.05 ± 29.42 mm²/min respectively, regardless of the ESD location. Comparative analysis between the first 10 and the second 10 ESDs showed a significant increase in dissection speed (43.72 ± 30.74 vs. 70.37 ± 22.09; p < 0.007).

Conclusion: Robotic colonic ESD is feasible in a preclinical model. The robotic platform and flexible instruments responded well to the stress testing. Comparing current results with previous studies performed by our group, robotic assistance outperforms conventional and mechanical platforms while carrying out colonic ESD. These preclinical results suggest that robotic assistance could be a shortcut to endoscopic expertise. The described robotic flexible endoscopic platform is ready for the first clinical case.

Disclosure: Nothing to disclose

References

P1407 DO HYPERMOBILE JOINTS PREDICT A PAINFUL COLONOSCOPY?

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Introduction: Patient perception of colonoscopy varies greatly; young slender women and irritable bowel syndrome (IBS) patients appear to be at risk for painful colonoscopy. Recent evidence suggests a high prevalence of connective tissue disorders referred to as “Hypermobility Spectrum Disorders” (HSD) in this population. Therefore, HSD might be associated with increased pain during colonoscopy.

Aims and Methods: In this study we aimed to compare pain perception during colonoscopy between HSD and non-HSD patients. We prospectively included patients undergoing a standard colonoscopy. Patients with a history of major tissue disorders referred to as “Hypermobility Spectrum Disorders” (HSD) in 18.51 mm, 95%-CI 10.56–26.47, p < 0.001).

were asked to report pain scores on a 100mm visual analogue scale (VAS). In addition, cephalic intubation time was measured, and endoscopists scored the difficulty of the procedure (100mm VAS).

Results: Of 201 included patients, 22 (10.9%) met criteria for HSD. HSD patients were more often female than subjects without HSD (86.4% vs. 48.6%, p = 0.001). A crude linear regression model demonstrated that pain scores were 13.39mm higher (95%-CI 0.07–26.53, p = 0.049) in HSD vs. non-HSD patients. When subsequently correcting for possible confounding factors, however, this difference in pain scores could be explained by a confounding effect of female gender. Indeed, female gender was the strongest predictor of a higher pain score (β = 18.15 mm, 95%-CI 10.56–26.47, p < 0.001). No other factors were found to be associated with patient pain score. Cephalic intubation time and perceived procedural difficulty did not differ significantly between HSD and non-HSD subjects. Colonoscopy time was an independent predictor of pain with a higher cephalic intubation time measured in female gender as a confounding factor explains the higher pain scores in HSD patients compared to non-HSD patients. In addition, performing colonoscopy is another key prognostic parameter in IBD patients. I-scan optical enhancement (OE) is a novel endoscopic pre-processing optical filter technology, in which the spectrum of the emitted wavelengths is reduced, thereby leading to enhanced visualization of the mucosa. Ten patients with IBD were enrolled in the study. Results showed that i-scan OE increased diagnostic accuracy for identifying inflammatory bowel diseases (IBD), recent evidence suggests that histologic healing is an important key prognostic parameter in IBD patients. I-scan optical enhancement (OE) is a novel endoscopic pre-processing optical filter technology, in which the spectrum of the emitted wavelengths is reduced, thereby leading to enhanced visualization of the mucosa. Ten patients with IBD were enrolled in the study. Results showed that i-scan OE increased diagnostic accuracy for identifying inflammatory bowel diseases (IBD), recent evidence suggests that histologic healing is an important i-scan OE with Cohen’s kappa was substantial (κ = 0.7).

Conclusion: Magnification endoscopy with i-scan OE in combination with virtual chromoendoscopy can render the endoscopic diagnosis in IBD more precisely.

Aims and Methods: Our aim was to evaluate whether i-scan OE in combination with high-resolution optical magnification endoscopy can accurately assess histologic inflammation in IBD patients. The in vivo assessment of histologic inflammation was made with optical magnification endoscopy in conjunction with i-scan OE by a total of four endoscopists. Targeted biopsies of the imaged areas were obtained and results were compared against established and validated histology scoring. Moreover, interobserver agreement was calculated.

Results: 82 IBD patients (29 CU, 53 MC) were consecutively enrolled (40 men, median age 43, range 19–72). A newly developed i-scan OE magnification score showed high accuracy, sensitivity and specificity for assessing the histologic level of inflammation and correlated strongly with histopathologic scoring (κ = 0.7, p ≤ 0.05). Furthermore, a prevailing amount of patients with mucosal healing on standard endoscopy showed signs of microinflammation on optical magnification endoscopy in combination with i-scan OE. Interobserver agreement for assessing microscopic inflammation with optical magnification endoscopy and i-scan OE with Cohen’s kappa was substantial (κ = 0.7).
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Introduction: Even if Split-dose regimen (SpD) [and Same-day regimen (SaD) for afternoon colonoscopies] is recommended by international guidelines1,2, its adoption is still suboptimal.

Aims and Methods: Our aim was to survey and improve adherence to SpD through a Plan-Do-Study-Act (PDSA) approach and to identify factors predicting its adoption.

The multicenter cross-sectional study consisted of 3 phases. Cycle1: survey of current practice; Intervventional phase: local spontaneous corrective measures after analysis of Cycle1 data; Cycle2: survey of modified practice. Every outpatient or inpatient scheduled for a complete colonoscopy was eligible.

Results: Differences were compared using a Student’s T or a Chi Square test as appropriate. Multiple stepwise selection logistic regression models were built.

Conclusion: Notwithstanding barriers limiting the spread of Split-dose regimens (SpD) new contact-type endoscopic Colonoscopy (EC) was able to differentiate neoplastic from non-neoplastic polyps using an automated computer-based decision support based on standard solution picture is not available until now. Technical support is therefore demanded in order to improve accuracy of optical predictions. Computer-assisted optical predictions (CAOB) approaches have recently been published but these approaches have focussed among users. Technical support is therefore demanded in order to improve accuracy of optical predictions.

Disclosure: Nothing to disclose

References
P1414 EFFICACY AND SAFETY OF ENDOCUTOSCOPY MUCOSAL RESSECTION FOR LARGE COLORECTAL LESIONS IN THE ELDERLY

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Introduction: Endoscopic mucosal resection (EMR) is a minimally invasive technique used for the treatment of superficial neoplasms of the gastrointestinal tract, including early carcinomas. There is limited data on the safety and efficacy of this technique for large colorectal lesions in elderly patients.

Aims and Methods: The aim of this study was to evaluate the efficacy and safety of EMR of large colorectal lesions (≥20 mm) in the elderly (≥75 years) and to compare the outcomes with those of younger patients (≤75 years).

Results: A total of 136 colorectal lesions were removed in 123 patients. Fifty-one EMR were performed on 44 patients ≥75 years and 85 EMR were performed on 79 patients ≤75 years. The median age in Group 1 was 80 years (range 75-87 years) and 67 years in Group 2 (range 47-74 years). There was no significant difference in sex ratio, lesion size and lesion distribution between the two groups. En bloc resection was performed in 29.4% (15/123) of all cases. The lesion size in Group 1 vs ≤75 years (Group 2) was 20 mm at our institution between January 2015 and December 2016. Patients were divided in two age groups considering 75 years as cut-off: ≥75 years (Group 1) vs ≤75 years (Group 2). The demographics of the patients, size and location of the lesions, technical aspects of the procedure, rate of endoscopic recurrence and complications were considered.

Results: A total of 136 colorectal lesions were removed in 123 patients. Fifty-one EMR were performed on 44 patients ≥75 years and 85 EMR were performed on 79 patients ≤75 years. The median age in Group 1 was 80 years (range 75-87 years) and 67 years in Group 2 (range 47–74 years). There was no significant difference in sex ratio, lesion size and lesion distribution between the two groups. En bloc resection was performed in 29.4% (15/123) of all cases. The lesion size in Group 1 vs ≤75 years (Group 2) was 20 mm at our institution between January 2015 and December 2016. Patients were divided in two age groups considering 75 years as cut-off: ≥75 years (Group 1) vs ≤75 years (Group 2). The demographics of the patients, size and location of the lesions, technical aspects of the procedure, rate of endoscopic recurrence and complications were considered.

Conclusion: EMR is a safe and effective procedure for the treatment of large colorectal neoplasms in the elderly, with outcomes similar to those obtained in younger patients.

Disclosure: Nothing to disclose.

References

P1414 UNDERWATER ENDOCUTOSCOPY MUCOSAL RESECTION (UEMR) FOR COLORECTAL (CR) LESIONS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Introduction: Underwater endoscopic mucosal resection (UEMR) for colorectal (CR) lesions has been described for overcoming the technical drawbacks of standard mucosectomy (EMR). This approach takes advantage of the behavior of water as a barrier preventing abdominal gas escaping from the muscular layer and aspirated into the liquid. Thus, luminal water infusion allows to achieve an alternative way to have the lesion lifted before being resected, without any submucosal injection. We performed a systematic review with meta-analysis to evaluate the efficacy of UEMR for the resection of CR lesions.

Aims and Methods: Electronic databases (Medline, Scopus, EMBASE) were searched up to March 2018. Studies including patients with CR lesions resected by the UEMR technique were eligible. The complete resection (primary outcome), en-bloc resection, oncological results, adverse events and complications were pooled by means of a random-effect model according to the degree of heterogeneity to obtain a proportion with a 95% confidence interval (CI).

Results: Ten studies were eligible for inclusion providing data on 508 lesions endoscopically removed in 433 patients (m/f = 239/194; ages ranging from 62.2 to 75 years). Six studies were performed in United States and the other in Europe; seven studies were prospective. The specific indications for performing UEMR, instead of standard EMR, varied widely across the studies: lesions localized to colon (8 out of 22 studies, above 15 mm in 1 and above 10mm in the others) (5/10 studies, 248 lesions), recurrence after EMR (1/10, 36 lesions), scarce accessibility (1/10, 27 lesions). Three studies included mixed cases and aimed either to evaluate the feasibility of the new technique (2/10, 124 lesions) or to compare it to the standard procedure (1/10, 73 lesions). Most of the lesions were located peripherally to the splenic flexure (309 lesions, 61%). The mean size of the lesion ranged from 15 mm to 33.8 mm.

Complete resection rate was 96.36% (CI 91.77–98.44) with a rate of 0.774). Patients with Sm2 invasion were referred for surgical treatment. During follow-up, no residual or relapsing lesions were identified in patients who underwent endoscopic and radiological evaluation.

Disclosure: Nothing to disclose.

References

P1416 DOES ENDOCUTOSCOPY SUBMUCOSAL DISSECTION REALLY DIFFER BETWEEN COLORECTAL AND RECTAL LESIONS? A WESTERN EXPERIENCE BY A SINGLE ENDOSCOPY CENTRE ON 505 PROCEDURES

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Introduction: In the treatment of early stage malignant and pre-malignant lesions, endoscopic submucosal dissection (ESD) is an effective, minimally invasive treatment modality which can provide en bloc and complete resection, when compared to other treatment modalities such as endoscopic mucosal resection and polypectomy.

Aims and Methods: In this study, we aimed to compare the effect of localization on ESD treatment success, in patients with pre-malignant and early-stage malignant colorectal lesions. Up to date, number of lesions included in this study is higher than any single-institutional publications in the Western literature. During April 2012 and April 2018, patients with a total of 2458 colorectal lesions were referred to our clinical unit to be treated with advanced endoscopic techniques. Colorectal ESD was performed on 541 lesions. Data were recorded prospectively and analyzed retrospectively by using t-test and a chi-square method. 8 patients with subepithelial lesions, 7 patients with tumors located on anastomosis line and 21 patients who didn’t have post-operative evaluation were excluded from the study. According to the localization of the lesions, ESD procedures were categorized as rectum (R-ESD) and colon (C-ESD).

The peroperative results of these two groups were compared.

Results: For pre-malignant and early-malignant lesions, 505 colorectal ESD procedures were performed in 486 patients. The overall en bloc and complete resection rates were 95.1% and 91.1% respectively for colorectal lesions. Numbers of lesions localized to rectum and colon were, 253 and 252 respectively. Between two groups, no differences were observed for age, gender, en bloc and complete resection rates, severity of dysplasia, rate of invasive carcinoma, utilization of submucosal or other knife, procedure times. (p > 0.05).

Lesions localized to rectum were larger than lesions localized to colon. Although procedure times were similar between groups, dissection rate was faster in rectal lesions. For controlling bleeding and providing pre-coagulation during the procedure, submucosal injection was utilized more in rectal lesions. Some significant differences in classifications of lesions (p < 0.05): Lateral spreading tumor non-granular (LST-N) type lesions were more frequent in colon group, while LST granular mixed type (LST-GM) lesions were more common in rectal group. Rate of malignancy was higher in rectal lesions; however no significant differences were observed (p > 0.05).

During procedure, utilization of clip was required for 14 lesions with mucosal damage. Delayed perforation was observed in 1 lesion. Except for the late perforation, all complications were treated with endoscopy. Usage of clip was higher in lesions located to colon (p < 0.05). Patients with Sm2 invasion were referred for surgical treatment. During follow-up, no residual or relapsing lesions were identified in patients who underwent endoscopic and radiological evaluation.

Disclosure: Nothing to disclose.
Endocytoscopic vascular pattern of colorectal lesions is useful for predicting pathological diagnosis.

Aims and Methods: A retrospective analysis was performed of all patients who underwent an endoscopy during a 2-year period, from January 2010 to January 2012, at a large non-tertiary endoscopy unit. Data was collected from endoscopy reports accessed from the hospital endoscopy reporting system (HICSS). Reports were reviewed for details of the endoscopy performed and follow-up endoscopies for recurrence at the site of the initial endoscopy. The size and morphology of polyp, location and histology was recorded along with EMR details including completeness of en-bloc resection and complications.

Results: A total of 437 patients underwent EMR during the study period. After exclusion for malignancy requiring surgery, incomplete follow-up, polyp size < 1cm and index EMR outside the study period, 241 cases were analysed. Of the 241 polyps, 63% (153) were > 2cm, 33% (2.5–7cm) had 9% (3.5–15 cm). Of the 241 polyps, 51% were located in the right colon and 35% in the left side. Most polyps were polypoid (79%) with the remaining being flat (15%) or sub-epithelial (6%). Duration of follow-up ranged from 3 to 60 months with a mean follow-up of 31 months (median 3 months). Residual/recurrent adenomas were successfully treated with further endoscopic resection and/or ablative therapy. In case of histologically, there was progression of severity of dysplasia/grading of adenoma in those patients who developed recurrence at long-term follow-up.

Conclusion: This study confirms EMR is a safe alternative to surgery for the management of large or difficult colon polyps with good long-term outcomes.

Disclosure: Nothing to disclose.

Reference:

Endoscopic submucosal dissection (ESD) is widely recognized as a safe and minimally invasive technique for the removal of large, non-polypoid colorectal lesions without resorting to surgery. In spite of high complete resection rates, local recurrence is not uncommon. Most studies have reported on short-term recurrence post EMR. We analysed our experience to determine long-term outcomes at 3 and 5 years post EMR.

Aims and Methods: A retrospective analysis was performed of patients who underwent an endoscopy at a general hospital in Japan from January 2009 to December 2018. Data was collected from endoscopy reports accessed from the hospital endoscopy reporting system. Patients with a history of cancer were excluded. The size and morphology of polyp, location and histology was recorded along with endoscopy details including completeness of en-bloc resection and complications. Polyp recurrence at subsequent endoscopies up to 5 years was also recorded.

Results: A total of 457 patients underwent EMR during the study period. After exclusion for malignancy requiring surgery, incomplete follow-up, polyp size < 1cm and index EMR outside the study period, 241 cases were analysed. Of the 241 polyps, 63% (153) were > 2cm, 33% (2.5–7cm) had 9% (3.5–15 cm). Of the 241 polyps, 51% were located in the right colon and 35% in the left side. Most polyps were polypoid (79%) with the remaining being flat (15%) or sub-epithelial (6%). Duration of follow-up ranged from 3 to 60 months with a mean follow-up of 31 months (median 3 months). Residual/recurrent adenomas were successfully treated with further endoscopic resection and/or ablative therapy. In case of histologically, there was progression of severity of dysplasia/grading of adenoma in those patients who developed recurrence at long-term follow-up.

Conclusion: This study confirms EMR is a safe alternative to surgery for the management of large or difficult colon polyps with good long-term outcomes.

Disclosure: Nothing to disclose.

Reference:
in 2/12 cases (17%) because the lesion was pT1sm1R0 with no pejorative qualitative criteria and in 2/12 cases (17%) we confirmed pT1sm2 lesion as on the initial resection but with negative positive deep margins on the second resection (one patient refused initially rectal surgery, rectal surgery was not possible for the second one) and we wanted avoid more than pT1sm2 lesion. In 2/14 patients (17%), surgery was recommended: 1 patient for R1 resection on the second procedure and 1 patient for pT1sm2R0 on the second procedure (pTis on the first) Regarding the secondary endpoints, only 1 patient presented a side effect which was a post polypectomy syndrome quickly controlled by an antibiotic treatment and by this no recurrence was notified. The median follow-up time was 569 days and no local recurrence has been observed in our patients.

Conclusion: In case of R1 resection for superficial adenocarcinomas without pejorative histology a second endoscopic resection in an expert center may be a safe way to evaluate the real risk of metastatic lymph node in order to avoid unnecessary surgery.

Disclosure: Nothing to disclose

References
P142 QUALITY ASSURANCE IN ENDOSCOPY: ABOVE AND BEYOND PROCEDURE-RELATED PERFORMANCE
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Introduction: In recent years considerable progress has been made to establish formal frameworks to ensure that quality services are delivered safely to patients. This was accompanied by considerable progress of the equipment available to deliver endoscopic services. While there are some studies assessing the procedural performance of specific equipment innovations, very little is known about the reliability of equipment and subsequent changes of reliability over time as well as the availability of equipment when time between repairs and repair time were taken into considerations.

Aims and Methods: We reviewed endoscopic service records of endoscopic equipment for a seven year time-period of a large tertiary teaching hospital delivering annually >12,000 endoscopic procedures. We aimed to capture the number of procedures done per scope, the number of repairs, costs per repair and time required for repair.

Results: In total 56 scopes (all from one supplier) were in use at the time of data capturing. While in 2011 on average scopes had a usefulness of 453 days until next repair (95% CI: 312–593), this dropped to 80 days (95% CI: 56–103) in 2017. This was associated with a significant increase of repair costs per 1000 procedures. At the same time the repair rate per 1000 procedures has substantially increased with the latest scope generations.

Discussion: Nothing to disclose.

P1423 DEVELOPMENT AND INITIAL VALIDATION OF A UNIVERSAL CLASSIFICATION FOR COLO-RECTAL POLYPS AND NEOPLASIA (UNICORN)
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Introduction: Identification and adequate characterization of colonic polyps is important in the prevention of colo-rectal cancer. Currently, the well validated classifications for colon polyps are based on image enhancement technology (IET). Magnification endoscopy is also required for some of the proposed algorithms. The uptake of such technology is not universal and learning curves are variable. High-definition white light endoscopy (HD-WLE) is used routinely by endoscopists. We developed a new classification and clinical algorithm using HD-WLE and proceeded to an initial validation.

Aims and Methods: The aim of our study was to develop and validate a classification and algorithm for colonic polyps using HD-WLE. In the first step, 10 experts developed the UNICORN classification by a series of consensus statements. Polyps were divided into Type 1a or hyperplastic polyps (HP), Type 1b or sessile serrated polyps (SSP), Type 2a or low-risk adenomas, Type 2b or high-risk adenomas and Type 3 or deep submucosal invasive cancer. In the next step, participants in 9 Endoscopy centres underwent training with a specially designed tutorial. Subsequently, 35 polyp images collected on HD-WLE from the 3 major endoscopic systems were provided. These included 16 images of Type 1, 18 images of type 2 polyps and 1 type 3. Participants were divided into experts and non-experts based on their level of experience and were asked to predict polyp type. Level of confidence of prediction was also recorded. Accuracy of prediction was calculated by measuring sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) as well as diagnostic effectiveness or accuracy.

Results: 12 experts and 15 non-experts participated in the validation using polyp images. Both groups achieved negative predictive values (NPV) >90% for HP, SSP and high risk adenomas. NPV was 86 and 81% respectively for low-risk adenomas. The expert group achieved diagnostic accuracy of 0.92 for HP, 0.93 for SSP, 0.87 for low risk adenomas and 0.92 for high-risk adenomas. The corresponding values for the non-experts were 0.91 for HP, 0.90 for SSP, 0.84 for low risk adenomas and 0.90 for high-risk adenomas. PPV was low for high-risk adenomas in the expert and non-expert group.

Discussion: Nothing to disclose.

Abstract No: P1423

Table 1: UNICORN validation results.

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<th>Characteristics</th>
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<td>Type of resection</td>
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<td>Piecemeal</td>
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Table 1: Characteristics and information about the malignant polyps of the study cohort

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<th>Margin clearance</th>
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<td>1mm clearance (R1)</td>
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</table>

Abstract No: P1421

Table 1: Characteristics and information about the malignant polyps of the study cohort

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<th>Mean polyp size (mm)</th>
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<td>sessile</td>
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<tr>
<td>pedunculated</td>
<td>10</td>
<td>22.7</td>
</tr>
</tbody>
</table>

NPV 93(89–95) 91(88–93) 97(94–98) 96(94–98) 86(81–90) 81(77–85) 97(94–98) 96(94–98)

Specificity 96(92–97) 96(94–98) 95(92–97) 91(88–93) 91(87–94) 93(90–96) 94(91–96) 92(89–94)

PPV 89(81–94) 90(83–94) 78(67–86) 67(57–75) 87(81–92) 89(83–93) 54(39–68) 45(33–58)

NPV 93(89–95) 91(88–93) 97(94–98) 96(94–98) 86(81–90) 81(77–85) 97(94–98) 96(94–98)
P1424 A SIMPLIFIED TABLE MIXING VALIDATED DIAGNOSTIC CRITERIA IS EFFECTIVE TO IMPROVE CHARACTERIZATION OF COLORECTAL LESIONS BY FELLOWS: THE CONECCCT CLASSIFICATION

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Introduction: Endoscopic characterization of colorectal neoplasia is a key point to choose in real time the best therapeutic option to treat effectively and safely each lesion. This characterization is based on 5 classifications, difficult to combine and to learn for non-experts. Thus, we mixed all the validated criteria in a single classification called CONECCCT to facilitate prediction and therapeutic choice. This study aimed to evaluate CONECCCT benefits in endoscopic characterization of colorectal neoplasia.

Aims and Methods: It is a prospective multicenter study involving all French gastroenterology interns and seniors who participated to usual bi-annual teaching session. Each participant performed a pre-test with 20 colorectal neoplasia (High quality pictures with chromoendoscopy) with 2 questions for each about histology prediction and adequate treatment to propose. Then, they followed a 30 min teaching session about CONECCCT and repeated a post-test with same 20 lesions in different order. In order to check that their progressions are sustainable in long time, we asked them to participate in a second session, 3–6 months later, during which they performed a test (T3M) with 40 colorectal (the last 20 lesions and 20 news) neoplasia with the 2 same questions.

Results: 419 persons (280 interns and 139 seniors) participated at first session and we analyzed 206 participants for T3M (96 persons were excluded because of matching problems). Mean rate of good answers progressed from 60.6% at pre-test versus 76.4% at post-test (p < 0.05) versus 70.5% at T3M (p = 0.05). Between pre Test and post Test, 345 (86.9%) participants progressed and mean progression per participant was 21.0%. Depending on histology, prediction results were significantly improved (p < 0.05) with 61.0% at pre Test and 78.5% at post Test. After the teaching program, overtreated patients reduced significantly from 30.1% to 15.4% (p < 0.05).

Between pre Test and T3M, 121 (76.6%) participants progressed and mean progression per participant was 12.9%. Depending on histology, prediction results were significantly improved (p = 0.05) with 61.0% at pre Test and 70.5% at T3M. Overtreated patients reduced significantly from 30.1% to 20.0% (p < 0.05).

Other interesting results are that among all French participants, 86.4% considered CONECCCT as helpful for prediction and 88.5% for treatment. 51.3% already used that classification.

Conclusion: CONECCCT classification teaching is effective to improve histology prediction and treatment choice regardless of lesion histology in gastroenterology interns and seniors. Overtreated patients reduced significantly thanks to CONECCCT.

Disclosure: Nothing to disclose

P1425 META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS SHOWS THAT ENDOCUFF INCREASES COLONOSCOPY ADENOMA DETECTION RATE

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Introduction: Endocuff—a plastic device with flexible projections—mounted on the distal tip of the colonoscope, promises improved colonic mucosa inspection and on advanced ADR (ADR). We performed literature searches in MEDLINE and Cochrane Library for randomized-controlled trials. Data were published as full papers in English language evaluating Endocuff-assisted (EAC) versus conventional colonoscopy (CC) in terms of ADR and AAD. The effect size on study outcomes was calculated using fixed or random effect model, as appropriate, and it is shown in OR[95%CI].

Results: We identified 6 studies; five parallel groups design and one tandem. Five studies evaluated the first-generation and the sixth one the Endocuff-Vision device. One study included screening examinations, another one evaluated FOBT-positive screening and surveillance examinations and four studies evaluated colonoscopies with mixed indications (screening, surveillance and symptomatic). ADR was reported in all 6 studies (3460 examinations). As compared to CC, ADR was significantly increased, ADR [OR(95%CI)=1.30(1.00–1.69); I²=67%]. Meta-analysis of data from 5 studies (2971 examinations) did not detect any difference between EAC and CC regarding AADR [OR(95%CI)=0.92(0.74–1.16); I²=0%]. There was no evidence of publication bias.

Conclusion: Our data provide evidence that EAC increases ADR compared to CC, without increasing AADR. Heterogeneity among the included studies calls for cautious interpretation of the results.

Disclosure: Nothing to disclose

P1426 COMPARISON OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING THE POCKET CREATION METHOD AND THE CONVENTIONAL METHOD FOR COLORECTAL LESIONS

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Introduction: Endoscopic submucosal dissection (ESD) is a widely used procedure for colorectal neoplasms. However, especially for intermediate colorectal lesions or flat colorectal lesions, it is still technically difficult because of the lack of counter-traction. Recently, the pocket creation method (PCM) was developed to overcome these technical difficulties, which facilitating ESD for such colorectal lesions creating a submucosal pocket under the lesion. However, it is still unclear whether the PCM is superior to the conventional method (CM) for colorectal lesions.

Aims and Methods: The aim of this study was to compare the clinical results of the PCM and CM for colorectal lesions. Between January 2016 and October 2017, a total of 87 colorectal ESD cases were performed at our institution. Retrospectively, they were divided into the PCM group (n = 40) and CM group (n = 47). All procedures were conducted using a water-jet colonoscope (PCF-290ZI; Olympus, Tokyo, Japan) and DualKnife (KD-655; Olympus, Tokyo, Japan). A small-caliber tip transparent hood (DH-29CR, Fujifilm, Tokyo, Japan) was used as the injection solution. For PCM, initial mucosal incision is made approximately 20mm in length at the distal side of the tumor after submucosal injection. Then, submucosal pocket under most of the tumor was created with Dual-J Knife. The lower side of the pocket was opened in a step-by-step manner toward the proximal side, and the tumor is resected. For conventional method, mucosal incision and submucosal dissection was performed from the proximal edge of the tumor. Then, additional mucosal incision was performed circumferentially, and submucosal dissection was made in the same manner.

For both groups, lesion size, procedure time, total amounts of midazolam, and ESD-related complications (hypotension, hypertension, hypoxia, and arrhythmia) were compared. SPSS version 14 (IBM, Armonk, NY, USA) was used for statistical analysis.

Results: Forty patients in the PCM group (16 male; 24 female; age range, 44–87 years; mean age, 75.5 years) and 47 patients in the CM group (21 male; 26 female; age range, 65–98 years; mean age, 77.3 years) were treated with ESD. The mean size of the resected lesions was 33.7 mm in the PCM group and 33.3 mm in the CM group (p < 0.05). ESD times for the PCM and CM groups were 51.7 and 54.6 minutes (p = 0.14), respectively. Midazolam doses for the PCM and CM groups were 2.87 and 2.5 mg (p = 0.23), respectively. En bloc resection rates for the PCM and CM groups were 97.5% and 97.9% (p = 0.45), and R0 resection rates were 88.2% and 75.0% (p = 0.17), respectively. Complications occurred in the PCM and CM groups as follows: hypoxia, 5.0% and 10.6% (p = 0.31); bradycardia, 2.5% and 10.6% (p = 0.17); tachycardia, 0% and 2.1% (p = 0.18); hypotension, 37.5% and 70.2% (p < 0.05); and hypertension, 32.5% and 23.4% (p = 0.18). Postoperative bleeding occurred in one case (1/40, 2.5%) of the PCM group; however, no perforations occurred in either group. Of note, even if the
lesion had submucosal fibrosis caused by a previous biopsy, en bloc resection was possible without any difficulty for the PCM group.

Conclusion: PCM is feasible, safe, and simple compared with the CM for colorectal lesions. Furthermore, it might be hugely advantageous during ESD for patients with fibrotic/scared colorectal lesions. However, further studies using unaided devices to perform the PCM are needed.

Disclosure: Nothing to disclose

P1427 LABEL-FREE MULTIPHOTON IMAGING AS A REAL-TIME DIAGNOSTIC TOOL FOR DISCRIMINATING COLORECTAL DISEASES

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Introduction: Accurate diagnosis of colorectal precancer and early carcinoma is crucial for cancer prevention and prognostic improvement. Various endoscopic technologies were developed to increase the diagnostic accuracy, and the biopsy-dependent pathology remains the golden standard. During routine endoscopy, random biopsy is performed as the gold standard to diagnose colorectal lesions. Without fluorescent label, multiphoton microscopic (MPM) imaging directly reveals live cellular morphology and tissue microenvironment based on intrinsic two-photon excited fluorescence (TPEF) and second harmonic generation (SHG) signal. As reported, its resolution and performance in vivo are comparable to the ex vivo histopathology. We thus aimed to initially investigate the original features of colorectal diseases under MPM, and evaluate its potential for real-time diagnosis in vivo.

Aims and Methods: Experimental and diagnostic cohorts were designed in this study. The multiphoton images of 40 fresh tissues were collected and confirmed pathological performance of colorectal normal tissues, hyperplastic polyps, adenomas and adenocarcinomas. Both morphological and quantitative features were recorded and analyzed to establish diagnostic standards with MPM. For the second cohort with 86 tissues, we distinguished the various colorectal diseases with conclusive MPM features.

Results: Through the investigation, the colorectal normal, hyperplastic polyps, adenoma and adenocarcinoma were presented difference in the crypt opening, gland structure, epithelial cells and collagen fibers. The epithelial nuclear area of normal cases were similar to hyperplastic tissues (31.36 ± 3.18 μm² and 32.14 ± 3.12 μm², respectively, P = 0.082) but apparently smaller than adenoma and adenocarcinoma of 57.41 ± 10.64 μm² and 86.62 ± 10.64 μm², P < 0.001). Cellular asynmetry were 0.79 ± 0.08, 0.77 ± 0.09, 0.39 ± 0.07 and 0.76 ± 0.10, respectively, indicating the nuclear elongation of adenoma evidently, while relative round in normal, hyperplastic and cancerous cells. Compared with normal tissues, the TPEF/SHG intensity ratio for collagen content was also similar in hyperplastic cases (0.27 ± 0.04 and 0.26 ± 0.02, P = 0.736) but decreased in adenoma and adenocarcinoma samples (0.22 ± 0.01 and 0.17 ± 0.02, P < 0.001). With the typical features, we preliminarily tested the diagnostic efficiency of real-time MPM, and found its sensitivity for distinguishing normal, hyperplastic polyps, adenoma and adenocarcinoma was 90.63%, 75%, 85.94%, 97.92%, while the specificity and adenocarcinoma was 90.63%, 75%, 85.94%, 97.92%, while the specificity was 99.29%, 95.14%, 95.37%, 94.36%, respectively.

Conclusion: The real-time multiphoton microscopic imaging can be effective to evaluate the bowel-cleansing efficacy. Using the Boston Bowel Preparation Scale (BBPS) to evaluate the bowel-cleansing efficacy. As bowel-cleansing agents, Using the Boston Bowel Preparation Scale (BBPS) to evaluate the bowel-cleansing efficacy.

Results: One hundred and thirty-three patients were included (68 in group A and 65 in group B), with a sex ratio = 0.85. The average age of patients was 52 ± 14.2 years [18–75]. The indication of colonoscopy was gastrointestinal bleeding or anemia in 50.3%, constipation in 17.2% of cases. Two groups were comparable for sex, history of constipation, taking all of the preparation, the duration after the last taking. but there was a significant difference for age classes and adherence to the Low-residue diet. There was significant difference in the rates of side effect (Group A: 49.5%, Group B: 23.1%) (p = 0.008) and acceptability (70.5% Versus 90.7% respectively) (p = 0.01).

In term of effectiveness, the Group B had a better mean BBPS compared with Group A (7.05 ± 1.5 vs. 6.43 ± 1.8) (p < 0.009), the BBPS greater than or equal to 6 was recorded in 89.2% versus 76.0% of patient respectively (p = 0.008). After adjustment for age classes and adherence to Low-residue diet, BBSP at Group B remained better than Group A.

According to our study, the efficacy of bowel preparation for colonoscopy can be improved by reducing the volume of Polyethylene glycol to two liters associated with Bisacodyl, this protocol is best tolerated and tolerated by the patients.

Disclosure: Nothing to disclose

P1428 TWO LIETERS OF POLYETHYLENE GLYCOL (PEG) WITH 15 MG OF BISACODYL VERSUS 4 LIETERS OF PEG FOR BOWEL PREPARATION TO COLONOSCOPY: PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Introduction: Bowel preparation is an essential step for successful colonoscopy in order to achieve complete visualization of the whole colonic mucosa, detection of abnormalities, and the rate of missed lesions is still not satisfying. Sedation increases quality and tolerability but also costs and timing of the procedures. The use of warm infusion in lieu of gas insufflation seems to improve colonoscopy performance decreasing insertion pain and the need for sedation, increasing cecal intubation rate and facilitating completion of difficult colonoscopy without reducing the adenoma detection rates.

Aims and Methods: Aim of the study was to evaluate tolerability of warm water infusion technique (WWI) compared to carbon dioxide (CO2) insufflation in terms of pain and need for sedation. Secondary aim was to compare the performance of the two techniques.

Prospective randomized controlled trial in which consecutive patients referred to undergo colonoscopy over a 4-month period were recruited. Pregnancy, age < 18 yrs, bowel resection, malignant stenosis, emergency were exclusion criteria. After the informed consent, patients were randomized into two arms: a) warm water preparation with no collagen b) CO2 insufflation with minimal patient’s weight based sedation. Patients completed a questionnaire regarding tolerability of the procedures and the level of pain after the colonoscopy expressed on a visual scale.

Cecal Intubation Time (CIT), Cecal Intubation Time (CIT), Total Procedure Time (TPT), Adenoma Detection Rate (ADR), Adverse Events (AEs) and bowel preparation and amount of sedation required were assessed. Procedures were performed by one doctor in training under supervision.

Results: One-hundred and four patients met the inclusion criteria (51F; 63 M; age 63 range 21–92; BMI 24.5, range 15.5–39.5) and 82 in the WWI group (44F, 38M; age 64 yrs, 21–92; BMI 24.8 15.5–39.5) and 82 in the CO2+sedation group (57F; 25M; age 62, 21–82; BMI 24, 16–34). There was no difference in terms of pain perception, CIT, CIT, TPT and bowel cleansing between the two groups (Tab. 1). Higher ADR was achieved in the WWI arm (p 0.02). Moreover, adverse events were significantly lower with water infusion compared to CO2+sedation (p 0.03). Finally, 3 patients required sedation during WWI to complete the procedure.

<table>
<thead>
<tr>
<th>Table 1. Results</th>
<th>CIT</th>
<th>TPT</th>
<th>Adenoma Detection Rate</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>WWI</td>
<td>8.67 (3.59)</td>
<td>18.31 (4.9)</td>
<td>20/82 (24.4%)</td>
<td>1/82 (1.2%)</td>
</tr>
<tr>
<td>CO2</td>
<td>8.39 (3.47)</td>
<td>18.21 (6)</td>
<td>20/82 (24.4%)</td>
<td>1/82 (1.2%)</td>
</tr>
</tbody>
</table>

Conclusion: Water Infusion colonoscopy was well tolerated and equally to intravenous sedation in terms of pain perception, procedure time and cecal intubation rate. Moreover, underwater colonoscopy in our study provided lower occurrence of adverse events and higher Adenoma Detection Rate (ADR).
The WWI technique seems to be a valid alternative to colonoscopy with sedation in young adults – especially in female patients – to achieve quality and painless colonoscopy when sedation is not available or contraindicated.

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**P1430 SCREENING COLONOSCOPY IN YOUNGER ADULTS—WHEN SHOULD WE START?**

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**Aims and Methods:** 440 consecutive patients with a complete colonoscopy including a double-contrast barium enema and polyp detection were prospectively analyzed between November 2007 and February 2018. Patients were categorized according to age and we determined ADR, AADR and CRC-rate for each group, also comparing male and female sex.

**Results:** Overall in 22.40% (n = 55381) of all patients, adenomas were detected, 27.8% within men and 17.2% (n = 33789) within women. Advanced adenoma detection rate (AADR) was 4.6% (n = 11266). Male-AADR (MAADR) was 5.7% and female-AADR (FAADR) 3.5%. In 0.77% (n = 1894) colorectal carcinomas were detected, 0.98% within male and 0.56% within female patients. According to age, ADR was 5.6% (3.3%; 4.3% within group of 30-34 year old individuals; 7.0% [3.8%; 8.5%] 35-39y; 11.7% [14.5%; 9.2%]; 40-44y; 15.0% [17.8%; 12.1%]; 45-49y and 17.1% [21.2%; 12.9%] in patients aged 50-54, where screening is already recommended. AADR was 1.2% [1.0%; 1.4%] 30-34y, 1.2% [1.0%; 1.4%] 35-39y, 2.6% [3.3%; 1.8%] 40-44y, 2.8% [2.6%; 2.9%] 45-49y and 3.1% [3.8%; 2.4%] 50-54y. Incidence of CRC was 0.30% [0.33%; 0.29%] 30-34y 0.32%; 0.53% 35-39y 0.55%; 0.77% 40-44y; 0.38% [0.32%; 0.45%] 45-49y and 0.33% [0.40%; 0.25%] 50-54y. Regarding localization, 50% of CRC in the group 30-34 years, 50% (35-39y), 47% (40-44y) and 44% (45-49y) were located in the rectum, compared to 0.38% in patients older than 50.

From 2008 to 2017, the overall incidence rates of adenomas in adults age 45–49 increased from 15.9% in 2008 to 20.9% in 2017; AADR 2.3% to 4.9% and incidence rate of CRC increases from 0.39% to 0.65%. In female patients, ADR was 12.6% vs. 20.7% (2008 vs. 2017); AADR 1.4% vs. 7.6% and incidence of CRC 0.34% vs. 0.32% (30-34y), 0.35% to 0.32% (35-39y), 0.52% to 0.44% (40-44y), 0.38% to 0.32% (45-49y) and 0.33% to 0.40% (50-54y). Regarding localization, 50% of CRC in the group 30–34 years, 50% (35–39y), 47% (40–44y) and 44% (45–49y) were located in the rectum, compared to 0.38% in patients older than 50.

**Conclusion:** In this large cohort of screening colonoscopies, we noticed quite similar incidence rates in patients aged 45–49, compared to those, whom screening colonoscopy is already recommended (30–54years): Incidences of adenomas (15.0% vs. 17.1%), advanced adenomas (2.8% vs. 3.1%) and colorectal carcinomas (0.38% vs. 0.33%). Compared to 2008, higher incidence rates of adenomas, advanced adenomas and colorectal carcinomas were documented in 2017, especially in female patients from 45 to 49, while we found no big changes within male individuals at the same age comparing 2008 and 2017.

Regarding this and to prevent more cases of colorectal cancer we should start screening colonoscopy at the age of 45, especially in female patients.

**Disclosure:** Nothing to disclose

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**P1431 USEFULNESS AND EFFICACY OF RETROFLEXION IN THE ASCENDING COLON DURING COLONOSCOPY FOR POLYPY AND ADENOMA DETECTION**

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**Introduction:** Missing polyps in the ascending colon during colonoscopy is a well-known problem. Polyp detection was divided in 3 categories: 1) detection in forward view (OR: 2.63, 95% CI: 1.25-5.50 p = 0.011), male gender (OR: 1.88, 95% CI: 0.99-3.58 p = 0.055), previous surgery (OR: 2.74, 95% CI:1.42-5.27 p < 0.01), the existence of adenomas in forward view (OR: 3.06, 95% CI:1.48-6.30 p < 0.01) and indication for colonoscopy—“barrett-up” (OR: 2.15, 95% CI:1.94-4.8 p = 0.07).

**Conclusion:** 1) Retroflexion in the ascending colon is safe and feasible in the vast majority of patients 2) It has an added value for polyp and adenoma detection in the ascending colon provided that forward view missed an important number of polyps.

**Disclosure:** Nothing to disclose

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**P1432 DOES THE ENDOSCOPIST’S GENDER INFLUENCE QUALITY PARAMETERS OF SCREENING COLONOSCOPY?**

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**Introduction:** Gender differences were shown in relation to less career satisfaction and lower career advancement for female gastroenterologists (Gerson LB et al, Gastroenterology 2007).

**Aims and Methods:** Data from 174,484 screening colonoscopies between 2007 and 2018 from private practices were analyzed within Austrian Certificate in Quality for Colorectal Cancer Screening. We evaluated the adenoma detection rate (ADR), advanced adenoma detection rate (AADR) andecal intubation rate (CIR). SR, complication rate and compared these quality measures between male and female endoscopists.

**Results:** From 189 endoscopists included in this study, 18.52% were female (27,370 screening colonoscopies, mean patient’s age = 61.07) and 81.48% were male (n = 147,478, mean patient’s age = 61.3). Female endoscopists had significantly more male patients (57, 56% (SD = 6.3% vs. 49, 43% (SD = 5.16), p < 0.001) while male endoscopists more male patients (50, 57% (SD = 5.16) vs. 42, 44% (SD = 6.39), p < 0.001).

No significant finding was found so far between gender of endoscopists and outcome of their performance. Thus, the aim of the study was to assess differences in quality measures and incidence of complications according to endoscopt’s gender.

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No significant finding was found so far between gender of endoscopists and outcome of their performance. Thus, the aim of the study was to assess differences in quality measures and incidence of complications according to endoscopt’s gender.

**Conclusion:** The study showed that more female patients were examined by female endoscopists while more male patients were examined by male endoscopists but it did not show any significant difference in the quality parameters in
Disclosure: Nothing to disclose

PI1433 UNDERWATER ENDOSCOPIC MUCOSAL RESECTION SHOWS TO BE MORE EFFECTIVE THAN EMR IN WORSE SCENARIOS WITH LESS ADVERSE EVENTS
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Introduction: Nowadays, endoscopic mucosal resection (EMR) is the usual technique for treatment of flat colorectal polyps, however underwater-EMR (U-EMR) has appeared as an attractive alternative. Despite its preliminary suitability, the real indication of U-EMR remains unclear. The aim of this study is to compare the feasibility, adverse events and recurrences of both techniques in a multicentric fashion.

Aims and Methods: We performed a prospective cross-sectional study in two referral hospitals from December 2016 to November 2017 in which lesions >15 mm resected by EMR or U-EMR were included. Both cohorts were matched on their baseline scoring (ratio 1:1) to avoid a selection bias using as reference the score in SMSA score. The margins of the scars were assessed to detect residual adenomatous tissue. A follow-up colorectum in 3–6 months and 12 months was scheduled.

Results: A total of 162 lesions were resected and analysed from 137 patients (59% male, 66% y.o), with an average size of 25 mm and 60% of them located in proximal colon. Histological assessment revealed carcinoma in 33/162 (20%), detecting in 8 of them (5%) deep mucosal invasive cancer (referred to surgery). Recurrence rate was achieved in 68% U-EMR versus 49% EMR (p >0.05), and less number of slides to reach complete resection were detected in U-EMR (2.59 +/- 0.24 vs 1.74 +/- 1.10, p <0.001). There were no significant differences between efficacy comparing size of the lesions, however U-EMR might trend to be more feasible in achieving en bloc and complete resection compared to EMR, in addition to more efficient (less time spent per procedure). In terms of adverse events, post procedural bleeding (10% EMR vs 2% U-EMR; p >0.05) and one perforation (EMR group) were described. In both groups early endoscopies (early-3months and late-12months), no differences were described between both techniques.

Conclusion: In real clinical practice U-EMR showed to be as effective and safer than traditional EMR especially in difficult cases. Furthermore, U-EMR yielded a feasible approach to prevent cavitary artefact, allowing an accurate pathologic assessment.

Disclosure: Nothing to disclose

PI1434 CHROMOENDOSCOPY WITH INDIGO CARMINI VERSUS ENDOLUMINAL COLONIC CARCINOMA DETECTION RATE IN A RANDOMIZED CONTROLLED TRIAL
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Introduction: Colorectal cancer (CRC) is one of the leading causes of death in the world. These deaths could be avoided by early detection of adenomas. There are some techniques to increase the adenoma detection rate (ADR) during colonoscopy, such as the chromoendoscopy with indigo carmine or the use of endocuff device. Indigo carmine highlights the surface topography of the mucosa while endocuff is a flexible long cap that is integrated into the tip of the colonoscope to flat the folds of colon. Both techniques seem to increase the ADR, but there is not direct comparison between the two methods.

Aims and Methods: The aim was to compare ADR of chromoendoscopy with indigo carmine versus endocuff. This is a randomized controlled trial performed in a single center from March 2016 to November 2017. The Institutional Ethical Committee approved the study and written informed consent was obtained in all cases. The inclusion criteria were patients over 50 years old with average risk for colorectal cancer and adequate Boston bowel preparation (≥6). Patients were randomly selected in a 1:1 ratio by a computer generator in blocks of four. Colonoscopies were performed using 10 mL of indigo carmine 0.8% in 250 mL of water or endocuff19 (Arc Medical Desing Ltd). ADR was defined as the proportion of patients with at least one adenoma (per-patient analysis). Mean adenomas per patient (MAP) was also calculated as the total number of detected adenomas in each group divided by the total number of patients in that group (per-adenoma analysis). ADR and MAP were compared for both groups using chi2 test and Student’s T-test respectively. P ≤ 0.05 was considered statistically significant. The preliminary results of the 30% of the total calculated sample size (n =150 per group) are shown here.

Results: A total of 92 patients were included but 6 were eliminated because they met the non-inclusion criteria. The selected 86 patients were randomized into the two groups, chromoendoscopy (n =44) vs endocuff (n =42). There were no differences in gender, age or quality of colonic preparation. The withdrawal time for chromoendoscopy was 15 ± 4 minutes whereas for endocuff was 12 ± 4 minutes (p =0.02). Histocarcinoid vascular conclusion was 91% in chromoendoscopy versus 89% in endocuff without statistical differences. The results of ADR and MAP analysis are described in the table below.

<table>
<thead>
<tr>
<th></th>
<th>Indigo carmine</th>
<th>Endocuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR (%)</td>
<td>31 (16–45)</td>
<td>31 (16–45)</td>
</tr>
<tr>
<td>Right</td>
<td>10 (7–19)</td>
<td>10 (7–19)</td>
</tr>
<tr>
<td>Transverse</td>
<td>13 (2–23)</td>
<td>13 (2–23)</td>
</tr>
<tr>
<td>Left</td>
<td>15 (4–27)</td>
<td>15 (4–27)</td>
</tr>
<tr>
<td>Rectum</td>
<td>5 (1–12)</td>
<td>5 (1–12)</td>
</tr>
</tbody>
</table>

Mean Adenomas per Patient, MAP (mean [95% CI])

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Right</th>
<th>Transverse</th>
<th>Left</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indigo carmine</td>
<td>1.20 (0.56–1.84)</td>
<td>0.10 (0.00–0.24)</td>
<td>0.39 (0.11–0.66)</td>
<td>0.16 (0.01–0.30)</td>
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</tr>
<tr>
<td>Endocuff</td>
<td>1.40 (0.60–2.60)</td>
<td>0.12 (0.00–0.24)</td>
<td>0.40 (0.11–0.66)</td>
<td>0.17 (0.01–0.32)</td>
<td></td>
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</tbody>
</table>


Disclosure: Nothing to disclose

PI1435 "LEAVE-IN-SITU STRATEGY" FOR DIMINUTIVE RECTAL ADENOMAS – A RANDOMIZED CONTROLLED Trial
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Introduction: Colonoscopy with polypectomy of adenomas reduces the incidence and mortality of colorectal cancers (1). With recent increment of the number of screening colonoscopies, it is reported that eradication of adenomas during colorectum can be a big burden for endoscopists (2). According to the Japanese Society of Gastroenterology guidelines (3), diminutive adenomas which has no evidence of carcinoma in their appearance are allowed to be left in situ, provided strict surveillance colonoscopies within 3 years (=leave-in-situ strategy”) are conducted, which is different from the European or American guidelines (4,5). However, the safety and efficacy of the “leave-in-situ strategy” of diminutive adenomas are unknown.

Aims and Methods: The aim was to retrospectively assess the safety and compliance of the “leave-in-situ strategy” of diminutive adenomas. Patients whose diminutive adenomas were not resected at the initial colonoscopies between April 2001 and November 2014 at a referral center were chosen as the subjects. All the subjects were asked to receive surveillance colonoscopies within 3 years. The primary outcome measure is the incidence rate of index lesions (ILs) at the surveillance colonoscopy within 3 years. The ILs were defined as follows: adenomas ≥10 mm, high grade dysplasias, villous adenomas, and invasive cancers. The secondary outcome measures included the rate of patients who received the 3-year surveillance colonoscopies and the number of the diminutive polyps which were detected at both the initial and surveillance colonoscopies.

Results: A total of 4816 patients were left untreated of diminutive adenomas (n =2502) at the initial colonoscopies. The incidence rate of index lesions at the surveillance colonoscopies was 2.5%/36,1543; 12 adenomas ≤10 mm, 22 high-grade dysplasias, and 2 invasive cancers. The rate of patients who underwent 3-year surveillance colonoscopies was 32.0% (1543/4816). The same
DIMINUTIVE ADENOMAS WERE DETECTED IN THE SURVEILLANCE COLONOSCOPY IN 63.2% (95% CI: 62.5–63.9) OF THE PATIENTS AND ITS QUALITY AS COMPARING TO THE NEGATIVE COLONOSCOPY.

CONCLUSION: “Leave-in-situ strategy” of diminutive adenomas can be acceptable whose rate of ILS in the surveillance colonoscopies is limited to 2.3% which is similar to those in the National Polyp Study (6). However, strict instruction to the patient is indispensable considering the low receiving rate of surveillance colonoscopies.

DISCUSSION: Nothing to disclose

References

P1438 LONG-TERM COLORECTAL CANCER INCIDENCE AND MORTALITY IN RELATION TO QUALITY OF A SINGLE NEGATIVE SCREENING COLONOSCOPY

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Aims and Methods: This study aims to determine the predictive effect of quality of negative screening colonoscopy on long-term risk of colorectal cancer (CRC) remains uncertain.

Methods: This study included 156,633 patients after single negative colonoscopy who were followed for CRC occurrence and death through the National Cancer Registry over median of 9.2 years up to 16.4 years. High-quality colonoscopy was defined as examination with cecal intubation, adequate bowel preparation (very good, good or sufficient according to Aronchick scale) performed by an endoscopist with more than 10 years of experience. High-quality negative colonoscopy (SIRs and SMRs) were calculated by comparison with values for general Polish population according to sex and 5-years age groups.

Results: Of the 156,633 individuals included into analysis, 365 CRC after negative screening colonoscopy, irrespective of its quality according to time from screening colonoscopy.

Quality of screening colonoscopy

<table>
<thead>
<tr>
<th>Time from screening colorectum (years)</th>
<th>SIR (95% CI)</th>
<th>SMR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1–3.0</td>
<td>0.23 (0.19–0.27)</td>
<td>0.07 (0.03–0.11)</td>
</tr>
<tr>
<td>3.1–5.0</td>
<td>0.12 (0.10–0.14)</td>
<td>0.05 (0.02–0.09)</td>
</tr>
<tr>
<td>5.1–10.0</td>
<td>0.16 (0.14–0.18)</td>
<td>0.07 (0.04–0.11)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>0.23 (0.19–0.27)</td>
<td>0.09 (0.05–0.13)</td>
</tr>
<tr>
<td>High</td>
<td></td>
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<tr>
<td>0.1–3.0</td>
<td>0.12 (0.10–0.14)</td>
<td>0.05 (0.02–0.09)</td>
</tr>
<tr>
<td>3.1–5.0</td>
<td>0.11 (0.09–0.13)</td>
<td>0.05 (0.03–0.08)</td>
</tr>
<tr>
<td>5.1–10.0</td>
<td>0.12 (0.10–0.14)</td>
<td>0.05 (0.03–0.09)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>0.15 (0.13–0.17)</td>
<td>0.07 (0.04–0.11)</td>
</tr>
</tbody>
</table>

Table 1. SIRs and SMRs of colorectal adenoma after negative screening colonoscopy according to quality according to time from screening colonoscopy.

Conclusion: Single high-quality negative colonoscopy was associated with significantly reduced risk of CRC and CRC mortality compared to general population (SIRs and SMRs) were 0.41 (95% CI, 0.37–0.46) and 0.22 (95% CI, 0.18–0.27), respectively. Negative high-quality colonoscopy was associated with colonoscopy technique (nurse's sedation training) are independent factors to consider while performing a colonoscopy.

Disclosure: Nothing to disclose

P1439 SEDOANALGESIA COMPLICATIONS DURING A COLONOSCOPY. WHICH FACTORS ARE INVOLVED?

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Introduction: Colorectal cancer ranks third among the most commonly diagnosed cancers worldwide. Colorensopy has been shown to reduce morbidity and mortality in screening programs. Colonoscopy due to sedation procedure has several complications being the most frequent the cardiorespiratory complications. The overall complication rate ranges from 0.1 to 0.2%, with a mortality of 0.0014%.

Methods: To determine which factors are related to the risk of developing a sedoanalgesia complication (SAC) during a colonoscopy with the objective of reduces the post-colonoscopy complications. All screening colonoscopies after a positive faecal immunochemical test were analyzed related with colonoscopy technique (nurse's sedation training) are independent factors to consider while performing a colonoscopy.

Results: After 67,946 colonoscopies, SAC rate was 0.12%. 64.4% were men. The patients had 16.5% were smoker, 25% had cardiopathy and neumopathy history respectively. The 16.9% of patient were treated with benzodiazepines, 6.4% with antipsychotic and 2.6% with opioids. 49.3% of the patients had polypectomy. Significant SAC: 50% had a moderate consumption of alcohol and the 12.5% were smoker. 28% had cardiopathy and neumopathy history, 25% were treated with benzodiazepines and the 12.5% with antipsychotics. 49.3% of the patients had polypectomy.

Firstly we made a univariate analysis. Patients-variables for the analysis were: age, sex, ASA, cardiopathy and neumopathy history, patient's toxic habits (tobacco and alcohol), IMC, Charlson Index, chronicity index, polypectomy and antipsychotic, benzodiazepine or opioids therapies. Colonoscopy technique variables: patient position, type of insufflation, type of sedation, type of oxygenation, colonoscopy assist or not by an anesthetist, hours until the patient recuperation, nurse’s sedation training and type of hospital. The variables with a significant result in the univariate analysis were: tobacco, alcohol, neumopathy history, polypectomy or not by an anesthetist, hours until the patient recuperation and nurse’s sedation training.

After a multivariate analysis SAC IP were: tobacco (OR:2.8; 95%CI:1.1–7.4), alcohol (OR:8.0; 95%CI:1.2–30.0), polypectomy (OR:0.4; 95%CI:0.2–0.8) and nurse’s sedation training (OR:0.4; 95%CI:0.2–0.9). The logistic model explained 73% of the complications (C95%: 0.65–0.80, p < 0.001).

Conclusion: The colonoscopy is a procedure with a small but not insignificant risk of complications in order to implement countermeasures. The study that we present shows that both variables related to the patient (toxic habits and polypectomy) and related with colonoscopy technique (nurse's sedation training) are independent factors to consider while performing a colonoscopy.

Disclosure: Nothing to disclose

References
P1440 IMPACT OF AN EDUCATIONAL INTERVENTION ON THE IMPROVEMENT OF QUALITY INDICATORS OF COLORECTAL CANCER SCREENING COLONOSCOPIES

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Introduction: The diagnostic accuracy of colorectal cancer screening colonoscopies (CRCSCs) depends on the adherence to quality indicators.

Aims and Methods: We aimed at evaluating the effects of an educational intervention on quality indicators of CRCSCs at a tertiary center. CRCSCs performed between 2005 and 2009 at a tertiary center were analyzed and a quality assessment was carried out. The results of CRCSCs evaluation and reporting were compared with optimal indicators recommended by the team of gastroenterologists and nursing staff in January 2011. 218 CRCSCs performed between 2011 and 2015 were evaluated and compared to 1545 CRCSCs performed between 2005 and 2009.

Results: Descriptive statistical analysis was performed and Chi-Square test was applied to compare quality indicators of CRCSCs between 2005 to 2009 and 2011 to 2015. Results: 218 CRCSCs were performed between 2011 and 2015. The mean age was 62.5 ± 10.7 years and 57% (1205) were women. Sedation was performed in 77% (1634) of the procedures. Colonoscopy was performed in 1336 (93%). Most common reasons for incomplete CRCSCs were: patient intolerance 46.3% (122), inadequate bowel preparation 20.4% (58) and technical difficulties 15.1% (43). Good or adequate bowel preparation was noted in 1786 (84%) patients. Photodocumentation of colonic landmarks (PCL) was performed in 97.3% (1785) of the cases. Polyp detection rate (PDR) was 34.3% (726) and polyps ≥1cm were detected in 13.4% (97) patients. Colorectal cancer (CRC) was detected in 0.5% (11) patients.

1545 CRCSCs were performed between 2005 and 2009. The mean age was 60.4 ± 10.7 years and 62% (958) were women. Sedation was performed in 32% (499) of the exams. The CIR rate was 91% (1336). Most common reasons for incomplete CRCSCs were: patient intolerance 40% (84), inadequate bowel preparation 35% (73) technical difficulties 18% (37). Good or adequate bowel preparation was noted in 1345 (87%) patients. PCL was performed in 93% (1248) of the cases. PDR was 33% (503) and polyps ≥1cm were detected in 16% (82) patients. CRC was detected in 0.3% (5) patients.

Conclusion: Although there was a significant improvement in the quality of the PCL indicator after the educational intervention, there was no improvement in cecal intubation rates despite a significant increase in use of sedation during colonoscopy. Additionally, our results suggest a need for better patient education to improve the quality of bowel preparation.

P1441 UTILITY OF 3D ENDOSCOPY IN MEASUREMENT OF COLON POLYP SIZE

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Introduction: Measuring colon polyp size is crucial in choosing an appropriate therapeutic option. However, currently available measurement procedures are not necessarily accurate. Depth and spatial information, which is lacking in conventional two-dimensional (2D) endoscopy, has become available with the use of 3D technology. In collaboration with a medical device company, by using a prototype three-dimensional (3D) endoscope currently in development, we conducted an ex vivo study to evaluate the utility of 3D endoscopy in measurement of colon polyp size.

Aims and Methods: We prepared models of colon polyps (protruding and flat lesions) ranging in size from 2 mm to 10 mm in 1 mm increments. A total of 220 measurements were made among 10 doctors (6 specialists and 4 non-specialists). A prototype 3D endoscope was used to measure polyp size either in 3D mode in combination with 3D glasses or in 2D mode. Randomization was performed by using envelopes containing the size of a model polyp and the mode of measurement to be used. Accuracy rate and measurement error (i.e., actual polyp size minus measured size) were compared between 3D and 2D endoscopy.

Results: Accuracy rate was 23.3% (24/103) by 2D endoscopy and 25.6% by 3D endoscopy (30/117); the difference was not significant. On the other hand, measurement error by 2D endoscopy (1.81 ± 1.88 mm) was significantly larger (p=0.05) than that by 3D endoscopy (0.92 ± 2.27 mm). Errors in measurements of flat polyps and protruding polyps were 2.25 ± 1.97 mm and 1.34 ± 1.69 mm, respectively, by 2D endoscopy, and 1.68 ± 1.62 mm and 0.2 ± 2.56 mm, respectively, by 3D endoscopy. Accuracy rate was 33.8% (27/80) with a measurement error of 0.96 ± 2.10 mm among non-specialists, and 19.3% (21/104) with a measurement error of 1.55 ± 2.14 mm among specialists; accuracy rate was significantly higher and measurement error was significantly smaller among non-specialists than among specialists.

Disclosure: Nothing to disclose

P1442 SCREENING COLONOSCOPY: DOES THE ADR VARIATES WITHIN A TRAINING CENTER? AN EXPERIENCE AT A LATIN AMERICAN TRAINING CENTER

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Introduction: Colonoscopy is considered the gold standard screening method for colorectal cancer (CRC), it allows the detection and resection of the adenoma-tous lesions. There are different markers which define colonoscopy-quality indicators. Measuring colon polyp size is crucial in choosing an appropriate therapeutic option. However, currently available measurement procedures are not necessarily accurate. Depth and spatial information, which is lacking in conventional two-dimensional (2D) endoscopy, has become available with the use of 3D technology. In collaboration with a medical device company, by using a prototype three-dimensional (3D) endoscope currently in development, we conducted an ex vivo study to evaluate the utility of 3D endoscopy in measurement of colon polyp size.

Aims and Methods: We prepared models of colon polyps (protruding and flat lesions) ranging in size from 2 mm to 10 mm in 1 mm increments. A total of 220 measurements were made among 10 doctors (6 specialists and 4 non-specialists). A prototype 3D endoscope was used to measure polyp size either in 3D mode in combination with 3D glasses or in 2D mode. Randomization was performed by using envelopes containing the size of a model polyp and the mode of measurement to be used. Accuracy rate and measurement error (i.e., actual polyp size minus measured size) were compared between 3D and 2D endoscopy.

Results: Accuracy rate was 23.3% (24/103) by 2D endoscopy and 25.6% by 3D endoscopy (30/117); the difference was not significant. On the other hand, measurement error by 2D endoscopy (1.81 ± 1.88 mm) was significantly larger (p=0.05) than that by 3D endoscopy (0.92 ± 2.27 mm). Errors in measurements of flat polyps and protruding polyps were 2.25 ± 1.97 mm and 1.34 ± 1.69 mm, respectively, by 2D endoscopy, and 1.68 ± 1.62 mm and 0.2 ± 2.56 mm, respectively, by 3D endoscopy. Accuracy rate was 33.8% (27/80) with a measurement error of 0.96 ± 2.10 mm among non-specialists, and 19.3% (21/104) with a measurement error of 1.55 ± 2.14 mm among specialists; accuracy rate was significantly higher and measurement error was significantly smaller among non-specialists than among specialists.

Conclusion: Accuracy rate of colon polyp size measurement was not high, and there was no significant difference between 2D and 3D endoscopy. Measurements tended to be larger and measurement errors were significantly smaller in 3D endoscopy than in 2D endoscopy. Also, measurement of protruding polyps tended to be larger and measurement errors than those of flat polyps. Accuracy rate was significantly higher and measurement error was significantly smaller among non-specialists than among specialists.

Disclosure: Nothing to disclose

[Comparison of quality indicators during the two study periods]

Disclosure: Nothing to disclose
In the left colon, 55 (31.4%) showed at least one high risk characteristic, 26 (29.3%) showed at least one high-risk tumor in the right colon and 17 (44.7%) in rectum. A statistically significant difference was found between the adenoma location and their high risk findings. Compared and corrected by the p-value through the Bonferroni method, statistically significant differences were found in the high-risk adenoma proportions found in the left colon compared with the transverse colon (p = 0.0024) and the right colon (p = 0.0013).

Left colon and rectum localization of adenomas, increases by 3 (p < 0.0001, OR = 3.73, IC 95%: 2.19–6.34) and 2 (p < 0.0001, OR = 1.99, IC 95%: 0.99–3.98) times respectively, the possibilities that the adenomas found at other segment of the colon or rectum may have to at least a high-risk characteristic. No significant association between risk adenoma and sex was found (p = 1.971).

Conclusion: Our global and adjusted by sex ADR are comparable to those recommended by the international guidelines. Formative stages under the supervision of an experienced observer do not influence on ADR. Despite right-sided adenomas were the most frequent, left colon and rectum adenomas showed a significant increase compared to the presence of the high-risk adenomas found at other segment of the colon or rectum. Therefore, the measurement of colonoscopy quality indicators in the colorectal cancer screening programs must be a goal from the earliest formative stages.

Disclosure: Nothing to disclose

P1443 WHO HAS MORE INCOMPLETE COLONOSCOPIES: SURGEONS, INTERNISTS OR GASTROENTEROLOGISTS?
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Introduction: Intubation of caecum is foundation for general impression of colorectal neoplasms. Intubation rate (ICR) correlates with high-risk adenoma colorectal cancer (PCCRC), (Baxter et al., Gastroenterology 2011).

Aims and Methods: Aim of the study was to investigate if surgeons, internists or gastroenterologists have higher rates of incomplete colonoscopies. Further to identify reasons for incomplete colonoscopy (complication, stenosis, pain, inadequate bowel preparation, others) and analyze the quality of bowel preparation (data collected since 2012). Therefore 264,116 screening colonoscopies performed by 294 physicians between 2007–2018, within the Austrian certificate of screening colonoscopy colorectal cancer (PCCRC), (Baxter et al., Gastroenterology 2011). A total of 42 (38%) patients had an injury in their right colon, 27 of them (24%) during the first evaluation and 11 (31%) during the second one.

Results: Injuries found were 23 (21%) ≤5mm, 12 (11%) ≤5-9mm and 7 (6%) >9mm. According to the Paris Classification, there were 16 (14%) 0-Is, 24 (22%) 0-Ia and 2 (1%) 0-IIb injuries. Histopathological examination showed 36 (32%) adenomatous injuries and 6 (5%) corresponding to sawing injuries.

Conclusion: The first evaluation was 22% and increased around 7.3% during the second evaluation, thus reaching a 29.3% TDA, with a statistically significant difference according to the Chi square Test. Average time before a second evaluation in the right colon was 1.36minutes (1.15–2 min).

Disclosure: Nothing to disclose

P1445 DOUBLE BALLOON-ASSISTED ESD VERSUS STANDARD ESD FOR SIGMOID LESIONS
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Introduction: Initial double balloon-assisted endoscopic submucosal dissection (ESD) for colorectal lesions requires a high skill level to complete. In particular, sigmoid colon lesions are thought to be amongst the hardest anatomical location for ESD. This is due to the sigmoid colon being more mobile with lack of peritoneal fixation. From this standpoint, we hypothesised that a double balloon-assisted technique could facilitate sigmoid colon ESD through stabilizing of the sigmoid colon.

Aims and Methods: A bespoke 3D-printed abdominal-pelvic anatomical housing was developed and an ex-vivo colon model mounted within it. A commercially available double balloon-assisted colonoscope was used in this study. A 3.0cm pseudo-polyp was created on the fresh porcine distal colonic mucosa with electrocautery. Six ESDs were performed against this 3.0cm pseudo-polyp without the double balloon sheath as control group, and with the double balloon sheath on the sigmoidoscope. The total procedure time, the number of perforation and the number of muscle layer damage were collected and compared. A single operator performed every procedure.

Results: There were no perforation in all of the procedures. The total procedure time and the number of muscle layer damage in each ESD were shown in the table. The mean total procedure time in Double balloon ESD group was 23.29 minutes and this was significantly shorter than 46.45 minutes in control group (p = 0.007). There was also a significant difference in the number of the muscle layer damage (1.5 vs 1.0, p = 0.009).

Conclusion: Double balloon technique may facilitate sigmoid colon ESD by reducing the procedure time and difficulty. We postulate that this is performed by ‘splitting’ that section of the sigmoid intestine reducing movement and increasing stability.

Disclosure: J. Milsom – Olympus research grant and Lumendi CAB member

P1446 DIAGNOSTIC Yield of SpyGlassDS for Bilary Tract Lesions
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Introduction: SpyGlassDS has been used as diagnostic or therapeutic tool for biliary tract lesions, and the feasibility of this device was reported in several studies. We investigated the utility of the SpyGlassDS for patients with biliary tract lesions.

Aims and Methods: We evaluated success rates of observation and sampling using SpyGlassDS for 34 patients who were performed cholangioscopy for the purpose of examine the biliary tract lesions at our hospital between November 2015 and December 2017. Successful observation was defined as the case in which SpyGlassDS reached the biliary tract lesion and obtained high-quality images

Our aim is to decide whether the performance of a second evaluation of the right colon would increase the adenoma detection rate (TDA)

Aims and Methods: A prospective study from September 2016 to May 2017 was performed.

All patients who underwent a CCR screening videocolonoscopy were included, with prior informed consent.

Every patient having a Boston Scale store of 2 or 3 in the right colon segment underwent a second evaluation of the right colon.[1]

Injuries found in the right colon were described according to location, size and Paris Classification; they were resected during the procedure.

The time required to perform the second evaluation of the right colon was evaluated.

Results: A total of 130 patients were included in the study between September 2016 and May 2017. 21 patients (16%) were excluded according to the Boston Scale <2 in the right colon; and 109 patients (84%) met the inclusion criteria, 69 (63%) men and 40 (36%) women, with an age range of 45–75 years. A total of 42 (38%) patients had an injury in their right colon, 27 of them (24%) during the first evaluation and 11 (31%) during the second one.

Injuries found were 23 (21%) ≤5mm, 12 (11%) ≤5-9mm and 7 (6%) >9mm. According to the Paris Classification, there were 16 (14%) 0-Is, 24 (22%) 0-Ia and 2 (1%) 0-IIb injuries. Histopathological examination showed 36 (32%) adenomatous injuries and 6 (5%) corresponding to sawing injuries.

TDA during the first evaluation was 22% and increased around 7.3% during the second evaluation, thus reaching a 29.3% TDA, with a statistically significant difference according to the Chi square Test.
enough to evaluate. Successful sampling was defined as the case in which sufficient amount of specimen was collected by SpyBite biopsy forceps. For 18 patients with cholangiocarcinoma who had undergone surgical treatment, we evaluated the concordance rate of horizontal extension of cancer between diagnosis using SpyGlass and SpyBite, and resected specimens. Horizontal extent of cholangiocarcinoma was diagnosed by SpyGlass as the presence of irregular papillary or granular mucosa or irregularly dilated and tortuous microvasculature that continuously spread from the main lesion.

Results: The rates of successful observation and successful sampling were 97.5% (87/90), 3.8% (3/76), respectively. Biopsy using SpyBite were not informative due to insufficient amount for pathological review in 9 cases. To evaluate horizontal extension in 18 (7) cholangiocarcinoma patients, 91 checkpoints were observed using SpyGlass and 30 samples were obtained using SpyBite. Comparison of SpyGlass imaging with the histological diagnosis in resected specimens revealed the diagnostic accuracy of 86.8% (79/91). The false positive rate was 11.0% (10/91), and the main cause of false positive was misdiagnosis for the inflammatory mucosa as carcinoma. Comparison between the photomicrograph and the resected specimen revealed an increased risk of missing carcinoma for 9.0% (45/50) and the false-negative rate of 6% (3/50), namely the diagnostic ability of the biopsy specimen was higher than that of visual images.

Conclusion: The ability to approach for the biliary tract lesion which we aimed to evaluate was good enough, especially in the advanced technique, evaluation for the second branch of the intrahepatic biliary tract was possible. That was very meaningful to decide the therapeutic option or the surgical form. Considering the results of visual images or the biopsy specimen, the accuracy was mostly satisfactory.

Disclosure: Nothing to disclose.

P1447 AMPULLARY RADIO FREQUENCY ABLATION: A NEW MINIMALLY INVASIVE APPROACH TO AVOID SURGERY?
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Introduction: Recently ERCP Guided RF probes were designed. This device has been already used in cholangiocarcinoma and pancreatic cancer with biliary obstruction.

This new treatment induces local coagulative necrosis by delivering thermal energy from high frequency current via bipolar probes and induced an immunomodulation.

We report our experience in ampullomas treated by combination of endoscopic resection and radio frequency ablation (RFA).

We aim to evaluate the feasibility, clinical efficacy and safety of biliary RFA a new minimally invasive approach.

Aims and Methods: In this study 9 patients (2 males and 7 females) average 70 (41–93) underwent prior endoscopic ampullectomy. Indications of biliary RFA were deep margins not free in 8/9 patients and a relapse in 1 case. Surgery was contra indicated due to comorbidities in 3/9 patients, but mainly because the ratio of potential bile duct cancer with low-grade dysplasia (n = 5). We used dedicated RFA probe manufactured by Taewoong Company (ELRA)16 of 8 mm length and 7 F. From July 2015 to September 2017 we performed 12 sessions of ampullectomy (4 patients with single session 1 patient with 2 sessions and 1 patient with 3 sessions for recurrence).

Technique: Finally a cholangiogram was obtained to clearly determine the location of the lesion and to access its length. The most often there was none defect or structure visible. The RFA probe was then introduced over the guide wire on the low part of common bile duct.

RFA energy was delivered over the selected period by the device usually 2 mm 10W; We used selected power and time settings recommended by manufacturers based on the results of preclinical studies. After withdrawing the probe a biliary stent fully covered metallic stent (n = 8) or accessory plastic stent (n = 4) was placed to ensure biliary drainage and avoid a delayed stricture. The most often a small plastic pancreatic stent (5F) was also placed to avoid acute pancreatitis and kept for a few days after check control checked their spontaneous migration after 1 month). Biliary stents were usually removed after 2.5 months (1–5 months) on average during a new ERCP to control the result and perform new biopsies on site.

Results: Feasibility: technical success was 100%. No complication such as angio- cothilia or pancreatitis occurred immediately after RFA ablation. All patients, except two, were discharged one day after procedure. Regarding late complications 2 biliary benign strictures in 2 patients at 4 and 7 months easily treated by a new stent. None pancreatic stricture with an average follow up of 12 month occurred. All patients are alive at the end of this study.

Clinical efficacy was accessed on absence of recurrence of ampuloma on biopsy with an average follow up of 11 months in 6/9 patients. 1/9 patient was lost before 2 months (78 years old). 2 patients presented recurrence. 1 with a recurrence after 22 months treated by a second RFA ablation and actually free of disease for 17 months. Last patient presented 2 recurrences after 2 and 7 months treated by RFA ablation with a good result for 4 months.

Conclusion: ERCP with RFA amputation is safe and seems to be an effective alternative in patients with a high risk for surgery (important co-morbidities) or patients who refuse surgery.

Further studies are mandatory to confirm these preliminary results.

Disclosure: Nothing to disclose.

P1448 POST-ERCP PANCREATITIS (PEP): MINIMIZING ROLE OF PANCREATIC DUCT (PD) STENTING WITH NON-INVASIVE COMBINATION THERAPY IN DIFFICULT CASES
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Introduction: ERCP data was retrospectively retrieved from our electronic database between July to December 2017. Approval of the local review board was sought. A total of 258 ERCP cases were reviewed with regards to patient demography, successful standard biliary cannulation (SBC), cases requiring DGT, peri-procedural rectal-steroidal anti inflammatory drug (NSAID), intravenous hydration with lactated Ringer’s (LR), PD stenting and common complication rates including PEP, infection and bleeding and perforation. Aim was to determine PEP rates in DGT cases and role of PD stenting in these situations. Data was analyzed using SPSS v20.

Results: From a total of 258 ERCP cases conducted, 13.5% (35 cases) failed SBC and required DGT to facilitate successful biliary access. Of all DGT cases, rectal NSAID was administered in 65%, PD stenting was performed in 23%, and hydration with intravenous LR was initiated in 33% as PEP prophylaxis. DGT cannulation rate following failed SBC was 83%. The incidence of PEP, infection, significant bleeding and perforation were 2.9%, 17.1%, 0% and 0% respectively. The rate of PEP in the subgroup without PD stent placed was only 3.7%. Impact of PEP prophylaxis was found to be significant for rectal NSAID (p < 0.01), PD stenting (p = 0.039) and LR hydration (p < 0.01). There was no PEP witnessed when at least 2 PEP prophylactic measures were instituted (either rectal NSAID and/or PD stent and/or LR drip).

Conclusion: Our data demonstrated PEP remained low despite performing DGT for difficult biliary access and PEP risk may be minimized even without PD stenting if at least 2 other PEP prophylactic measures are undertaken such as using rectal NSAID and LR drip. This suggests PD stenting may not be critical in the setting of DGT if deemed challenging. A longer prospective study is intended to evaluate this finding.

Disclosure: Nothing to disclose.

P1449 COMPARISON OF THE DIAGNOSTIC SENSITIVITY OF A NOVEL PERORAL CHOLANGIOSCOPY-GUIDED TARGET BIOPSY TO THAT OF CONVENTIONAL ENDOSCOPIC TRANSPAPILLARY FORCEPS BIOPSY IN PATIENTS WITH SUSPECTED BILE DUCT CANCER
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Introduction: Endoscopic transpapillary forceps biopsy has been used for the histopathological confirmation of bile duct cancer. However, its sensitivity has been reported to be around 30%. To improve the sensitivity, peroral cholangioscopy-guided target biopsy has been attempted as an alternative. However, its fragility and impaired maneuverability have hindered its popularity. Recently, a new disposable-type peroral cholangioscope with better maneuverability, SpyGlass DS16, was developed. Some studies have shown that this cholangioscopic has a high sensitivity.

Aims and Methods: To compare the diagnostic sensitivities of POCS-guided target biopsy and conventional endoscopic transpapillary forceps biopsy in patients with suspected bile duct cancer.

This retrospective cohort study included 1) patients with suspected bile duct cancer and 2) patients who underwent both the biopsy methods at our institutions between November 2010 and November 2017. The primary endpoint of this study was the diagnostic sensitivity for malignancy. The specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and sample size of both methods were also compared.

Results: A total of 40 patients were included. Their final diagnoses were bile duct cancer (n = 32), gallbladder cancer (n = 2), and benign or inflammation stricture (n = 6). Sensitivity, specificity, PPV, NPV, and accuracy of the conventional method were 71%, 100%, 0%, 32%, and 80% and the SpyGlass-guided targeted biopsy were 50%, 100%, 0%, 47%, and 60%, respectively. The mean sample sizes for the conventional method and for SpyGlass-guided targeted biopsy were 1.69 ± 2.10 mm2 and 0.43 ± 0.47 mm2, respectively (P < 0.01).

Conclusion: The diagnostic sensitivity was rather high for conventional endoscopic transpapillary biopsy compared with SpyGlass-guided target biopsy.
P1450 ASSESSMENT OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN THE ELDERLY - IS ERCP REALLY SAFE IN THE ELDERLY?

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Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is important for diagnosis and therapeutics for cholangiopancreatic disease. Several studies demonstrated its safety in the elderly. But most of those reports assessed only complication rates of ERCP.

Aims and Methods: We retrospectively analyzed the clinical records of consecutive patients (n=299) undergoing ERCP between November 2016 and December 2017. We divided them into two groups: group A (n≥75 years old and group B <75 years old. Patient attributes, ERCP success rate, complication rate, hospitalized days and changes of PS were compared between two groups using chi-square test or t-test. The multivariate regression model was applied to find the risk factors of the prolonged hospitalization and the worsening of PS.

Results: A total of 299 patients was divided into two groups: group A (n=123, mean age: 82.5±5.3), and group B (n=176, mean age: 62.3±9.6).

Patients in Group A were more likely to have hypertension, chronic kidney disease and poor PS. Findings for other characteristics were similar between two groups.

All patients underwent ERCP successfully. No significant differences were observed between two groups regarding major ERCP-related complications (pancreatitis, bleeding, cholangitis and so on), while only the rate of pneumonia was higher in group A (P=0.037).

Hospitalization for 20 days or more was noted in 33 patients (26.8%) in group A and in 24 patients (13.6%) in group B (P=0.0043). The worsening of PS was observed in 19 patients (15.4%) in group A and in 4 patients (2.3%) in group B (P<0.0001).

The multivariate regression model identified that the complications (Odds Ratio [OR]:3.81, 95% Confidence Interval [CI]:1.69–8.57, P=0.0012) and the older age (OR:5.86, CI:1.10–3.72, P=0.024) were independent risk factors for the prolonged hospitalized days, and it also identified that the older age (OR:5.86, CI:1.89–18.2, P=0.0022), complications (OR:3.33, CI:1.03–10.8, P=0.045) and malignancy (OR:2.75, CI:1.03–7.32, P=0.043) were independent risk factors for the worsening of PS. Especially, Combinations of the older age and complications placed patients at increasingly higher risk of the prolonged hospitalization (OR:4.02, CI:1.40–11.5, P=0.0097) and the worsening of PS (OR:9.89, CI:2.81–34.8, P<0.0003).

Conclusion: We found that the risk of pneumonia, the prolonged hospitalization and the worsening of PS after ERCP are significantly higher in the elderly. We should perform ERCP carefully in the elderly.

Over 75 years old Under 75 years old p-value

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Disclosure: Nothing to disclose.

P1451 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY OF ACUTE CALCULOUS CHOLANGITIS IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction: Endoscopic Retrograde Cholangiopancreatography (ERCP) has become the standard treatment of choice for treating acute calculous cholangitis, but little is known about its outcome and safety in patients with liver cirrhosis (LC).

Aims and Methods: The objectives of this study were to analyze outcomes, efficacy and safety through a retrospective study of ERCP in patients with liver cirrhosis. A cross-sectional retrospective analysis of 59 ERCPs of 51 patients with LC performed at tertiary academic hospital over 5years was conducted. The patients (LC group) were subdivided into two groups based on their Child-Pugh classification (CP-class): 32 with CP-class A (LC-A), 14 with CP-class B (LC-B) and 5 with CP class C (LC-C).

Results: Procedural outcomes and post-procedural complications (bleeding or perforation) did not differ significantly among three groups. The 30-day, procedure-related adverse events included post-ERCP pancreatitis (n=5, 8.47%), hemorrhage (n=2, 3.39%), cholangitis (n=5, 8.47%), and death (n=2, 3.39%). There was a higher rate of adverse events in patients with LC-C compared with those with LC-A and LC-B (11.4%, 5.3%, and 6.1%, respectively; P=0.034). There was no correlation between the risk of significant hemorrhage and CP class, even in those who underwent an endoscopic sphincterotomy. No patients experienced worsening of the CP score 1 month after ERCP compared with the baseline score. During a median observation period of 44 months, the recurrence rates of cholangitis were similar between the three groups (recurrence rates: 8.1 vs. 7.5 vs 6.4%, P=0.625). The overall mortality rate was increased in the LC-C group (1-year mortality rates: 4.3 vs. 6.3 vs. 12.7%, respectively).

Conclusion: The adverse events seen in patients with liver cirrhosis are not different from those seen in the general population of patients undergoing ERCP, although patients with Child C have higher adverse event rates compared with those with Child A and B.

Disclosure: Nothing to disclose.

P1452 RADIONFREQUENCY ABLATION (RFA) FOR INTRABILIARY EXTENSION OF ADENOMA OF THE PAPILLA OF VATER: PRELIMINARY RESULTS

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Introduction: Endoscopic snare papillotomoy (ESP) of adenoma of the papilla of Vater after papillectomy appears feasible and effective in more than 85% of the cases. Intrabiliary extension of the adenoma can limit the curative intent of the endoscopic resection.

Aims and Methods: Radiofrequency ablation (RFA) of the intraductal extension was evaluated in consecutive patients with adenoma of the papilla of Vater after papillectomy.

Endoscopic resection was performed with an en-bloc-resection without submucosal injection and placement of a 5 french prophylactic pancreatic stent. Possible intra-biliary extension was assessed on cholangiogram and after traction with an inflated extraction balloon: in case of suspected intrabiliary extension, biopsies were performed and a biliary stent was placed. RFA was planned during a subsequent procedure 1 month later. RFA was performed with the VIVacombo™ generator (STARmed, South Korea) and an 18 or 33 mm long bipolar catheter (ELRA), power setting 10 W, 80’, 2 minutes. A 7 french pancreatic stent was placed before RFA and 2-3 biliary plastic stents were inserted to prevent stenosis. All the stents were removed 3 months later and intrabiliary biopsies performed. In case of positive biopsies RFA was repeated.

Results: Between March 2016 and April 2018, 7 patients (6, mean age 67.3 years) underwent ESP for adenoma of the papilla of Vater with intrabiliary extension. Liver function tests were normal in all the cases. Final histology resulted in 1 case of adenocarcinoma; the patient refused surgery and accepted RFA. RFA was performed one month after ESP (6 cases with a pancreatic stent in place, 1 without due to failure in replacement). The patient without the pancreatic stent developed severe post-RFA pancreatitis which resolved with conservative treatment. After a mean follow-up of 13 months, 4 patients have no evidence of residual intrabiliary adenoma on biopsies, 2 patients are under treatment, while the patient with adenocarcinoma accepted duodenal pancreatectomy due to repeated biopsies positive for adenocarcinoma (table 1).

Conclusion: RFA ablation of intrabiliary extension of adenoma of the papilla of Vater after papillectomy appears feasible and effective. According to our small experience, RFA should be performed with a pancreatic stent in place to reduce the risk of pancreatitis. Further data and extended follow-up are needed.

Disclosure: Nothing to disclose.

[Table 1]
P1453 ASSOCIATION BETWEEN PREDICTIVE FACTORS AND RADIATION EXPOSURE DURING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Introduction: The objectives of this study were to analyze the dose of radiation to which the physician is exposed during endoscopic retrograde cholangiopancrenography (ERCP) and to identify predictive factors of radiation exposure during the procedure. Further, we evaluated the characteristics of patients and procedural factors associated with prolonged fluoroscopy time.

Methods: A cross-sectional retrospective analysis of 780 ERCPs performed at tertiary academic hospital over 48-month period was conducted. The primary outcome of interest was the radiation exposure during ERCP as determined by fluoroscopy time and additionally to determine the association between variables and radiation exposure. And we correlated them with age, sex, body mass index (BMI), diagnosis, duration of procedure, procedure name, and procedure complexity.

Results: As a result of analysis of the 780 ERCPs performed for 2 years, the mean fluoroscopy time was 5.07 minutes (95% confidence interval (CI), 4.87–5.26). The mean radiation durations were as follows: choledolithiasis was 5.76 minutes (95% CI, 4.75–6.80); malignant biliary obstruction was 6.13 minutes (95% CI, 5.91–6.35); pancreatic disease was 5.28 minutes (95% CI, 4.45–6.28); benign biliary structure was 5.32 minutes (95% CI, 5.02–5.94). There was no significant difference between the two expert endoscopists in present study. Multivariate analysis revealed that prolonged duration of fluoroscopy was related to specific factors of patient including higher BMI (BMI > 27.5 kg/m2) (+ 4.1 minutes; 95% CI, 2.56–5.63), mechanical lithotripsy (+ 4.85 minutes; 95% CI, 0.45–9.25), needle knife (+ 4.5 minutes; 95% CI, 2.15–6.86), and malignant biliary obstruction (+ 2.34 minutes; 95% CI, 0.15–4.53).

Conclusion: ERCPs are associated with significantly higher radiation exposure of the specific procedure. The endoscopists should be aware of the determinantal factors including patients who were obese, mechanical lithotripsy, malignant biliary obstruction and the use of a needle-knife, affected the fluoroscopy time during ERCP.

Disclosure: Nothing to disclose

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P1454 ENDOSCOPIC RESECTION MAY BE CURATIVE FOR AMPULLARY CARCINOMA: RESULTS OF A EUROPEAN MONOCENTRIC RETROSPECTIVE STUDY

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Introduction: The treatment of ampullary carcinomas is based on duodenopancreactectomy (DP). However, in the absence of poor prognostic factors (submucosal invasion, lymphovascular embol (LV), budding, poorly differentiated carcinomas were sporadics. Monobloc resection was achieved in 77%. A prophylactic pancreatic stent was inserted in 72% (divisum pancreas = 2, insertion failure = 4). Morbidity was 18% (delayed bleeding = 3, severe AP = 1). No procedure-related death was observed.

Histopathological examination showed well or moderately differentiated carcinoma in respectively 45% and 13%, and lymph nodes were observed respectively in 9% (n = 2) and 4.5% (n = 1). Pathological subtype was classified into intestinal (n = 16) or biliary (n = 11) subtypes. In 13% (n = 2) and 5% (n = 1) respectively 2 and 1 cases being unclassifiable. Microscopic deep margins were positive in 50%. Carcinomas was staged Du0, Du1 and Du2 respectively in 20 (91%), 1 (4.5%) and 1 (4.5%). Eleven patients with R0 resection of Du0 carcinomas without lymphovascular invasion were followed-up a mean of 24 months, only 1 local recurrence. This relapse in low grade dysplasia was successfully treated by intraductal biliary radiofrequency. Eleven resections had positive deep margins (Du0 = 9, Du1 = 1, Du2 = 1). Among these 11 patients, 3 patients had PD (PT0N0 = 1, PT1N0 = 1, PT0N1 = 1) and 8 patients were followed-up. Of these patients, 5 had local recurrence which were treated by surgery (n = 1), chemoradiotherapy (n = 1), radiofrequency (n = 1) or best supportive care (n = 2). Local recurrence rate after endoscopic resection of Du0 adenocarcinoma with R0 margins (R0) was 9% (n = 1). Endoscopic approach provides curative treatment for adenocarcinoma in 64% in intent to treat but in 100% for R0 Du0 carcinoma.

Conclusion: EA is a validated treatment for cancers that do not invade beyond the oddi sphincter. This technique makes it possible to avoid surgery in almost 60% of cases. A positive deep margin is associated with a higher risk of local recurrence, justifying surgery.

Disclosure: Nothing to disclose

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P1455 ENDOSCOPIC SNARE PAPILLECTOMY: LONG TERM RESULTS IN 173 CONSECRUENT PATIENTS

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Introduction: Ampullary adenomas represents 5% of the neoplasia of the gastrointestinal tract. The premalignant nature of ampullary adenoma justify their radical excision.

Aim of this study is to evaluate the results and the long-term follow-up of endoscopic snare papillectomy (ESP) of ampullary tumor.

Aims and Methods: Consecutive patients undergoing ESP between October 1999 and February 2018 were identified from an electronic database. The following data were recorded: size of the ampullary lesion, pre-and post-endoscopic resection histology, complications, local recurrence rate and survival. Endoscopic follow-up was scheduled after 1, 3, 6 and 12 months for the first year, and then yearly for the following 5 years.

Results: ESP was performed in 173 consecutive patients (89 M, mean age 60.5). En bloc resection was possible in 88% of patients. 28 patients (16.2%) had familiar adenomatous polyposis (FAP).

Biliary sphincterotomy with or without insertion of a plastic stent was performed after papillotomy in 77 patient (44.5%); a pancreatic stent or a naso-pancreatic drain, with or without pancreatic sphincterotomy was inserted in 95 (54.9%) patients, 14 had a pancreas divisum and in 8 cases pancreatic stent placement failed. The following adverse events were recorded:

- delayed bleeding (n = 16, 9.2%); 2 cases that required angiography.
The present series reports the results of ESP after more than 4-year median follow-up. ESP is effective with favorable long-term outcomes; multidisciplinary is team needed to manage complications. The high incidence of residual/recurrent ade-

Table 1. Follow-up results in 146/173 (84.4%) after endoscopic snare papilllect-

Table 1. Follow-up results in 146/173 (84.4%) after endoscopic snare papillectomy (ESP).

Disclosure: Nothing to disclose

P1456 ENDOSCOPIC OR COMBINED ENDO/PERCUTANEOUS MANAGEMENT IN COMPLEX BILE DUCT INJURIES

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Introduction: Bile duct injuries (BDI) occur most often after biliary tract surgery, with laparoscopic cholecystectomy representing the leading cause. Reconstrucative biliary surgery is considered standard treatment for the most severe form of biliary injuries, also known as complex BDI. Recent studies have suggested a role for an endoscopic or combined endoscopic/percutaneous approach in selected patients.

Aims and Methods: We report our experience with a variety of endoscopic or combined endoscopic/percutaneous techniques to re-establish biliary drainage in patients with complex BDI and biliary exclusion.

Results: We identified 15 symptomatic patients with complex BDI and biliary exclusion who were treated by various endoscopic or combined endoscopic/percutaneous methods to recreate a communication with the excluded bile ducts. In 6 patients, BDI occurred after cholecystectomy. In 5 patients, biliary reconstruction was performed using a TIPSS-200 set, initially developed for insertion of transjugular intrahepatic portosystemic shunts (TIPS) Successful drainage of the excluded bile ducts with resolution of symptoms was possible in 14 patients, either through recreation of bili-biliary continuity (10 patients) or by creating a biliary drainage tract (3 patients) or by both techniques (1 patient). Mean duration of the biliary repermeabilisation procedure was 107 min (range 59–180). No immediate severe complication occurred. Complete internalization of biliary drainage was possible in 14 patients. An average of 7.4 additional ERC/PCP procedures per patient were performed after the initial reper-

P1457 NATURAL HISTORY OF BILIARY CAST SYNDROME AFTER LIVER TRANSPLANTATION: A PROSPECTIVE CHOLANGIOGRAPHIC EVOLUTION STUDY

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Introduction: Biliary cast syndrome (BCS) is a rare complication after liver trans-

Disclosure: Nothing to disclose

P1458 HOLMIUM LASER LITHOTRIPSY TO TREAT DIFFICULT BILIARY AND PANCREATIC STONES USING PERORAL SINGLE OPERATOR CHOLANGIOPANCREATOSCOPY

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Introduction: In tertiary centres 5–10% of bile duct stones are difficult to clear with conventional ERC techniques. Similarly, most pancreatic stones cannot be removed.

Recently, it has been possible to treat complex calculi under direct vision with peroral single operator cholangiopancreatoscopy (POC) using Holmium (Ho) laser lithotripsy.
Conclusion: Cholangiopancreatoscopy-guided Holmium laser lithotripsy appears to achieve complete ductal clearance. Stones were cleared in all patients undergoing lithotripsy. Complications were mild, aspiration pneumonia (2) and pancreatitis (1). The mean number of stones per patient was 3 (range 1-7). The mean largest biliary stone was 13mm (range 3–30mm) and pancreatic stone 9mm (range 8–10mm). Mean procedural time was 48 minutes for bile duct stones and 29 minutes for pancreatic stone cases.

Laser power settings were higher for pancreatic stones (8-8 30 and biliary 8–10 W). Complications were mild, aspiration pneumonia (2) and pancreatitis (1) from 21 procedures. There were no ductal injuries. Stones were cleared in all the patients undergoing lithotripsy.

Conclusion: Cholangiopancreatoscopy-guided Holmium laser lithotripsy appears to be safe and effective at treating difficult biliary and pancreatic stone disease, with pancreatic stone disease being more challenging to manage. Further studies are required.

Disclosure: Nothing to disclose.

P1459 BIOPSY IN COMBINATION WITH BRUSH CYTOLOGY CAN IMPROVE THE CHARACTERIZATION OF MALIGNANT BILIARY STRICTURES DURING ERC

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Introduction: Brush cytology is systematically performed during endoscopic retrograde cholangiopancreatography (ERCP) to characterize biliary strictures. However, it has a low sensitivity in detection of malignant strictures.

Aims and Methods: The aim of this retrospective study was to verify if biopsies improve the characterization of malignant biliary strictures. We reviewed 186 patients with biliary strictures who underwent endoscopic brush cytology. The brush cytology was performed between January 2010 and December 2017. Brush cytology was performed at the site of biliary stricture at least ten times and at least two fragments were obtained for histopathological diagnosis. Final diagnosis was based on cytology/biopsy, percutaneous biopsy, surgery, or clinical follow-up.

Results: The mean age was 69.6±14.2 years and 111 (59.7%) were patients were males. Single stricture of the main bile duct was documented in 96.8% (n=180). The majority of stenoses was located in the proximal and distal thirds of the biliary duct (51.1% and 27.4%, respectively). Malignant strictures were identified in 76.9% of patients with pancreatic cancer (n=66) and cholangiocarcinoma (n=61) being the most frequent aetiology. Biopsies were performed in 97 (52.2%) patients.

For detection of malignancy, brush cytology alone had a sensitivity of 34.27% (95% IC: 26.54–42.66), a specificity of 97.67% (95% IC: 87.71–99.94) and an accuracy of 48.92%. For pancreatic cancer specifically, brush cytology presented a sensitivity of 34.85% (95% IC: 23.53–47.58) and specificity of 100%, and for cholangiocarcinoma a sensitivity of 36.07% (95% IC: 24.16–49.37) and specificity of 100%. Biopsy alone had a sensitivity of 30.43% (95% IC: 19.92–42.69), specificity of 96.43% (95% IC: 81.65–99.91) and accuracy of 49.48%. A combination of brush cytology and biopsies yielded a slight increase in sensitivity to 38.46% (95% IC: 30.45–46.96). ERC was repeated in 72 (38.7%) patients and cytology repeated in 22 (27.3%), 6 of which detected malignant stricture that was not previously identified. Conclusion: Combination of brush cytology and biopsies during ERCP can increase detection of malignant biliary strictures when compared to cytology alone. Cholangioscopy-guided biopsies may improve the characterization of these malignant strictures.

Disclosure: Nothing to disclose.

P1460 ENDOSCOPIC MANAGEMENT OF BILE DUCT STONES IN PATIENTS WITH SURGERY-RELATED ANATOMY: EVALUATION OF NEWLY DEVELOPED SHORT TYPE DOUBLE BALLOON ENDOSCOPE

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Introduction: Endoscopic retrograde cholangiography (ERC) is an endoscopic procedure that is applied worldwide for the examination and treatment of biliary stones. However, the success rates for the use of conventional endoscopic devices for the treatment of biliary stones had been unsatisfactory in patients with surgically altered gastrointestinal (GI) anatomy. Recently, many papers proved that the development of the balloon-assisted endoscope (BAE) could achieve superior outcomes in the feasible, however, these studies observed in various sizes of total number of object patients and the success rate was overall wide ranging.

Aims and Methods: The aim of this study was to evaluate a large case series of ERC using short type DBE for common bile duct stones in postoperative patients. From February 2006 to October 2017, ERC using short-type DBE (DB-ERC) was performed in 210 postoperative patients (325 procedures). We retrospectively studied the success rate of reaching the blind end, the success rate of complete ERC related interventions, the mean procedure time, and adverse events.

Results: The success rate of reaching the blind end was 98.5% (320/325). By type of reconstruction methods, the success rate of reaching the blind end was 98.1% (202/206) in Roux-en-Y(R-Y) reconstruction, 99.1% (106/107) in B-II gastrectomy, 100% (106/107) in jejunal interposition. The mean time to reach the blind end was 9.4 minutes. By type of reconstruction methods, the mean time to reach the blind end was 19.5 minutes in Roux-en-Y(R-Y) reconstruction, 11.4 minutes in B-II gastrectomy, 10.5 minutes in jejunal interposition. The success rate of complete ERC related interventions was 97.5% (312/320). By type of reconstruction methods, the success rate of complete ERC related interventions was 98.5% (199/202) in Roux-en-Y(R-Y) reconstruction, 96.2% (102/106) in B-II gastrectomy, 91.7% (11/12) in jejunal interposition. The procedure time was 76.9 minutes. By type of reconstruction methods, the mean procedure time was 96.6 minutes in Roux-en-Y(R-Y) reconstruction, 61.6 minutes in B-II gastrectomy, 55.1 minutes in jejunal interposition. The occurrence of adverse events was 9.2% (30/325). By type of reconstruction methods, the occurrence of adverse events was 8.7% (18/206) in Roux-en-Y(R-Y) reconstruction, 10.3% (11/107) in B-II gastrectomy, 8.3% (11/12) in jejunal interposition.

Conclusion: ERC using a short-type DBE for biliary stones is highly effective and safe in patients with altered gastrointestinal anatomy. DB-ERC is a promising therapeutic modality in such patients and should be selected as the first-line policy.

Disclosure: Nothing to disclose.
Aims and Methods: that demonstrated a positive impact in preventing PEP. Lactated Ringer (LR) and pancreatic duct stenting are recommended measures.

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Indications: Endoscopic retrograde cholangiopancreatography (ERCP) has become an integral part in the therapeutic armamentarium when dealing in patients with cholelithiasis. However, when choosing the proper extraction device, data are inconsistent, with selection being, often, a matter of the endoscopists’ preferences.

Aims and Methods: We conducted a single-center prospective randomized controlled study to access success rates for basket versus balloon catheters for small stones for the first time in Europe. In a non-inferiority setting, 180 patients with bile duct stones were randomized in a basket and a balloon catheter group. Inclusion criteria were fluoroscopically bile duct stones ≤10mm in diameter and a common bile duct (CBD) diameter ≤15mm. The primary endpoint was the rate of complete bile duct clearance for each extraction method used. Secondary endpoints included time comprised and the amount of radiation dose recorded in each ERCP session, as well as any reported adverse events.

Results: Balloon was non-inferior to basket stone extraction (OR 3.35, 95% CI 1.56–7.14). Complete clearance was achieved in 69 out of 82 patients (84.1%) in the basket catheter group versus complete clearance in 79 out of 84 patients (94%) in the balloon catheter group (p = 0.03). This seems to hold especially true for patients with few stones and of small size (≤2 stones, p = 0.043) and stone diameter <5mm, p = 0.032). Complete stone clearance in the basket group patients took longer than complete stone clearance in the balloon group (4.52 and 4.06 min, respectively, p = 0.015). Higher median radiation doses for stone clearance were recorded in the basket versus the balloon catheter group (155.43 Gy vs 124.54 Gy, p = 0.015).

Conclusion: In conclusion, our study showed that balloon was non-inferior to basket stone extraction. More prospective future studies with proper methodology will enhance our knowledge and provide us with more robust data regarding complete stone clearance and catheter type.

Disclosure: Nothing to disclose

P1464 SAFETY AND EFFICACY OF EUS-GUIDED GALLBLADDER DRAINAGE (EUS-GBD) COMBINED WITH ERCP IN THE SAME SESSION


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Introduction: ERCP is increasingly being combined in a single-session with other endoscopic procedures such as EUS staging, screening for CBD stones, removal (for failed cannulation) duodenal stenting or cholangioscopy. EUS-guided gallbladder drainage (EUS-GBD) is an emerging option for acute cholecystitis in non-surgical candidates. Patients with acute cholecystitis often need CBD stone removal. Combination of ERCP for CBD stones and EUS-GBD might be appealing in some patient subsets, but there is virtually no objective evidence to support this combined approach to gallstone disease.

Aims and Methods: To assess the safety and efficacy of EUS-GBD combined with ERCP in the same session.

Single-center retrospective cohort study comparing outcomes of EUS-GBD alone to those of ERCP combined with EUS-GBD in the same session between June 2011 and May 2017. Lumen-apposing metal stent (LAMS, Axios®) were used in both groups. Exclusion criteria: ERCP or EUS-GBD used for salvage of one another (e, transcytic GB drainage after failed EUS-GBD or EUS-GBD for failed biliary drainage at ERCP), EUS-guided biliary drainage (EUSBD) in the same session, and ERCP within 5 days (before/after) EUS-GBD. Epidemiologic, procedural, and clinical outcome data were analyzed with Wilcoxon, Chi-square and Fisher tests where appropriate. Primary endpoints were rates of technical success, clinical success and adverse events.

Results: Sixty-four consecutive patients underwent EUS-GBD between June 2011 and May 2017. 19 patients were excluded: in 11 the indication for either ERCP or EUS-GBD was salvage of a failed tandem procedure, 5 had EUS-guided biliary drainage in the same session and a further 3 had another ERCP within 5 days of the index procedure. Forty-five patients met inclusion/exclusion criteria: 24 EUS-GBD and 21 ERCP-GBD combined with ERCP. Baseline patient characteristics were comparable in both groups. There were no significant differences in technical (100% vs 91.7%) and clinical success rates (90.5% vs 91.7%) of EUS-GBD in the combined versus the single procedure groups. The rate of adverse events (23.8% vs 20.9%) and the rate of technical failures (14.3% vs 35.7%; p = 0.10) during LAMS deployment were also comparable. Results are detailed in Table 1. Technical success of EUS-GBD was 100% and 81% of patients required sphincterotomy and stone extraction.

Conclusion: While ERCP combined with EUS-GBD maintains similar rates of technical and clinical success to EUS-GBD alone, a combined procedure does not appear to increase adverse events. Despite the limitations of our study, these findings are encouraging and warrant further evaluation before this therapeutic approach can be generalized.

Disclosure: Nothing to disclose

[Table 1]
Disclosure: This abstract has been presented in ESGE days 2018 and has been accepted for DDW 2018.

P1465 EUS ANATOMY OF THE PancreaticoBiliary SYSTEM IN A SWINE MODEL: THE WISE EXPERIENCE

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Introduction: The swine model has been described as a realistic tool for EUS training [1]. Papers extensively describing EUS swine anatomy are lacking in the current literature, though.

Aims and Methods: The aim of the article is to describe both linear and radial EUS pancreatobiliary swine anatomy.

We report the animal lab experience of the WEO (World Endoscopy Organization) International School of EUS (WISE) group at ASAN Medical Center in Seoul. 2 young pigs were sedated under general anesthesia, endotracheal intubation and mechanical ventilation. Both radial and linear array echoendoscopes were used for delineation of pancreatobiliary anatomy and videos were recorded.

Results: Consistent with other reports about the aorta, crura of the diaphragm, celomic trunk, superior mesenteric artery, pancreas, common bile duct, gallbladder, portal vein, kidneys, spleen and hepatic hilum. Images obtained were comparable to human EUS findings, even if with some remarkable differences.

Conclusion: Swine model confirmed to be a highly realistic training model for EUS. To the best of our knowledge swine EUS anatomy has not been reported to date. We believe that this image-provided description of swine pancreatobiliary anatomy can be a useful tool for EUS training in the setting of in-vivo hands-on sessions.

Disclosure: Nothing to disclose

Reference


P1466 PREDICTIVE FACTORS FOR THE ASSESSMENT OF THE Ki-67 INDEX IN Pancreatic NeuroEndoCRINE TUMORS DIAGNOSED BY ENDOSCOPIC ULTRASONOGRAPHY

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Introduction: Endoscopic ultrasonography (EUS)-guided puncture is the standard of care for tissue sampling of pancreatic masses. For pancreatic neuroendocrine tumors (P-NET), obtaining material that allows a complete anatomopathological examination with Ki-67 index quantification is essential for its adequate characterization. However, the factors that enable it are unclear, namely the advantage of fine needle aspiration (FNA) versus fine needle biopsy (FBN).

Aims and Methods: The aim of this study is to evaluate in patients with P-NET diagnosed by EUS the factors that potentially influence the ability to obtain adequate samples allowing complete anatomopathological examination with assessment of the Ki-67 index.

Retrospective study of all patients with P-NET with histological diagnosis by EUS at our institution between January 2013 and December 2017. The size of the lesion, location of the lesion, tissue acquisition technique (FNA vs FNB) and needle gauge were analysed.

Results: Twenty-one procedures were performed in 20 patients: 11 women (55.0%) and 9 men (45.0%) with a median age of 54 years (range 27–82 years). The median lesion size was 25mm (range 8–70mm). In 61.9% (n = 13) of the procedures an adequate sample allowing a complete anatomopathological examination (with Ki-67 index quantification) was obtained. The Ki-67 index compatible to the analysis methods was 72.5% in lesions <20mm (8/11) vs 50.0% in lesions ≥20mm (5/10), p = 0.290; 64.3% in body/ tail lesions (9/14) vs 57.1% in head/uncinate lesions (4/7), p = 0.751; 53.8% of the cases with FNA (7/13) vs 75.0% with FNB (6/8), p = 0.339; 70.0% with 22G needle (7/10) vs 54.5% with 25G needle (6/11), p = 0.469. There were no complications associated with the procedure.

Conclusion: Characteristics of the lesion and puncture technique did not significantly influence the ability to obtain material for complete anatomopathological examinations in P-TNE. However, the size of the sample does not allow a definitive conclusion. The authors recommend that this study be replicated in a larger sample of patients, possibly in a multicenter study.

Disclosure: Nothing to disclose

P1467 DIAGNOSIS AND OUTCOME OF MEDIASTINAL FOREGUT DUPLICATION CYSTS: THE ROLE OF EUS

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Introduction: Mediastinal foregut duplication cysts (FDC) are rare dysembryogenic lesions originating from the ventral portion of the endodermal primitive foregut. The diagnosis, follow-up and outcome of these lesions have been reported in only few case reports and small retrospective studies. 1, 7

Aims and Methods: Aim of this study was to assess the role of endoscopic ultrasound (EUS) in the diagnosis and follow-up of FDC.

Forty-five patients who had been referred for EUS for mediastinal lesions suspected of being FDC between 01.01.2009 and 01.02.2017 were identified by using the ICD-10 code Q39.8 from the patient registry of EUS of Helsinki University Hospital. All patients’ baseline characteristics (gender, age, symptoms and signs), gastroscopy, computer-tomography (CT) findings (density, localisation), EUS findings (echogenicity, localisation, final diagnosis), surgical intervention, histologic findings and complications were reviewed. Data are presented as number with percentage when categorical and as median and range when continuous.

Results: All the patients (n = 45, 17 males, median age 55 years; range: 27–79) underwent EUS for a suspected FDC after endoscopy and/or chest-CT. In 31 patients (69%) the lesion was an occasional finding. Gastroscopy was performed in 22/45 (49%) showing a submucosal lesion in 19/22 (86%). Chest-CT was performed in 36/45 (80%) and the final diagnosis was consistent with a fluid lesion in 15/36 (42%) and with a solid lesion in the remaining 19 patients; normal finding was found in 2 patients. In CT images, lesions were localized outside the oesophageal wall in 22/36 (61%) of the patients and inside in the remaining 12.5.

Conclusion: EUS, the final diagnosis was consistent with a FDC in 44/45 (98%) and normal in 1. Biopsy was not routinely performed because of the risk of infection. Thirty-four lesions (77%) were localised inside the oesophageal wall and 10 outside.

Disclosure: Nothing to disclose

References


P1469 THE DIAGNOSTIC EFFICACY OF CONTRAST ENHANCED-ENDOSCOPIC ULTRASONOGRAPHY IN DIFFERENTIAL DIAGNOSIS OF GASTRIC GASTROINTESTINAL STROMAL TUMOR (GIST) AND NON-GASTROINTESTINAL STROMAL TUMOR

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Introduction: Gastrointestinal stromal tumours (GISTs) represent the largest group of subepithelial tumors (SETs) of the upper gastrointestinal tract. The differential diagnosis of GISTS is important because of malignant potential, in contrast to other SETs. Endoscopic ultrasound (EUS) and contrast-enhanced endoscopic ultrasound (CE-EUS) is frequently used to diagnose GISTS, however, the characteristic features to distinguish GISTS from other SETs are still unknown.

Disclosure: Nothing to disclose
Aims and Methods: The aim of this study is to find specific features on CE-EUS in patients with GIST with the aim of differentiating GIST with other SEPs. We retrospectively reviewed the findings of CE-EUS of 25 hypoechoic tumors, located in gastric or muscular layers in 25 patients from January 2014 to December 2016. The presence and degree of tumor vessel in the SEPs was evaluated. In addition, the texture of the tumor was described according to a contrast pattern as hypoenhancement, iso-enhancement, and hyper-enhancement. The results were compared to histological diagnosis, in which obtained by EUS-guided fine needle aspiration with biopsy or surgical resection.

Results: Seventeen SELs were diagnosed as GIST by histological results. 6 SELs were diagnosed as leiomyoma and 2 SELs were schwannoma. In 14 of 17 GIST's tumor vessel was observed and in 8 non-GIST's tumor vessels were not observed. On statistical analysis, the presence of tumor vessel was significantly related to GIST (OR=7.782; 95% confidence intervals = 1.8–10.0; P < 0.001). 1 or 2 tumor vessels (1+ in 5 cases, 2 or 3 tumor vessels (2+) in 6 cases, more than 3 tumor vessels (3+) in 3 cases and no tumor vessels in 3 cases. The sensitivity, specificity, and positive predictive value with vessel enhancement were about 100%, 66.7%, 77.4% and 84%. In GISTs hypoenhancement was observed in 5 cases, iso-enhancement in 11 cases and hyperenhancement in 1 case. In 8 of non-GISTs, hypoenhancement was observed in 5 cases, isoenhancement in 11 cases and hyperenhancement in 1 case. The tumor vessels (3+) in 5 cases, 2 or 3 tumor vessels (2+) in 6 cases, more than 3 tumor vessels (3+) in 3 cases and no tumor vessels in 3 cases. The sensitivity, specificity, and positive predictive value with vessel enhancement were about 100%, 66.7%, 77.4% and 84%. In GISTs hypoenhancement was observed in 5 cases, iso-enhancement in 11 cases and hyperenhancement in 1 case.

Disclosure: Nothing to disclose

P1470 SLOW-PULL TECHNIQUE FINE-NEEDLE BIOPSY WITH 20-GAUGE NEEDLE (SPUTNQ-20G STUDY) VERSUS STANDARD SUCTION OF SOLID PANCREATIC LESIONS: A MULTICENTER RANDOMIZED TRIAL

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Introduction: Standard endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) of solid pancreatic lesions involve the use of no-suction or suction aspiration techniques. A new aspiration method, the stylet slow-pull technique, consists in the slow withdrawal of the needle stylet to create minimum negative pressure. New generation of stylets could facilitate the slow-pull technique.

Aims and Methods: We compared EUS-FNB performed with the stylet slow-pull technique versus the standard suction technique in patients with solid pancreatic lesions. We evaluated blood contamination and adequacy of the samples, FNB diagnostic accuracy and complications. EUS-FNB were performed with a 20-gauge needle (EchoTip ProCore with ReCoil Stylet). The ReCoil Stylet has an automatic recoiling capability designed to help users to manage more easily the stylet and reduce the risk of contaminating the samples. After completion of the endosonographic examination, the pancreatic mass was evaluated with color Doppler to avoid the involvement of vessels. The needle was slowly withdrawn from the lesion, the stylet was pulled back, and the core was defined as an architecturally intact-looking piece of tissue deemed sufficient for histological evaluation. Samples positive for malignancy were considered as “true positive”.

Results: Two-hundred and thirty samples were collected. In 90% of the patients (n = 210), the final diagnosis was histology on EUS-FNB, surgical specimen or clinical follow-up.

Discussion: As both slow-pull and standard suction techniques are comparable offering high diagnostic sensitivity and accuracy. The technique versus the standard suction technique in patients with solid pancreatic lesions is a safe procedure with high diagnostic accuracy and few complications. All EUS-FNB were performed with a 20-gauge needle (EchoTip ProCore with ReCoil Stylet). The ReCoil Stylet has an automatic recoiling capability designed to help users to manage more easily the stylet and reduce the risk of contaminating the samples.

Disclosure: Nothing to disclose

P1471 DO WE NEED ENDOCOSIC ULTRASONOGRAPHY IN THE WORKUP OF PATIENTS WITH ACHALASIA?

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Introduction: The etiology of primary achalasia of the lower esophageal sphincter is unknown. Endoscopic ultrasonography (EUS) is advised in the workup of achalasia patients to rule out secondary achalasia or pseudoachalasia, and search for a collagenosal pallidal wall thickening. The purpose of this study was to assess the clinical contribution of EUS findings in achalasia.

Aims and Methods: We conducted a single-centre retrospective study at a tertiary referral center. We included all patients with an endoscopic ultrasonography for the workup of a suspected esophageal motility disorder from January 2012 to December 2017.

Results: Seventy-one patients were included, 54% were men, with a mean ± (SD) age of 61 ± 14 years. Mean ± (SD) Eckardt score at time of the EUS was 7 ± 2. EUS was strictly normal in 27 (38%) patients, and showed an esophageal wall thickening in 44 (62%) patients. The inner circular muscle layer was the most frequently affected, with a mean ± (SD) thickness of 2.9 ± 2.3 mm. Three cases of secondary achalasia were diagnosed: 2 esophageal carcinomas and one eosinophilic esophagitis, all three diagnosed at mucosal biopsies. Sixty percent of the patients had never received a treatment at the time of EUS and 82% were treated later. EUS was performed after the treatment in 18 (25%) patients. The most frequent treatment was an esophagogastric myotomy in 48% of the patients (per oral endoscopic myotomy in 20% and surgical myotomy in 3%), while 20% and 13% of patients were treated with pneumatic dilatation and botulinum toxin injection, respectively. The occurrence of a wall thickening was not significantly associated with the type of esophageal motility disorder or achalasia subtype, the Eckardt score, the integrated relaxation pressure at manometry, or a previous treatment. There was no statistical correlation between the presence of a wall thickening at EUS and therapeutic outcomes after any of the achalasia treatments.

Conclusion: In our work, the contribution of endoscopic ultrasound findings was limited. The presence of an esophageal wall thickening was not predictive of achalasia subtype or treatment outcome.

Disclosure: Nothing to disclose

P1472 EUS ELASTOGRAPHY STRAIN RATIO IN THE DIFFERENTIAL DIAGNOSIS OF GASTROINTESTINAL SUBEPITHELIAL LESIONS: RESULTS OF A MULTICENTER STUDY

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Introduction: Real-time endoscopic ultrasound elastography (EUS-E) allows for the quantification of tissue stiffness and has proven to be useful to better characterize soft tissue masses. Strain ratio (SR) measurement has been introduced as a method to minimize the operator bias by providing semi-quantitative data. Studies on EUS-E with SR in gastrointestinal subepithelial lesions (SELs) are lacking.

Aims and Methods: Aim of this study was to assess the efficacy of EUS-E with SR in differentiating SELs. Retrospectively collected data from consecutive patients with SELs evaluated by EUS-E with SR at three centers were analyzed. EUS-E was carried out using the Olympus compact ultrasound processor EU-ME2. Two different areas were selected for SR. Area A included the biggest possible area of the lesion without surrounding tissue, while area B was selected in the peritumoral healthy gastrointestinal wall. The SR was calculated as the quotient of B/A. Every time, 3 measures of SR were recorded and the mean value for each measurement was evaluated. SR was calculated as the quotient of B/A. Every time, 3 measures of SR were recorded and the mean value for each measurement was evaluated.

Results: A total of 57 SELs were included. The mean lesion size was 36.4 mm (SD 20.8 mm). The lesion locations were esophagus (n = 7), stomach (n = 38), duodenum (n = 10) and rectum (n = 2). The final diagnosis of SELs were histology on EUS-FNB, surgical specimen or clinical follow-up.

Conclusion: The results indicate that EUS-E with SR may improve differential diagnosis of SELs, being SRs of GIST higher than those of leiomyoma. The cut-off of 13.3 may be helpful to differentiate between GIST and leiomyoma.

Disclosure: Nothing to disclose
Ongoing, Re-intervention was required in 110 (27%) subjects. The need for Re-
cluded 155 (38%), Group C included 42 (10.3%) subjects. During EUS guided
were included in the study group. Group A included 211 (51.7%), Group B
Disclosure:
Nothing to disclose
higher in PFC containing severe necrotic contents. Whereas disconnected pancreatic duct is significantly
Normal Pancreatic duct can be seen in majority of subjects with PFC containing
Pancreatic necrotic contents in PFC significantly impacts manage-
Conclusion:
Results:
G. Delconte
2

Aims and Methods:
Fondazione IRCCS Istituto Nazionale dei Tumori, Pathology Department,
Fondazione IRCCS Istituto Nazionale dei Tumori, Diagnostic and Therapeutic
The mean size of the target lesion was 79 mm (range: 25–190). FNB
sarcomas, 1 leiomyoma, 1 schwannoma, 6 GISTs, 1 glioma, and 1 desmoid-type
The aim of the study was to evaluated clinical performance of
the effect of these pancreatic necrotic contents in PFC on treatment strategy and
Acute severe pancreatitis can be necrotizing and frequently compli-
tents which has important implications on management and outcome. However,
the extent of these pancreatic necrotic contents in PFC on treatment strategy and
more importantly on the subsequent pancreatic ductal anatomy not clearly
Aims and Methods: The objective of this study is to evaluate whether the severity of necrotic contents in pancreatic fluid collections impacts the treatment strategy and pancreatic ductal anatomy.
Severe acute pancreatitis with symptomatic PFC were included after an informed consent from Jan 2013 to December 2017. PFCs were classified into 3 distinct groups based on severity of necrotic contents, Group A) (≤15% SD; Group B) 15–40% SD; Group C) >40%. Subsequently EUS-guided drainage done using either short covered b-flanged metal stent or plastic stents. After drainage, subjects were reassessed at 48–72 hours & Re-intervention including, Nacoso-tic duct (NCT) placement with irrigation and Direct Endoscopic Necrosectomy were performed if required. All subjects underwent MRCP fol-
lowed by ERCP between 4-8 weeks after the complete resolution of PFC to define the abnormalities in Pancreatic duct (PD) & were compared between 3 PFC subgroups. A p value <0.05 was considered statistically significant.
Results: (350 males, median age 32 years, range 5–69 years) were included in the study group. Group A included 211 (51.7%), Group B included 155 (38%), Group C included 42 (10.3%) subjects. During EUS guided drainage, 270 underwent metal stent, 136 underwent plastic stents placement. Overall, necrosectomy was required in 10% of subjects. The need for Re-
tervention was significantly higher in Group C (SD >40%) compared to Group B & A (40.4% vs. 29.8% vs. 22.2%, p = 0.06). 340 out of 408 subjects had both MRCP and ERCP and included in final analysis. Of these, 42 (12.4%) subjects had normal PD, 35 (10.3%) had leak in PD, 20 (5.9%) had leak in PD & PD fistula and 11 (3.2%) had dilated PD with calcui & majority of subjects (n = 232, 68.2%) had cut-off in PD (Disconnected pancreatic duct). Normal PD was present significantly higher in Group A (SD 15%) compared to Group B & C (61.9% vs. 23.8% vs. 14.2%). Similar trends were observed among Group A, B, & C for PD leak (71.4% vs. 28.5% vs. 0%), PD stenosis (75% vs. 25% vs. 5%). However, PD cut off (Disconnected pancreatic duct) was observed significantly higher in Group C (SD >40%) compared to Group A (80.5% vs. 57.7%, p = 0.001).
Pancreatic necrotic contents in PFC significantly impacts management strategy and subsequent Pancreatic ductal anatomy. PFCs with severe necrotic contents require aggressive treatment strategy including Re-intervention. Normal Pancreatic duct can be seen in majority of subjects with PFC containing necrotic contents. Whereas disconnected pancreatic duct is significantly higher in PFC containing severe necrotic contents.
Disclosure: Nothing to disclose

P1474 A NEW 19 G ENDOSCOPIC ULTRASOUND CORE NEEDLE FOR THE HISTOLOGICAL DIAGNOSIS OF MESENCHYMAL TUMORS: A FEASIBILITY STUDY

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Introduction: Different type and size of histological needles for Endoscopic Ultrasound guided Fine Needle Biopsies (EUS-FNB) have been developed, however the appropriate core length in which they should be used has to be defined. The diagnosis of mesenchymal tumors (MT) often requires tissue for molecular studies (i.e. ISH, FISH, NGS) beside H&E and immunohistochemistry.

Aims and Methods: The aim of the study was to evaluated clinical performance of a new three points 19 G core needle with opposing bevels design in the setting of MT. Prospectively collected data from consecutive patients who underwent EUS-FNB with a 19 G core needle characterized by a three-points design for suspected abdominal and/or gynecological MT at a single referral center were analyzed. Procedures were performed by a single operator between July 2017 and February 2018.

Results: Fifteen patients were managed. The procedure was technically feasible in all patients. Biopsy was performed through the rectum, the duodenum, and the stomach. Respectively, 2, 7 and 6 procedures per patient were performed, although hemostatic clips were used to control mild gastric bleeding at the point of the needle passage for 2 patients. Biopsies showed in 2 cases malignancies other than MT one being a lymphoma and one a pelvic metastasis from ovarian cancer. Among 13 patients diagnosed MT (10 M, mean age 54±16.7 years) and FNB lead to a diagnosis in 12 cases (accuracy, 92.3%); 2 sarcomas, 1 leiomyoma, 1 schwannoma, 6 GISTs, 1 glioma, and 1 desmoid-type fibromatosis. The mean size of the target lesion was 79 mm (range: 25–190). FNB was non-diagnostic in a patient with a large mass located behind the gastric wall with lipomatous radiological features. Quality of biopsy was examined showing, that although a mean number of 1.4 passes (range: 1-2) were performed based on gross visual inspection, adequate core tissue was available after the first pass for all patients. In 10 out of 12 diagnostic cases additional molecular studies were performed.

Conclusion: This is the first report, to the best of our knowledge, on 19 G histological EUS needle with a novel three points design and showed both feasibility and safety of the procedure. This study showed a high rate of biopsied core tissue which was adequate for a full histological and molecular evaluations, supporting this new device as a promising tool when a pathological diagnosis is needed for patient management such as the case of MT.

Disclosure: Nothing to disclose

P1475 DIRECT ENDOSCOPIC NECROSECTOMY IN SUPER-INFECTED FLUID COLLECTIONS IN NECROTIZING PANCREATITIS USING LUMEN-APPOSING METAL STENTS: BETTER OUTCOME WITH EARLY INTERVENTION

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Introduction: In the last decade a paradigm shift in the treatment of necrotizing pancreatitis from more invasive surgical strategies toward less invasive percuta-
ous and endoscopic techniques took place. Infected necrosis is a dreaded complication requiring an intervention. Nevertheless the optimal timing of first intervention is unclear and consensus data are sparse.

This retrospective two-center study evaluates immediate direct endoscopic necrosectomy using lumen-apposing metal stents in case of proven or suspected super-
fection.

Aims and Methods: 60 patients with a mean age of 53.1 years were included between 6/12 and 2/18. Etiology of pancreatitis was alcoholic (n = 18), biliary (n = 23), after surgery (n = 1), hyperglycemia (n = 1), post-ERCP pancreatitis (n = 3) and unknown (n = 14). Pancreatic necrosis was diagnosed by contrast-enhanced computed tomography. Infection of necrosis was confirmed by presence of gas in the CT-scan or suspected based on clinical or biochemical markers of infection or sepsis. In case of infection a lumen apposing metal stent (hot-AxiosTM, Stent, Boston scientific, Marlborough, Massachusetts, USA or NAGITM, Stent, Taewoong medical, wolgot-myeon, South Korea) via trans-
jejunal access was performed. Time to necrosectomy and steerable direct endoscopic necrosectomy was performed until resolution of the necrotic debris. The patient-cohort was divided in an early group receiving first necrosectomy within the first 30 days and a late group obtaining the intervention more than 30 days after first proof of necrosis. The C-reactive-protein as marker of inflam-
matory activity was recorded.

Results: The mean CRP was 219.2 ± 134.9 mg/l and 56 ± 74 mg/l before and after intervention, respectively. The mean time between first proof of necrosis and first intervention was 20 ± 3.1 days. Mortality was achieved in 84.7%. 4.9 ± 3.4 necrosectomies were performed per patient. The mean stay on the intensive-care-unit was 5.4 ± 11.5 days, on intermediate-care-
early-care-unit were 2.2 ± 6.1 days. Mean follow-up was 19 ± 12.4 months.

Conclusion: Our retrospective data reveal an advantage of early timed endoscopic intervention over a delayed approach in necrotizing pancreatitis. Direct endo-
scopic necrosectomy in combination with lumen apposing metal stents shows a trend to less mortality and saving in ICU-capacity when its performed in an early stage of disease. Further randomized investigations should concretise the optimal timing of intervention.

Disclosure: Nothing to disclose

P1476 ADEQUACY AND DIAGNOSTIC YIELD OF A NOVEL CORE BIOPSY NEEDLE (SHARKCORE FNB NEEDLE) IN THE DIAGNOSIS OF SUBEPITHELIAL LESIONS: OUR SERIES

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Introduction: Subepithelial lesions of the gastrointestinal tract are commonly encountered during routine upper and lower endoscopy, diagnosed incidentally because of their asimptomaticity. They are frequently located in the stom-
mach, but also found in the esophagus and duodenum. Endoscopic ultrasound (EUS) plays a fundamental role in the detection and management of these
lesions, both for the ability to identify the original layer and the ultrasound pattern to predict the possibility of a histological, immunohistochemical and molecular diagnosis, through Fine Needle Biopsy (FNB).

Aims and Methods: The aim of the study is to assess adequacy and diagnostic yield of a novel core biopsy needle (Sarkhore FNB needle Medtronic). We reported EUS-FNBS performed at our Center between September 2015 and March 2018, to further investigate suspicious subepithelial lesions found at upper and lower endoscopy.

Results: Out of 923 EUS, 123 were performed with suspicious of submucosal lesions, finally identifying 109 (average size 16 mm, range 1–35 mm). FNB (Sharkhore FNB needle Medtronic, 22G, average of 3 passes), was performed in 22 cases (average dimension 30 mm, 12 female), only one patient experimented mild and self-limiting intraluminal bleeding during FNB. The material resulted adequate in 95% of cases, resolving diagnostic in 10 cases (C21GIST: 8 leiomysarcoma and 1 gastric splenosis). Therefore in 16 cases the sample allowed the immunohistochemical analysis, in 7 cases molecular tests. In 4 cases surgery was performed, with a concordant diagnosis with FNB in 3 of them.

Conclusion: Our series demonstrates FNB (Sharkhore FNB needle Medtronic) adequacy of 90% and diagnostic yield of 86%.

Disclosure: Nothing to disclose

References


P4177 CONNECT YOUR NEEDLE TO YOUR SMARTPHONE TO INCREASE EUS-FNA DIAGNOSTIC YIELD? ESGE RESEARCH GRANT 2016 PRELIMINARY RESULTS

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Introduction: Diagnostic yield of endoscopic ultrasound fine needle aspiration (EUS-FNA) in solid pancreatic masses depends on the lesion characteristics, needle diameter, presence of aspiration, number of passes and presence of rapid on site evaluation. We aim to prove that high needle acceleration through aspiration syringe. Aspired material was fixed in alcohol and processed by the Cytoblock procedure. Slides for each pass were scored for accuracy by the


Results: 21 patients with locally advanced or metastatic pancreatic cancer on CT were included. Using a 22-gauge needle, two “fast” and “slow” passes were performed in a randomized order, each with ten “to and fro” fanning passes (66.6% versus 44.4%, p = 0.0001). The tissue acquisition adequacy of 90% and diagnostic yield of 86%

Disclosure: Nothing to disclose

P4178 THE PREVALENCE OF SMALL BOWEL AND COLONIC POLYPS IN PATIENTS WITH SPORADIC DUODENAL AND/OR AMPULLARY ADENOMAS – A PROSPECTIVE CASE CONTROL STUDY

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Introduction: Sporadic duodenal and/or ampullary adenomas are found in 1–3% of patients referred to upper endoscopy. Patients with duodenal adenomas have a 3-7-fold increased risk of colorectal neoplasia above the normal population. It is unknown whether these patients have a clinically significantly increased risk of small bowel neoplasia. Video capsule endoscopy (VCE) identifies Small bowel (SB) polyps in up to 75% of familial adenomatous polyposis (FAP) patients. Our aim was to investigate the prevalence of SB polyps occurring in association with large (≥10mm) sporadic duodenal or ampullary adenoma patients using VCE.

Aims and Methods: A single-centre prospective case control study was performed. Patients with ≥10mm duodenal and/or ampullary adenoma were approached to participate in the study (Adenoma group). Patients with FAP were excluded. The control group comprised patients undergoing VCE for the evaluation of obscure gastrointestinal bleeding (OGB) or Iron deficiency anemia (IDA) within the same study period.

Results: Over 20 months, 194 patients were enrolled in the study. The mean age was 65 (IQR 24–91) and 49% were male. There were 94 control patients and 99 adenoma cases (Duodenal adenomas n = 74 (75%), mean size 10mm (IQR 10–80mm); Ampullary adenomas n = 25 (25%), mean size 25mm (IQR 10–80mm)). 91% of duodenal adenomas were in the second part of the duodenum. Five patients (adenoma group) were excluded from analysis due to inadvertent aspiration of the capsule (1), technical failure (2), inability to swallow the capsule (1) and non-adenomatous lesion (1).

There were no SB polyps in either group. One adenoma patient had an incidental finding of active bleeding, most likely from an angiodyplasia, but otherwise no significant small bowel findings were obtained.

Colonoscopy was performed in 82% and 84% (p=0.705) of the adenoma and control groups, respectively. Colonic polyps were found more frequently in the adenoma group than controls (61% vs 41%, respectively (p=0.009)). Overall, 43% of patients in the adenoma group had at least one colonic adenoma vs. 21% in the control group (p=0.002). The polyps were<10mm in 87% and 95%, conventional adenoma in 76% and 71% (p=0.537) and sessile serrated polyps in 10% and 2%, respectively (Table 1). Advanced colonic polyps (HGD, >10mm Villous histology) were found in 21% of the adenoma group and 5% of the control group (p=0.02).

Conclusion: This is the first prospective case control study to show the negligible risk of colonic sporadic SB polyps in patients with sporadic duodenal and/or ampullary adenoma patients. We have also confirmed the increased risk of colonic adenoma in this population, even in comparison to a control group at potentially greater risk of colonic pathology. Our data indicate that VCE for SB polyp screening in this group of patients is not necessary. However, colonoscopy is mandatory due to the high prevalence of colonic adenomas including advanced polyps.

P4179 VIDEO CAPSULE ENDOSCOPY HAS A HIGHER DIAGNOSTIC YIELD WITH SIMILAR TECHNICAL SUCCESS IN OLD-ELDERLY COMPARED TO YOUNG-ELDERLY PATIENTS

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Introduction: Video capsule endoscopy (VCE) is a non-invasive procedure that evaluates the small bowel (SB). The use of VCE in the elderly is rising mainly due to an increased rate of investigations for obscure gastrointestinal bleeding. While previous studies in the elderly demonstrated delayed gastric transit time (GTT) with normal SB transit time (SBTT), detailed data is lacking regarding motility and diagnostic yield in these age groups.

Aims and Methods: To evaluate the diagnostic yield and transit times in different age categories among elderly patients.

All consecutive VCEs performed from 01/2010 to 12/2017 in a single tertiary center were reviewed. Inclusion criterion was age≥65 years. Exclusion criteria were technical malfunction or inability to swallow. The cohort was divided into two age groups: 65-79 years (young-elderly, YE) and ≥80 years (old-elderly, OE). Complete SB visualization was defined by cecal documentation. GTT and SBTT were calculated and expressed as median (range min-max).

Indications, TTs and diagnostic yield were compared between groups.
From April 2016 until April 2018, 111 individuals (mean age 61 years) were included in the study. The interim analysis of results is presented. The methods of acceptance were evaluated based on the questionnaire of patients. Complications were assessed as serious (bleeding, perforation) or mild to moderate. The rate of bleeding complications by NOAC seems to be comparable to that of warfarin but a previously assumed increase in gastrointestinal bleeding complications was meanwhile confirmed. The risk of bleeding in the setting of suspected small bowel bleeding (SSBB) in patients taking antiendothelins or anticoagulants has been poorly investigated.

Introduction: Antiendothelin and anticoagulant therapy is increasingly being used for cardiovascular prevention. Novel direct-acting oral anticoagulants (NOAC) represent a recent, alternative, family of drugs. Rate of bleeding complications by NOAC seems to be comparable to that of warfarin but a previously assumed increase in gastrointestinal bleeding complications was meanwhile confirmed. The risk of bleeding in the setting of suspected small bowel bleeding (SSBB) in patients taking antiendothelins or anticoagulants has been poorly investigated.

Methods: Aim of this study was to evaluate diagnostic yield using video capsule endoscopy in OGB patients taking antiendothelins or anticoagulants. This is a retrospective review of chronic users of antiendothelins or anticoagulants who underwent VCE for SSBB. Small bowel findings were evaluated using Miracam VCE (Intromedic, Korea). Results: 264 patients (134 women, mean age 72.3 years, 55% occult SSBB) underwent VCE from January 2014 to March 2018 for SSBB. 162 out of 264 patients were taking antendothelins or anticoagulants agents. 44 patients were taking 100 mg of enterico-coated aspirin, 24 taking thienopyridine (ticlopidine or clopidogrel), 39 taking aspirin combined with thienopyridine (combined group), 27 taking warfarin and 28 patients taking NOAC (20% dabigatran, 32% apixaban, 48% rivaroxaban). Diagnostic yield in this specific cohort was 52%. Signs of clinical lesions were most frequently detected in the “combined” group (74.3%) among the five groups (aspirin group 52.2%, NOAC group 50%, warfarin group 48.1%, thienopyridine group 41.6%) (p = 0.037).

Conclusion: The risk of small bowel bleeding associated to antendothelin or anticoagulant therapy seems to be increased in patients taking the combination of aspirin and thienopyridine and preventive strategies in this group should be established. The risk related to novel oral anticoagulants seems to be similar to that for warfarin and aspirin alone.

Disclosure: Nothing to disclose.
Introduction: A typical capsule endoscopy case generates several thousand images, with abnormalities often confined to a just few frames. The use of rapid reading software has become common place in an attempt to reduce reading times. There is concern that use of such software may result in an unacceptable number of missed lesions. Omni Mode is novel EndoCapsule software algorithm, which aims to intelligently remove duplicate images whilst maintaining lesion detection. Here we present the interim results of a multi-centre European study of the use of Omni Mode in daily clinical practice.

Aims and Methods: This study took place across 9 European centres, using real life cases. Patients undergoing a clinically indicated capsule endoscopy had their case read at their local centre using standard reading, with every captured frame reviewed for any ‘pragmatic ‘real life’ approach was adopted, with readers using their usual viewing mode and speed. These cases were then anonymised and randomly allocated to another centre where this was read using Omni Mode. Detected lesions and reading time was recorded, with findings compared between both viewing modes. All lesions were reviewed and classified according to type and severity using the P-Classification. Where lesions were missed, a review of the Omni Mode reading stream was conducted at 10fps, to determine whether they were missed by the viewer or had been excluded by the software.

Results: Here we report the preliminary results for the first 210 cases analysed. The patient population undergoing capsule endoscopy had a mean age of 60.8 years (range 18-91), with a Male to Female ratio of 1:1.1. The investigation of anaemia or overt gastro-intestinal bleeding accounted for 68% of cases. A total of 1732 lesions were identified, which were classified according to the P-Classification as P0 (927), P1 (550) and P2 (255). Lesions were identified using both reading modes in 48.3% (n=856). 320 lesions seen in normal mode were missed using Omni Mode, of which 229 were P0, 66 were P1 and 25 were P2. When the viewing stream in Omni mode was evaluated, it was noted that only 4% (n=13) of the missed lesions were removed from the reading stream (P0 2%, P1 8%, P2 0%). A greater proportion of lesions were missed during standard reading, that using Omni Mode (n=516).

Conclusion: These preliminary results suggest that Omni mode has an acceptable accuracy and is associated with a significant reduction in reading time. Missed lesions using the standard reading mode were less likely to be due to loss of concentration due to time spent and the tendency to use faster reading speeds. Disclosure: Nothing to disclose

P1484 FEASIBILITY AND SAFETY OF ROBOTICALLY CONTROLLED MAGNETIC CAPSULE ENDOSCOPY IN THE VISUALIZATION OF UPPER GASTROINTESTINAL TRACT
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Introduction: Visualization of the upper gastrointestinal tract with capsule endoscopy was not possible because of the large cavity of the stomach and the lack of controlled movements. The Ankon robotically controlled magnetic capsule endoscopy (MACE) system has been developed to investigate the stomach visualization. The present prospective study was designed to evaluate the feasibility and safety of the Ankon MACE system in the visualization of the upper gastrointestinal (GI) tract in humans.

Aims and Methods: Our current prospective study enrolled 75 consecutively selected patients under the age of 40, with upper GI complaints or dyspepsia, but without any alarm symptoms. All subjects swallowed the Ankon MACE after drinking of one liter of clear water for gastric distension. An external robotic system with automatic preset programs applied to maneuver the MACE in the upper GI tract and generate a targeted magnetic field. The primary outcomes were the feasibility and usability of the MACE, including the quality of gastric preparation (excellent:4 good:3, moderate:2, poor:1), the level of visualization (complete, partially complete, none) of the Z line, the entire gastric mucosa (cardia, fornix, corpus, antrum), the duodenal bulb and the Vater papilla. We also assessed the feasibility of the esophageal withheld and active pyloric passage of the MACE with the targeted magnetic field.

Results: MACE was successful in all 75 patients with good to excellent visualization (mean score: 3.37) of the stomach and the entire small bowel without any complication or capsule retention. The visualization of the Z line was possible in 67/75 (89%), which was assessed as complete in 23 and partially complete in 44 patients. The mean stationary time for MACE in the esophagus was 1 min and 32 sec. Complete visualization of the cardia, fundus, corpus, antrum, angulus and duodenal bulb was possible in 100%, 100%, 100%, 100% and 100% respectively. We were able to visualize the Vater papilla in only 20 patients. The possibility of successful pyloric passage of the MACE with the targeted magnetic field without administration of intravenous metoclopramide was possible in 55 patients (73.3%). The following MACE 10 patients under the upper GI endoscopy to take history due to the following pathologies detected by MACE, such as one patient with gastric lymphoma, three patients with hyperplastic polyps, five patients with severe erosive gastritis and one patient with duodenal ulcer.

Conclusion: Our present study proved that robotically controlled MACE is easy to perform, non-invasive, safe method with excellent maneuverability in the upper GI tract, and has a future potential to detect and diagnose upper gastro-intestinal disorders including esophageal, gastric and small bowel pathologies.

Disclosure: Nothing to disclose

P1485 INVESTIGATING IRON-DEFICIENCY ANAEMIA WITH SMALL BOWEL CAPSULE ENDOSCOPY: IS HAEMOGLOBIN A RELIABLE PREDICTOR OF POTENTIALLY BLEEDING LESIONS?
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Introduction: Capsule endoscopy (CE) is a first-line diagnostic tool for iron-deficiency anemia (IDA) evaluation after a negative bidirectional endoscopic study. Whether haemoglobin level is a predictor of potentially bleeding lesions (P2) in small bowel capsule endoscopy (SBCE) remains controversial.

Aims and Methods: Determine the influence of haemoglobin levels on diagnostic yield of SBCE for P2 lesions in patients with IDA. Prospective single-center study including consecutive patients submitted to SBCE over 12 years for IDA. The minimum value of haemoglobin observed between the diagnosis of IDA and the performance of the exam was considered. The lesions were described using Saurin et al. classification.

Results: 289 patients were included, 211 females (73.0%), mean age of 61.6±18.7 years. The overall diagnostic yield was 60.6%, with identification of 100 P2 lesions (34.6%). A statistically significant association was found between the presence of P2 lesions and haemoglobin levels (68.3±17.6 vs 58.1±18.3, p<0.001), male gender (36.0% vs 22.2%, p=0.02), haemoglobin levels (8.6±2.0 g/dL vs 9.3±1.7 g/dL, p=0.003), smoking habits (23.0% vs 12.7%, p=0.03), diabetes (10.0% vs 3.7%, p=0.004), Charlson index (5.2±3.2 vs 3.5±3.4, p<0.001), arterial hypertension (70.0% vs 49.7%, p=0.001), chronic kidney disease (31.0% vs 19.6%, p=0.04), heart failure (39.0% vs 20.1%, p=0.001), chronic obstructive pulmonary disease (47.4% vs 7.4%, p<0.001) and proton pump inhibitors use (62.0% vs 48.7%, p=0.04). At logistic regression analysis only haemoglobin levels (p=0.02) were independently associated with the diagnosis of P2 lesions. Although haemoglobin levels showed a weak discriminative capacity for the diagnosis of P2 lesions (AUC=0.60, p=0.005), values ≤7.7 g/dL were associated with a higher likelihood detection of P2 lesions.

Conclusion: Haemoglobin values may help guiding the decision to study the small-bowel in patients with IDA, since values ≤7.7g/dL are predictive of potentially bleeding lesions.

Disclosure: Nothing to disclose

Reference

P1486 BULKING AND LAXATIVE EFFECTS OF KIWIFRUIT DIETARY SUPPLEMENTATION: NOVEL MRI IMAGING INSIGHTS
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Introduction: Chronic constipation affects approximately 17% of the population worldwide and remains an important unmet need as patients are often dissatisfied with treatment. Kiwifruit may offer an alternative to traditional laxatives and have been shown to increase stool volume and frequency (1). Using novel validated non-invasive MRI techniques (2,3), we assessed fluid distribution in the small and large intestine and colon volumes.

Disclosure: Nothing to disclose

Reference
Aims and Methods: A two-period crossover trial of kiwifruit versus control in healthy participants recruited from the general population. Participants underwent MRI scans on the third day, including a fasted scan, meals, and scan 4 h after first meal. Participants underwent MRI scans on the third day, including a fasted scan, meals, and scan 4 h after first meal. Results: The study was completed by 14 participants, 6 male, 8 female, with a mean age of 26 (range 21–33) years. SBWC AUC was markedly increased in participants consuming kiwifruit, 59.4 l/min as compared to control arm of the study (243.2 ± 46.2 l/min; P = 0.004). Transit time did not change (P = 0.11). Stool frequency was significantly increased during the kiwifruit week (1.60 ± 0.24 stools per day) compared to the control per month. The average increase in size was of 5.2 mm, with the largest difference being of 12 mm at 24-month follow-up. 3.2% (n = 2) of those radiologically followed-up developed concomitant PADC in our cohort of 141 BD-IPMN patients with surveillance imaging was of 2.1% (in 48) whereas the general population-matched lifetime risk in Malta is 1.5% (in 68), resulting in a relative risk of 1.4. The risk increases further to 3.4% (1 in 29) when BD-IPMNs measuring < 10 mm are excluded, with a relative risk of 2.3.

Conclusion: BD-IPMNs lacking complex features still harbour the potential for interval growth. The risk increases further with larger BD-IPMNs. The relative risk of concomitant development of pancreatic adenocarcinoma in our patient cohort was found to be higher than the general population. Given these findings, active long-term surveillance is warranted in all incidental BD-IPMNs, even in the absence of complex features, especially if over 10 mm in size.

Disclosure: Nothing to disclose.

References

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Introduction: Patients presenting to the Emergency Room with abdominal pain frequently undergo urgent CT scans, often revealing bowel wall thickening (BWT). In the absence of guidelines to address the issue, endoscopic evaluation is carried out in most of them, while only a proportion of patient have significant pathology. The study aims to evaluate the clinical relevance of such BWT and assess predictors of significant pathology on endoscopic evaluation.

Aims and Methods: Patients referred to Gastroenterology Service from the Emergency Department at Hamad General Hospital with bowel wall thickening on CT scans between July 2015-July 2017 were retrospectively analyzed. Apart from the CT features, correlation of endoscopic findings to clinical presentation, laboratory parameters and histopathology were studied.

Exclusion Criteria: 1. Patients who underwent endoscopic evaluation were included in final analysis.
2. In the case of a negative endoscopy, patient had follow up of at least 6 months to exclude GI Condition.
3. Patients with known GI Pathology (IBD, malignancy).
4. Evidence of luminal obstruction, stricture or mass on CT scan.

Results: 109 of 160 referred patients satisfied criteria for study inclusion. Endoscopic appearance was normal in 37(109/33.9%). Significant findings

P1488 SIGNIFICANCE OF BOWEL WALL THICKENING ON EMERGENCY ROOM CT SCANS
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Introduction: Patients presenting to the Emergency Room with abdominal pain frequently undergo urgent CT scans, often revealing bowel wall thickening (BWT). In the absence of guidelines to address the issue, endoscopic evaluation is carried out in most of them, while only a proportion of patient have significant pathology. The study aims to evaluate the clinical relevance of such BWT and assess predictors of significant pathology on endoscopic evaluation.

Aims and Methods: Patients referred to Gastroenterology Service from the Emergency Department at Hamad General Hospital with bowel wall thickening on CT scans between July 2015-July 2017 were retrospectively analyzed. Apart from the CT features, correlation of endoscopic findings to clinical presentation, laboratory parameters and histopathology were studied.

Exclusion Criteria: 1. Patients who underwent endoscopic evaluation were included in final analysis.
2. In the case of a negative endoscopy, patient had follow up of at least 6 months to exclude GI Condition.
3. Patients with known GI Pathology (IBD, malignancy).
4. Evidence of luminal obstruction, stricture or mass on CT scan.

Results: 109 of 160 referred patients satisfied criteria for study inclusion. Endoscopic appearance was normal in 37(109/33.9%). Significant findings
confirmed as chronic pathology were found in 41/109 (37.6%) patients. Of these, 21 (19.1%) had IBD (13 Crohn’s Disease (11.9%), 8 Ulcerative Colitis (7.3%), and 9 (8.3%) had Tuberculosis, 10 (11.0%) had malignancy. Mucosal abnormalities but normal or acute inflammation on histopathology were observed in 31/109 (28.4%) patients. Segment based diagnosis and distribution in Table 1. A previous report had no correlation with significant findings. Symptom duration was the strongest predictor of significant endoscopic findings (> 2 weeks 25/35, 71.4% vs < 2 weeks 16/74, 21.6%; P < 0.001). Features such as blood in stool, fever and weight loss were also positively associated with having significant findings. Laboratory parameters, WBC, Hemoglobin, INR, Albumin and CRP were not correlated with IBD. Mean Hemoglobin (10.5 ± 2.1 vs 12.8 ± 1.9; P = 0.001) and Albumin (27.5 ± 6.7 vs 35.4 ± 10.8; P = 0.008) were significantly lower in the malignancy group. Calprotectin was done in 36/109 patients. Mean Hemoglobin (10.5 vs 12.8; P = 0.001) and Albumin (27.5 ± 6.7 vs 35.4 ± 10.8; P = 0.008) were significantly lower in the malignancy group. Calprotectin was done in 36/109 patients. Mean Calprotectin was significantly higher with IBD and TT (199.5 ± 299.8 vs 809.9 ± 540.8; P < 0.001).

Four radiologically reported parameters – fat stranding, lymphadenopathy, vascular engorgement and pelvic free fluid were analyzed from CT reports. Of these only fat stranding was associated with IBD or TT (20/46, 44% vs 10/52, 19%; P = 0.001).

Conclusion: One-third of study patients had significant pathology (IBD/TT/ Malignancy). Two thirds of patients have a negative endoscopy or acute inflammatory findings on endoscopy. Prospective data may guide patient selection for endoscopic evaluation in patients with Bowel Wall Thickening on CT scans.

<table>
<thead>
<tr>
<th>Normal or Crohn’s</th>
<th>Ulcerative</th>
<th>Acute Disease</th>
<th>Colitis</th>
<th>Tuberculosis</th>
<th>Malignancy</th>
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<td>1</td>
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<td>Junction (3)</td>
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<td>0</td>
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<tr>
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<tr>
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<td>Total</td>
<td>68</td>
<td>13</td>
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</table>

[Segment based diagnosis and distribution]

Disclosure: Nothing to disclose

References

Fluorescence imaging with EP-HMRG would be useful for detection of early carcinoma of the esophagus.
Results: Of the 8 PICRCs, 3 were detected at subsequent BCSP procedures, one at 1 year surveillance, and 2 following re-invitation for screening at 2 years. Five were detected outside the BCSP.

Conclusion: 1. The PICRC-3y in the BCSP is 6.35%, higher than the rate in the published literature (4.4%-7%) and the corresponding rate for Post Colonooscopy Colorectal Cancer (PCCRC) over the same period (2.5%).

2. CTC is commonly reserved for patients who are either deemed unsuitable for colonoscopy, or in whom colonoscopy has failed, meaning that there are likely to be substantial differences between the populations undergoing each examination. 3. PICRC and CTC are different populations, having CTC more likely to be fraught with greater co-morbidity, the higher rate of PICRC when compared to colonoscopy may relate to the difficulty of investigating such patients, who may not be fit enough for, or refuse an intervention even if a lesion is found.

Disclosure: Nothing to disclose

Reference

P1491 IN VIVO DIAGNOSIS OF FOOD ALLERGY WITH CONFOCAL ENDOMICROSCOPY

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Introduction: The immune-mediated adverse reaction to food is defined as food allergy. Food allergy can be divided into IgE mediated or non-IgE mediated food allergy. In the majority of cases, while light endoscopy is unremarkable in patients with food allergy and hence, obtaining several biopsies within the upper and lower GI tract is an integral part in the work-up of suspected food allergy. Within this study, we aimed to assess the potential of probe-based confocal laser endomicroscopy (pCLE) as an advanced endoscopic imaging technique allowing for in vivo microscopic imaging of the intestinal mucosa for the diagnosis of food allergy.

Aims and Methods: 29 Patients with suspected food allergy manifesting with dietary-induced abdominal pain and diarrhea were included. From all patients detailed clinical information were obtained including parameters of food allergy or intolerance and diagnostic criteria of irritable bowel syndrome. In all patients ileocolonoscopy was performed using high-definition endoscopes with digital chroendoendoscopy. Intestinal lavage with quantification of a large panel of markers of food allergy or intestinal inflammation including TNF, food specific IgE and eosinophilic cationic protein was performed in the terminal ileum, the cecum and the rectosigmoid junction in all patients. At these sites real-time microscopic imaging with pCLE was performed after intravenous contrast with 10% fluorescein.

Results: Of 29 patients (mean age 53 years) with suspected food allergy manifesting with dietary-induced abdominal pain and diarrhea, were included. From all patients detailed clinical information were obtained including parameters of food allergy or intolerance and diagnostic criteria of irritable bowel syndrome. In all patients ileocolonoscopy was performed using high-definition endoscopes with digital chroendoendoscopy. Intestinal lavage with quantification of a large panel of markers of food allergy or intestinal inflammation including TNF, food specific IgE and eosinophilic cationic protein was performed in the terminal ileum, the cecum and the rectosigmoid junction in all patients. At these sites real-time microscopic imaging with pCLE was performed after intravenous contrast with 10% fluorescein.

Conclusion: Without fluorescent label, multiphoton imaging (MPM) could directly reveal tissue architecture based on two-photon excited fluorescence (TPEF) and second harmonic generation (SHG). In this study, we aimed to explore the feasibility of MPM to assess the gastric tumor morphology and infiltration.

Aims and Methods: Unstained slides of 18 fresh gastric tissues with different T staging were examined by multiphoton microscopy. Morphological and quantitative analysis were studied. Nuclear area was defined as the area of the nuclear profile and the boundary. Collagen content was the ratio of the SHG pixels over whole pixels.

Results: Gastric normal and tumor tissues under different T stages were visually presented with cellular and subcellular features on fluorescent imaging. Nuclear area of normal and cancerous cells were 32.01 ± 2.89μm² and 38.41 ± 6.09μm² (P < 0.001). Collagen contents were quantified by 0.087 ± 0.012 in normal mucosa but 0.020 ± 0.007 in cancerous mucosa (P < 0.001). All results were correlated well with the paired H&E stained slides.

Conclusion: Our findings support the proving potential of MPM for judging T staging of gastric cancer. Without staining intervention, TPEF and SHG on MPM could objectively and quantitatively indicate the subcellular and molecular changes during carcinogenesis. With the advancement of deep penetration, self-focusing multiphoton and 3D visualization, label-free multiphoton imaging combined with endoscopy could be further introduced to realize a real-time in vivo assessment of tumor invasion clinically.

Disclosure: Nothing to disclose

P1493 DO WE UNDERESTIMATE THE ROLE OF HYPOTHALAMIC-PITUITARY-ADRENAL AXIS ACTIVATION BY GLP-1/GLP-1 RECEPTOR AGONIST TREATMENT? FIRST DATA FROM GLP-1 RECEPTOR POSTION EMISSION TOMOGRAPHY OF THE HUMAN PITUITARY

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Introduction: We have developed a technology for in vivo imaging of the GLP-1/glucagon receptor (GLP-1R) using Ga-68-NODAGA-exendin (Ga-68-NODAGA-exendin) for PET/CT (position emission computed tomography / computed tomography), This technology enables non-invasive in vivo quantification of radiotracer uptake into tissues, representing a measure for GLP-1R density. During clinical studies measuring beta cell mass with this technology in patients with diabetes, we have observed a high uptake into the dorsal pituitary. Here, we analyse the first in human imaging data of the pituitary and formulate a hypothesis concerning the role of pituitary GLP-1R signaling.

Aims and Methods: Pituitary uptake in Ga-68-NODAGA-exendin for PET/CT scans obtained in prospective clinical studies in patients before and after bariatric surgery was quantified. Patients with type 2 diabetes (T2D) and morbid obesity (body mass index (BMI) >40 or BMI >35 with co-morbidity) prior to or 1 year after bariatric surgery were included. PET/CT from pelvis to skull was performed one hour after injection of 100 MBq of Ga-68-NODAGA-exendin. The maximum standardized uptake value (SUVmax) was measured in a volume of interest (VOI) placed in the sella turcica.

Results: To date, we have collected data from 4 patients after bariatric surgery (the last patients from a finalized cross-sectional analysis pre/post bariatric surgery) and 9 patients before bariatric surgery (from an ongoing longitudinal study). Analysis of these data revealed a marked inter-individual difference in the pituitary radiotracer uptake but also a clear higher uptake in patients prior to bariatric surgery. The uptake ranged from 0.83 to 2.8 (average 1.81 ± 0.99) in the post bariatric surgery group and from 1.9 to 9 (average 4.5 ± 2.46) in the pre bariatric surgery group, with only a slight overlap between groups. No uptake in other tissues was observed, except in one post-stomach surgery patient with a history of a goiter.

Conclusion: Although the number of patients analysed so far is limited and we have switched to whole-body scanning only during a running a cross-sectional study in order to assess the tissue distribution of GLP-1R in humans, the highly non-invasive in vivo quantification of radiotracer uptake into tissues, representing a measure for GLP-1R density, during clinical studies measuring beta cell mass with this technology in patients with diabetes, we have observed a high uptake into the dorsal pituitary. Here, we analyse the first in human imaging data of the pituitary and formulate a hypothesis concerning the role of pituitary GLP-1R signaling.

Disclosure: Nothing to disclose

References
PI1494 SPATIO-TEMPORAL MAPPING OF GASTROINTESTINAL MOTILITY USING MRI AND COMPUTER POST-PROCESSING: A PROOF OF CONCEPT STUDY

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Introduction: MRI is increasingly used to assess gastrointestinal motility and post-processing methods add value through objectively assessing the presence or absence of contractile activity. Such metrics often do not offer insights into the nature of contractile action, their presence or absence. Greater insight may be needed to determine how changes in contractile frequency, amplitude or contraction length may be associated with gastrointestinal symptoms. The aim of this proof of concept study was to evaluate preliminary validation of an MRI based method to generate a spatio-temporal map of contractile activity in the stomach and colon.

Aims and Methods: Two cohorts of subjects were selected displaying 1) gastric (n=24) and 2) colonic motility (n=20). Subject preparation and disease status was heterogeneous to provide a spectrum of motility on which to test the spatio-temporal motility assessment technique. The technique involved delineating the boundaries of the inner and outer border of the gastrointestinal tract. A series of diameter measurements were made automatically at a 2mm interval orthogonal to the central axis of the lumen. These measurements were automatically propagated through the time series using a previously validated image registration algorithm. Contractions were quantitatively summarised with two methods measuring 1) Normalised Contraction Plot (NCP) and 2) Combined Velocity Distance (CVD). Both metrics were correlated against a three-point subjective but consensus scoring system for the gastric data and a previously validated numerical, semi-quantitative scoring system for the colonic data.

Results: Good correlation was seen between reader scores and both motility metrics (NCP, R=0.85, P<0.001; CVD, R=0.93, R<0.001) in the gastric data. Good correlation was also seen between the reader scores and the two metrics in the colonic data (NCP, R=0.82, P<0.001, CVD, R=0.78, R<0.001).

Conclusion: Spatio-temporal mapping of the stomach and colon correlates well with subjective scoring of both a consensus and quantitative means of assessing contractile activity in the gastrointestinal tract.

Disclosure: Alex Menys is the CEO of Motient Ltd.

PI1495 SHORT-TERM AND LONG-TERM OUTCOMES OF SELF-EXPANDABLE METALLIC STENT PLACEMENT AS A BRIDGE TO SURGERY FOR MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: In Japan, self-expandable metallic stent (SEMS) placement for malignant colorectal obstruction has been performed from 2012. However, SEMS placement as a bridge to surgery (BTS) is not recommended in the Evidence-Based European Society of Gastrointestinal Endoscopy (EBESE) Guideline. Additionally, malignant effects of SEMS placement as BTS on long-term outcomes have not been broadly recognized. Therefore, we retrospectively reviewed the records of patients to clarify the safety and efficacy of SEMS placement and showed the long-term outcomes of BTS.

Aims and Methods: Three-hundred-ninety-two patients who underwent surgery for colorectal cancer (pStages II, III, and IV) in our hospital from May 2012 to August 2017 were reviewed. Of the 392 patients, 54 patients with malignant colorectal obstruction underwent BTS (group A), and 338 patients without malignant colorectal obstruction underwent surgery (group B). First, we evaluated short-term outcomes of the BTS group. Second, we compared long-term outcomes between the two groups as the 3-year overall survival (3yOS) and 3-year disease-free survival (3yDFS) rates for each group.

Results: Patients' mean ages were 70 years (group A) and 73 years (group B), and the male-to-female ratios were 25:29 (group A) and 182:156 (group B). Tumor sites (ecum:ascending/transition/descending/sigmoid/rectum) were 2/6/5/32/1 (group A) and 135/57/60/19 (group B). In group A, we treated 45 patients (83.3%), and synchronous multiple cancers in the proximal colon were found in 8 patients (14.8%). The only severe complication of SEMS placement was one case of perforation due to obstructive colitis. Regarding long-term outcomes, 3yOS/3yDFS rates were 95%/83.1% (group A) and 88%/81.9% (group B) in pStage B, and 66.2%/57.3% (group A) and 87.2%/66.2% (group B) in pStage III. The 3yOS rates were 42.0% (group A) and 35.1% (group B) in pStage IV. No significant differences were observed between the groups in long-term outcomes (median follow-up periods were 763 days in group A and 738 days in group B), until the Kaplan-Meier method and long-rank test.

Conclusion: SEMS placement can be effectively and safely performed, and contribute to preoperative evaluation of the proximal colon. According to long-term outcomes, the BTS group was not inferior to the normal surgery group despite the high malignant potential due to malignant colorectal obstruction. These findings suggest that the malignant effects of SEMS placement as BTS on long-term outcomes may be small in cases in which the perforation rates were low.

Disclosure: Nothing to disclose

PI1496 THE BOUGIECAP: A NEW METHOD FOR TREATMENT OF OESOPHAGEAL STRICTURES

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Introduction: Non-malignant strictures in the upper GI tract are often treated endoscopically by using polyvinyl Savary-Gilliard dilators. However, the drawbacks to this technique are the lack of direct optical feedback of the bougie and the need for fluoroscopic guidance during the procedure. A novel device, BougieCap (Ovesco, Tuebingen, Germany), allows direct optical control of bougienage.

Aims and Methods: Patients with a benign stenosis of the oesophagus and with or without recent adverse reactions recruited from two endoscopy centres for planned dilation with the BougieCap. The device, which is a single-use trans- parent conical cap, is fixed to the tip of the endoscope. Different sizes for standard gastroduodenoscopy and pediatric scopes are available. For the bougienage procedure, the endoscope is positioned frontally in the stenosis. Under direct vision, pushing forward with the endoscope enables the conical cap to dilate the mucosa in the area of the stenosis by the conversion of longitudinal force vectors into radial force vectors. Endoscopic procedure could be repeated sequentially with a larger sized cap if necessary. Primary endpoint of the study was success of endoscopic dilation. Secondary endpoint was improvement of symptoms of dysphagia as assessed by Dysphagia Handicap Index (DHI) before and 14 days after bougienage (dysphagia score 0: No dysphagia; able to eat normal diet; 1: Moderate passage: able to eat some solid food; 2: Poor passage: able to eat semi-solid foods; 3: Very poor passage: able to swallow liquids only; 4: No passage: unable to swallow anything).

Results: 23 patients (m/f, 11/12) underwent the procedure, mean age was 69.9 years (range 58.7-87). Etiology of stricture was benign (n=20) and malignant (n=3) (caustic ingestion (n=2) or unknown (n=1)). Median diameter of strictures was 9 mm (±2.3). Successful dilation with BougieCaps was possible in 91% (n=21) of patients. Symptoms of dysphagia decreased from a mean dysphagia score of 3.0 (±0.6) before endoscopic treatment to 1.7 (±0.7) 14 days after treatment (Mann-Whitney, p < 0.0001). A stiff guide-wire was used in 4 cases to aid with bougienage, exclusively using a pediatric scope. In two cases with a narrow stricture and no usage of guide wire treatment failed as a result of high resistance at the site of stricture causing buckling of the endoscope in the pharynx. Of average 2.3 (±0.2) BougieCaps of subsequent sizes were used per patient. No severe complications were reported. Adverse events were loss of 2 BougieCaps in the stomach causing no symptoms.

Conclusion: Endoscopic treatment of benign stenoses using the BougieCap enables direct visual control of the bougienage procedure and therefore of mucosal damage within the area of strictures. This might help to adapt endoscopic treatment to even more precisely to the structure. Symptoms of dysphagia are improved in short-term follow-up. Additional wall guidance is reasonable for selected cases (narrow lumen, pediatric scope).

Disclosure: Nothing to disclose

PI1497 SHORT AND LONG-TERM RESULTS OF SELF-EXPANDABLE METAL STENTS FOR ACUTE MALIGNANT COLORECTAL OBSTRUCTION

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Introduction: Self-expandable metal stents (SEMS) are widely used as an alternative to surgery for palliation purposes or as bridge-to-surgery (BTS) in acute malignant colorectal obstruction (MCRO), despite concerns about the effect of stenting on long-term clinical outcomes (long-rank test).

Aims and Methods: Our aim was to evaluate SEMS clinical success, AEIs and impact on short and long-term outcomes. We performed a retrospective study from 92 consecutive patients with acute MCRO that used SEMS in a tertiary center between January 2010 and December 2017.

Results: Forty-nine patients placed SEMS as BTS and 43 for palliative purposes. The median age of the patient population was 69 years (IQR 61–79), and 55.4% of the patients were male. Most of the obstructions (96.7%) were on the left colon. At the time of the procedure, based on additional imaging studies after colonic stenting and perioperative findings, 72.8% of patients (n = 67) had lymph node invasion and 58.7% (n = 54) had metastatic disease. Long-term clinical
success was achieved in 84.8% of the patients, with no significant differences between palliation and BTS groups (81.4% vs. 87.8%; p = 0.562). Clinical success was higher when tumor location other than sigmoid (94.3% vs. 78.9%; p = 0.047) and when shorter SEMS (≤110 mm) were placed (100% vs. 64%; p = 0.002). Immediate and post-procedure AEs occurred in 6.5% and 17.3% of the patients, respectively, with significant differences between the palliative and BTS group. The main post-procedure AEs were perforation (n = 6) and stent re-obstruction (n = 6). Nineteen percent of the palliative cohort were considered clinical failures, with 87.5% of them requiring further surgery; 11.6% of the patients in the palliative group were left with a permanent stoma; surgery-related AEs did not occur in patients with previous SEMS AEs; the occurrence of SEMS AEs did not influence overall survival. Twelve percent of the patients in the BTS group were considered clinical failures. Surgery was performed after a median time of 10 days (IQR: 7–15) following an urgent in 12.2% of patients; 16% of the BTS group were left with a permanent stoma. SEMS immediate (p = 0.542) and post-procedure AEs (p = 0.360) were not associated with tumor recurrence. Patients with post-procedure SEMS AEs had an inferior overall survival (median: 161 vs. 117 months; HR: 1.447; p = 0.047). In the multivariate Cox analysis, only SEMS-related AEs were independently associated with overall survival estimation (HR 4.06, 95% CI 1.2–13.7; p = 0.024).

Conclusion: SEMS allow relief of acute MCRO, yet AEs are seen in almost 20% of patients. Main contributors for surgery after stent failure are perforation and stent re-obstruction. SEMS should be the first line option for palliation even in patients with longer life expectancy. In the BTS setting, SEMS-related AEs decrease survival.

Disclosure: Nothing to disclose.

P1498 TWO DECADES AFTER THE FIRST, WHAT ARE THE OUTCOMES OF DUODENAL STENTING: EXPERIENCE OF A FRENCH TERTIARY CENTER ABOUT 220 CASES
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Introduction: Malignant gastric outlet obstruction (MGOO) often complicates the natural history of pancreatic adenocarcinoma but not only. However, the use of gastroduodenal self-expandable metal stents (GD-SEMS) has improved life’s quality of these patients. In current practice, the effectiveness of these GD-SEMS seemed imperfect and we wanted to report our results including all neoplastic diseases.

The main aim was to evaluate patients’ diets using the level of oral intake score (LOIS; 0: no oral intake, 1: liquids only, 2: solid, 3: full diet). The secondary endpoint was the evaluation of the complication rate, the median survival, the endoscopic duodenal reinsertion rate, the endoscopic biliary reinsertion rate, as well as the attempt to identify groups where the efficiency would be better or worse.

Aims and Methods: We retrospectively included all patients who underwent one or more GD-SEMS between January 2011 and December 2016 in our center (Pouls-Calmettes Institute Marseille, France). All data was calculated using the computerized record of each patient including dietary assessments and medical observations.

Results: We included 220 patients (women = 56%, mean age = 67 [29–94]). Median time of hospitalization was 7 days [1–52]. 50% of patients had pancreatic adenocarcinoma and another one had another malignant disease. WHO score was inferior or equal to 3 in 122/220 cases (55%). The two most frequent locations of MGOO are second duodenum (91/220 = 41%) and genu superius (46/220 = 21%). 66% of the patients (145/220) had already undergone oncological treatment before the first stent placement and 34% (75/220) had received no treatment. Median LOIS before GS-SEMS was 0[0–2] and median LOIS after was 2[0–3]. Median increase of LOIS was 2 (p < 0.001). This increase of LOIS patients was more important for patients with general state preserved (WHO score <3): 1.90 vs 1.40; p < 0.001. The complication rate was 2%/4 (220) with 3 perforations. The median survival was 4 months. At 1 month, the duodenal reinsertion rate and the biliary reinsertion rate were respectively 27% and 19%. During follow-up, 150/220 (68%) patients needed only one duodenal procedure and 70/220 (32%) had multiple duodenal procedures. The median permeability of GD-SEMS was 2.3 months and GD-SEMS was significantly more effective in the WHO score <3 group versus WHO score ≥2 group (3.81 vs 1.51; p < 0.001). Median permeability was also better significantly in the subgroup oncological treatment post GD-SEMS than subgroup no oncologic treatment post GD-SEMS (4.76 vs 1.25; p < 0.001). No significantly difference was observed between subgroups pancreatic cancer and other malignant diseases (2.37 vs 2.17; p = 0.733).

Our study is in agreement with the data of the literature. GD-SEMS are thought imperfect, effective on dysphagia with a low risk of complications (2%). Unlike the clinical impression we had, multiple endoscopic procedures are not systematic since they concern only 32% of patients. The duration of hospitalization is usually long probably because it is about fragile patients whose duodenal stricture is not the only health problem. Given the very low median survival (4 months), this endoscopic treatment seems to always be adequate or even sufficient in most cases. However, the subgroup analysis makes it possible to identify a subgroup for which the efficiency is better and more durable (WHO score <3, palliative chemotherapy post GD-SEMS). This subgroup could represent in the future the good candidates for endoscopic bypass.

Disclosure: Nothing to disclose.

P1499 BARIATRIC ESOPHAGEAL STENTS AND ENDOSCOPIC SUTURING SYSTEM FOR ENDOSCOPIC MANAGEMENT OF POST-LAPAROSCOPIC SLEEVE GASTRECTOMY LEAKS: A SINGLE-CENTER EXPERIENCE
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Introduction: Sleeve gastrectomy (SG) is one of the most popular bariatric surgical procedures, with a five-year survival rate of 94% and a total weight loss of 60%. However, SG morbidity is still high, with the most feared complication after laparoscopic sleeve gastrectomy (LSG), causing significant morbidity and mortality. Endoscopic treatment with fully covered self-expandable metal stents (FC-SEMS) may offer a useful non-invasive approach in this setting. Beta™ esophageal stents (Taewoong Medical Co., Gyeonggi-do, South Korea) are FC-SEMS specifically designed for post-bariatric leaks to reduce risk of migration. Moreover, endoscopic suturing with APOLLO OverStitch™ has been described as a therapeutic approach for large gastrointestinal leaks.

Aims and Methods: In this study, we aimed to report our experience in managing post-LSG leaks with Beta™ esophageal stents and APOLLO OverStitch™ suturing referred to our institution from June 2014 to July 2017. Type of endoscopic treatment, number of procedures, outcome and complications were analyzed.

Results: Thirteen patients treated using Beta™ esophageal stents for post-LSG leaks were included in this retrospective analysis. Eight patients (61.5%) received previous unsuccessful endoscopic treatments (pig-tail plastic stent, clips, conventional FC-SEMS). Eight patients (61.5%) who presented with larger leaks underwent combined endoscopic treatment with endoscopic suturing and TRB™ stent, while 5 patients (38.5%) with smaller leak were treated using only Beta™ stent. The overall success rate was 92.3% (12/13). One patient finally underwent gastroectomy after failure of multiple endoscopic procedures. A total of 16 Beta™ stent were placed, which were left in place for a median of 27 days (range 16–53). No stent migration or serious adverse events were observed during a mean follow-up of 3.6 months (range 0–11).

Conclusion: In our experience, endoscopic management of post-LSG leaks with Beta™ stent is safe and effective, with high rate of clinical success and no significant adverse events. The combined approach with APOLLO OverStitch™ endoscopic suturing system seems safe and effective in case of larger leaks. Further multicentric randomized controlled trial is needed to confirm these data.

Disclosure: Nothing to disclose.

P1500 ETOLOGICAL SPECTRUM AND RESPONSE TO ENDOSCOPIC BALLOON DILATION IN PATIENTS WITH BENIGN GASTRIC OUTLET OBSTRUCTION
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Introduction: Peptic ulcer disease (PUD) related gastric outlet obstruction (GOO) is known to respond favourably to endoscopic balloon dilation (EBD). However, data on efficacy of EBD for other etiologies of benign GOO is sparse.

Aims and Methods: We aimed to compare response of EBD among different etiologies of GOO.

Records of all patients with benign GOO who underwent EBD at our tertiary care centre between January 1998 to December 2017 were analysed. Dilation was performed using commercially available over-the-scope (TAELEN™) and BETATM stent, while 5 patients (38.5%) with smaller leak were treated using only Beta™ stent. The overall success rate was 92.3% (12/13). One patient finally underwent gastroectomy after failure of multiple endoscopic procedures. A total of 16 Beta™ stent were placed, which were left in place for a median of 27 days (range 16–53). No stent migration or serious adverse events were observed during a mean follow-up of 3.6 months (range 0–11).

Conclusion: In our experience, endoscopic management of post-LSG leaks with Beta™ stent is safe and effective, with high rate of clinical success and no significant adverse events. The combined approach with APOLLO OverStitch™ endoscopic suturing system seems safe and effective in case of larger leaks. Further multicentric randomized controlled trial is needed to confirm these data.

Disclosure: Nothing to disclose.
Endoscopic dilation is an efficient treatment for benign oesophageal strictures. By multivariate analysis, significant independent risk factors for LNM were found. Our study aimed to evaluate factors associated with a tumor-negative resection margin after gastrectomy and to evaluate the influence of hospital volume. The association of patient- and disease-related characteristics with irradicality was tested with multivariable regression analysis. The registration of complications according to the ECCG platform was validated.

**Aims and Methods:** This study aimed to evaluate factors associated with a tumor-negative resection margin after gastrectomy and to evaluate the influence of hospital volume. The association of patient- and disease-related characteristics with irradicality was tested with multivariable regression analysis.

**Results:** In total, 2799 patients were included. An irradical resection was seen in 263 (9.5%) patients. Factors associated with irradicality were: tumor located in the proximal stomach (OR[95% CI]: 2.44[1.46–4.03]), extensive tumor (OR: 2.33[1.40–3.88]), extent of invasion (OR[95% CI]: 2.987[1.100–8.111]), submucosal invasion (OR[95% CI]: 2.987[1.100–8.111]), and Lauren type (OR[95% CI]: 2.15[1.00–4.64]).

**Conclusion:** Tumor location, cT, pN, histological subtype and tumor differentiation are associated with irradicality. The association of irradicality with an annual hospital volume of <20 resections may underline the need for further centralization of gastric cancer care in the Netherlands.

**Disclosure:** Nothing to disclose.

**Reference**

rate and mortality in the Netherlands were comparable with the outcomes of the European Society for Medical Oncology. However, anastomotic leakage and pneumonia were more frequently reported in the Netherlands.

Disclosure: Nothing to disclose

References

P1505 NATIONALWIDE OUTCOME OF GASTRECTOMY WITH EN-BLOC PARTIAL PANCREATECTOMY FOR GASTRIC CANCER
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Introduction: Radical gastrectomy is the cornerstone of the treatment for gastric cancer. For tumours invading the pancreas, an en-bloc partial pancreatectomy may be needed to obtain a radical resection.

Aims and Methods: The aim of this study was to evaluate the outcome of gastrectomies combined with partial pancreatectomy for gastric cancer. Patients who underwent gastrectomy with or without a partial pancreatectomy for gastric cancer operation for intraduodenal junction cancer between 2011–2015 for gastric cancer were selected from the Dutch Upper GI Cancer Audit (DUCA). Outcome parameters were the pathological resection margin (pR0) and Clavien Dindo grade III post-operative complications. The association between partial pancreatectomy and severe postoperative complications was analysed with multivariable logistic regression. Overall survival was estimated using the Kaplan Meier method and subgroups were compared using log-rank test.

Results: Of 196 patients that underwent a gastrectomy, 55 patients (2.8 per cent) also underwent an en-bloc partial pancreatectomy. A pR0-resection was achieved in 45 of 55 patients (82 versus 85 per cent in the group with no additional resection, p = 0.82). Clavien Dindo grade III complications occurred in 21 of 55 patients (38 versus 17 per cent). Pancreatectomy increased the odds of having a Clavien Dindo grade III complication (OR: 3.13, 95 per cent c.i. 1.78–5.90). Median overall survival [95 per cent c.i.] of patients with partial pancreatectomy was 15[5–23.2] months, for patients with and without perioperative systemic therapy, it was 20[13–27.7] and 8[5–14.3] months, and for patients with R0 and R1/R2 resection it was 20[11.8–28.3] and 4[0–10.9] months.

Conclusion: Gastrectomy with partial pancreatectomy is associated with an pR0-resection rate of 82 per cent but an 3-fold increased risk for postoperative mortality.

Disclosure: Nothing to disclose

P1506 ROOT-CAUSE ANALYSIS OF SERIOUS ADVERSE EVENTS AFTER SURGERY FOR GASTRIC CANCER
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Introduction: In the Netherlands and Rotterdam region, postoperative mortality after surgery for gastric cancer was considerably higher than for any other type of cancer surgery.

Aims and Methods: To determine modes of failure and to develop proposals for preventive measures to decrease mortality, confidential review meetings were organised and supervised by a committee of experts.

Gastric cancer patients operated between 1999 and 2008 were selected from the regional cancer registry for 16 hospitals in the south-western part of the Netherlands. Per hospital, a maximum number of 9 cases with postoperative death or prolonged hospital stay were selected for review. Chart review was performed within the regional hospitals using an incident analysis tool the so-called Prevention and Recovery Information System for Monitoring and Analysis (PRISMA methodology). The primary goal of PRISMA is to systematically identify and classify causes of errors. Causes of error were classified into technical, organisational, human, patient-related or not specified using the Eindhoven Classification Model.

Results: The review comprised 106 patients with a median age of 74 years. There was considerable heterogeneity in protocols concerning diagnostic work up, surgery, postoperative care and treatment of complications between hospitals and surgeons. The most frequent technical complication was anastomotic leakage (n = 27) or duodenal stump dehiscence (n = 11). Some 56% of the operations were classified as high-risk procedures because of patient frailty or the extent of the cancer. Human error was considered contributory in 65% of the cases, mostly for not adapting the treatment plan or related to insufficient preoperative examination. Organisational failure was less important, with ‘culture of overconfidence’ listed as the main factor.

Conclusion: A qualitative approach is able to highlight modes of failure for gastric cancer surgery. This study shows that serious adverse events for gastric cancer surgery often tend to occur when three or more contributing causes coalesce, i.e. patient-, surgeon- and organisational factors. Outcome after gastrectomy for cancer could possibly be improved by regional audits that will reveal areas for improvement and stimulate standardization of (surgical) protocols.

Disclosure: Nothing to disclose

P1508 THE IMPACT OF BODY POSITION ON GASTRIC EMPTYING AFTER PANCREATICODUODENECTOMY
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Introduction: Abnormal gastric emptying velocity is a common complication after surgery of the upper intestine. Particularly after pancreaticoduodenectomy (PD), gastric emptying can be impaired (pylorus preserving procedure) or accelerated (classic Whipple procedure – pylorus resection). In this trial we aimed to study the impact of body position in gastric emptying in patients after PD and its impact on postprandial glucagon-like peptide-1 (GLP-1), insulin and glucose plasma concentrations.

Aims and Methods: 38 patients after PD, 19 subjects in sitting and 19 in supine position, were studied 2–118 (median: 19) months after the operation. Median age was 63 years, the male/female ratio 1:1, and body mass index 22.6 kg/m2. 21 of the patients had undergone a pylorus preserving PD and 17 a classical Whipple procedure. All subjects ingested a mixed liquid test meal containing 1 g acetylmonophen to measure gastric emptying. Before the meal and 10, 20, 30 and 60 minutes thereafter venous blood was drawn for the measurement of GLP-1, acetylmonophen, glucose, and insulin.

Results: Fasting glucose, fasting insulin, the early integrated concentrations of acetylmonophen and GLP-1 (0–30 min.) as well as integrated concentrations over 8 and 30 minutes of glucose and insulin were presented in Table 1. Gastric emptying speed revealed to be different between sitting and supine body position (Figure 1, Table 1). Postprandial GLP-1, insulin and glucose plasma concentrations showed no differences between the groups. Velocity of gastric emptying did not influence integrated insulin and glucose concentrations (0–60 min.). Body position had no impact on postprandial early integrated GLP-1 plasma concentrations.

Conclusion: Body position – sitting vs. supine – showed to have a significant effect on gastric emptying speed in patients after PD, sitting subjects emptied their stomachs faster. Be that as it may, no further impact of body position on postprandial glucose, insulin and GLP-1 plasma levels could be shown.

<table>
<thead>
<tr>
<th>Siting body position</th>
<th>Supine body position</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value*</td>
<td>p-value*</td>
</tr>
<tr>
<td>Acetylmonophen</td>
<td>Acetylmonophen</td>
</tr>
<tr>
<td>integrated 0–30 (mg/l × min)</td>
<td>322.5 (251.5–486.5)</td>
</tr>
<tr>
<td>Glucose</td>
<td>Glucose</td>
</tr>
<tr>
<td>fasting (mg/dl)</td>
<td>98 (88–114)</td>
</tr>
<tr>
<td>integrated 0–60 (mg/dl × min)</td>
<td>8005 (6705–9715)</td>
</tr>
</tbody>
</table>

Body position

(continued)
[Table 1. Acetaminophen, glucose, insulin and GLP-1 plasma concentrations after Pd in sitting and supine body position (median and quartiles).]

| GLP-1 | Sitting body position | Supine body position | p-value
|-------|-----------------------|----------------------|---------|
| fasting concentration | 3.9 (4–7.3) | 5.3 (2.9–8.8) | n.s.
| (mU/l) | integrated 0–60 | 10289 (775.1–2143.3) | 1067.7 (678.2–2550.6) | n.s.
| (mU/l x min) | 17 (12–20) | 16.5 (12.75–18.25) | n.s.
| GLP-1 | integrated 0–30 | 2270 (1405–2894) | 1322.5 (767.5–3170) | n.s.
| (pmol/l) | *Wilcoxon-test |

References

P510 LONGSTANDING POSTOPERATIVE FLUID COLLECTION INFLUENCES RECURRENT OF PANCROBATITARY MALIGNANCY
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Introduction: Postoperative abdominal fluid collection (PAFC) is frequently observed after surgery for pancreaticobiliary adenocarcinoma. The duration of PAFC differs among patients, and little is known about the effects of the presence and duration of PAFC. The aim of this study was to evaluate the effects of PAFC on the outcomes of surgery for pancreaticobiliary adenocarcinoma.

Aims and Methods: Data from 187 consecutive patients with pancreaticobiliary adenocarcinoma who underwent curative surgery between August 2005 and February 2017 were analyzed retrospectively. The presence of PAFC was evaluated on the APACHE II, fistula with an abscessed intra-abdominal communicating collection and the dominant model AT approach according to the type of fistula have not been evaluated. Thus, the originality of this study rests on the evaluation of the effectiveness of the EID according to the type of fistula.

Conclusion: The incidence of PAFC in patients with pancreaticobiliary adenocarcinoma after surgery was 76.5%, and 49.7% had longstanding PAFC. The presence of PAFC was not associated significantly with recurrence of pancreaticobiliary adenocarcinoma. However, longstanding PAFC was associated with the recurrence of pancreaticobiliary adenocarcinoma.

Disclosure: Nothing to disclose.

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Introduction: Fistulas are the main complication of sleeve gastrectomy (SG). Several types of fistulas are distinguished according to their communication with an abscess and/or an over-diaphragmatic involvement (Type I to III). Management with an endoscopic internal drainage (EID) using a double-pigtail stent has shown encouraging results. To our knowledge, the results of this approach with the type of fistula have not been evaluated. Thus, the originality of this study rests on the evaluation of the effectiveness of the EID according to the type of fistula.

Aims and Methods: This is a retrospective analysis of a prospective uncentered cohort of patients who developed a fistula after SG. The type of fistula was always classified initially by a CT scan with oral opacification: fistula without a communicating abscess (Type I), fistula with a communicating abscess (Type II), fistula with an abscessed intra-abdominal communicating collection and sodiuphagic (Type III). Our treatment algorithm consisted solely of the insertion of a naso-jejunal feeding tube (NJFT) for Type I fistulas and the placement of a NJFT with EID with or without surgical drainage depending on the septic status for type II and III fistulas. Several types of fistulas are distinguished according to their communication with an abscess and/or an over-diaphragmatic involvement (Type I to III).

Disclosure: Nothing to disclose.
The mean estimated size of the defect was significantly higher in type II and III versus type I, 2.8 mm (1–4) for type I, 11.2mm (5–20) for type II and 10 mm (5–15) for type III. The average scheduled endoscopic session required was significantly higher in type III (p = 0.001) I, II versus III), 2 (1–3), 2.7 (2–5) and 5.2 (2–10) for Type I and II, and III respectively. Number of unscheduled reinterventions were significantly higher in type III (p = 0.003). The NJFT was left in place significantly higher in type III (p = 0.001).

Conclusion: Our study shows that it is essential to characterize the type of fistula before the endoscopic treatment of post-sleeve fistulas to better guide the proper management. Our treatment algorithm is available for Type I and II with high clinical success rate. In addition, postoperative monitoring of patients is essential in order to detect a fistula as early as possible and avoid type III fistula requiring a complex endoscopic treatment with low success rate.

Disclosure: Nothing to disclose.

### P1512 EFFICACY OF ENDOSCOPIC VACUUM-ASSISTED CLOSURE WITH SELF-EXPANDABLE METALLIC STENT FOR POSTOPERATIVE ANASTOMOTIC LEAK OF GASTRIC CANCER


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**Introduction:** Post-operative anastomotic leak is a life-threatening complication with a high mortality rate at gastrointestinal surgery. Endoscopic vacuum assisted closure (EVAC) has been attempted as a new non-surgical treatment option for anastomotic leakage replacing previous self-expanding metal stents (SEMS). There were many reports of EVAC treatment for post-esophagectomy anastomotic leakage, but not for post-gastrectomy.

**Aims and Methods:** Between Jan 2007 and Feb 2018, total 39 cases of anastomotic leak occurred in patients who underwent gastrectomy for treatment of gastric cancer. Among them, 28 patients were treated with SEMS only, 7 patients were treated with EVAC following after SEMS failure, and 4 patient was initially treated with EVAC only. We compared clinical characteristics and therapeutic outcomes between patients treatment with EVAC or EVAC after SEMS (N=11) and patients treatment with only SEMS (N=28). Our aims are to compare the clinical outcomes of SEMS with EVAC treatment as a new anastomotic leak after gastrectomy and to discuss the efficacy of EVAC.

**Results:** Median follow up duration was median 17 months (range 0–48). All cases with EVAC treatment were healing successfully (11/11, 100%). Two cases of treatment failure occurred in patients who treated with SEMS (2/28, 7.1%). Median duration of EVAC treatment was shorter than SEMS treatment (15 days [range 6–47] in EVAC and 36 days [range 7–108] in SEMS). Relatively larger size leakage was treated successfully with EVAC treatment (median 2.1cm in EVAC and 1.0cm in SEMS). The anastomotic stenos was occurred in one patient of EVAC treatment (1/11, 9.1%) and in six patients with SEMS treatment (6/28, 21.4%) within 1 year.

**Conclusion:** As well as SEMS, EVAC can be the effective endoscopic treatment option for anastomotic leakage after gastrectomy. Considering the size of anastomotic leakage may be important in determining treatment options. Further large number randomized controlled trials are needed to define efficacy and benefit of EVAC.

### P1513 SURGICAL RESECTION FOR TREATMENT OF COLORECTAL POLYPS: A SINGLE CENTRE RETROSPECTIVE COHORT STUDY

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**Introduction:** In January 2014, the Dutch bowel screening program was introduced to reduce the mortality rate of colorectal cancer. Because of this program a rise in endoscopically found colorectal polyps is expected, which in turn will increase the number of surgical resections.

**Aims and Methods:** The aim of this study was to evaluate complications of surgically resected colorectal polyps and compare the amount of surgical resections and encountered malignancies before and after implementation of the Dutch bowel screening program.

This retrospective cohort study included patients who underwent surgical removal of colorectal polyps between January 2012 and December 2017. Patients with preoperatively established malignancy and polyposis were excluded.

Results: 143 patients were included. The surgical procedure was a segmental colectomy in 115 patients (80.4%). The procedures were laparoscopically in 79.7% (n = 114). Major complications (Clavien-Dindo ≥ 3b) occurred in 7 patients (4.9%), without mortality. The anastomotic leakage rate was 3.5% (n = 4).

In 2012, 3.2% of all conducted colonoscopies resulted in surgery (n = 18), compared to 5.8% in 2016 (n = 30). The overall malignancy rate before the implementation of the screening program was 28.9%, compared to 22.4% after the implementation (p = 0.46). High-dysplasia was seen in 77.4% of encountered adenomas before the implementation compared to 42.5% after implementation (p = 0.001).

**Conclusion:** After the implementation of the screening program the amount of surgically resected colorectal polyps almost doubled. Nevertheless the malignancy and high-grade dysplasia rate decreased.

Disclosure: Nothing to disclose.

### P1515 NAVIGATION SURGERY FOR LATERAL LYMPH NODE DISSECTION USING THREE-DIMENSIONAL PELVIC MODEL PRODUCED BY 3D PRINTER


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**Introduction:** Recent prevalence of three-dimensional (3D) printer has enabled to produce 3D model of internal organs easily. Although the usefulness of 3D model has been demonstrated in regard to parenchyma organ such as liver1 and kidney2, there are few reports as to the intestine. Total mesoenteric excision (TME) with lateral lymph node dissection (LLND) is the standard treatment for locally advanced rectal cancer in Japan. The branching patterns of iliac arteries and veins vary among individuals. Therefore, it is important to understand individual variations in advance of LLND. The anatomy of pelvic vessels is being evaluated using reconstructed 3D image of iliac arteries and its branches in selected patients in our institution3.

Here, we aimed to address the usefulness of pelvic 3D model as a navigation modality in LLND.

**Aims and Methods:** We selected patients who underwent resection of the rectum with LLND from June 2017 to March 2018. First, we made 3D images from enhanced computer tomography (CT). Arteries and veins were reconstructed using volume rendering technique. Vessels, nerves, ureters, muscle, and metastasized lymph nodes were reconstructed by defining as region of interest. Then, a pelvic 3D model was produced using the reconstructed 3D image.
Aims and Methods: The aims of this study were to evaluate the quality of TME, and the secondary endpoint was short-term patient demographics, operative details, and surgical outcome. The primary endpoint was the quality of TME, and the secondary endpoint was short-term patient demographics, operative details, and surgical outcome.

RESULTS

A total of 10 patients were operated with a mean age of 70 years (range 57–87). operation time was 226 minutes (156–263). There were no intraoperative complications. The average number of harvested lymph nodes was 9 (8–22). Overall positive margin rate was 0%. The hospital stay was 14 days. The median operative time was 226 minutes (156–263). There were no intraoperative complications. The average number of harvested lymph nodes was 9 (8–22). Overall positive margin rate was 0%. The hospital stay was 14 days.

Conclusion: A pelvic 3D model appeared useful as navigation in LLND and teaching residents and students pelvic anatomy.

Disclosure: Nothing to disclose

References


P1516 FEASIBILITY OF 2-TEAM TATME FOR LOWER RECTAL CANCER: SHORT-TERM OUTCOMES OF INITIAL TEN CASES

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Introduction: Transanal total mesorectal excision (tTME) seems to be a novel down-to-up approach for benign and malignant rectal disease. In addition, laparoscopic and taTME simultaneously (2-team tTME) against lower rectal cancer might be more promising approach. The aim of this study was to evaluate the short-term outcomes of 2-team tTME for lower rectal cancer.

Aims and Methods: A retrospective review was conducted on initial ten patients who underwent 2-team tTME from November 2017 to April 2018 in our single institution. All information was carefully reviewed and collected, including patient demographics, operative details, and surgical outcomes. The primary endpoint was the quality of TME, and the secondary endpoint was short-term adverse events in the patient treated with 2-team tTME against lower rectal cancer.

Results: Mean ages were 68 years, and 7 patients in male. The average BMI was 23.3 ± 2.8 kg/m². The average tumor distance from anal verge was 4.0 ± 2.0 cm. The median operative time was 226 minutes (156–263). There were no intraoperative complications including organ injury and conversion to open surgery. The median number of harvested lymph nodes was 9 (8–22). Overall positive CRM (≤1 mm) was 10% (n = 1) and 0%. Although postoperative complications were occurred in 8 patients (80%), there were no severe complications (Clavien-Dindo classification ≥ Grade3). The median length of hospital stay was 14 days.

Conclusion: Our results suggest that 2-team tTME for lower rectal cancer appears to be an oncologically safe and feasible with acceptable short-term outcomes. Further studies with more patients and longer follow-up are needed.

Disclosure: Nothing to disclose

P1517 THE BENEFICIAL USE OF STW 5 IN DSS-INDUCED COLITIS IS PARTLY DUE TO REBALANCING THE CHANGES IN GUT MICROBIOTA INDUCED BY DSS

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Introduction: DSS-induced colitis has been shown to affect rodent gut microbiota. STW5 (Iberogast®), a standardized medicinal preparation hydro-alcoholic herbal preparation, was shown to be effective in functional dyspepsia and irritable bowel syndrome and was shown experimentally to be effective against DSS-induced colitis through anti-inflammatory and antioxidant properties. Present study was designed to show whether the beneficial treatment of DSS-induced colitis with STW5 also involves its effect on gut microbiota.

Aims and Methods: The experimental model of colitis was induced in Wistar rats by administering 5% DSS in drinking water for 7 days. Treatment with STW5 was started at the same time as DSS administration by giving it orally once daily in a dose of 2 and 5 ml/kg. Rats were sacrificed 24 hours later and fecal samples from cecum were collected to study the taxonomic diversity of gut microbiota. Selected main microbial phyla and genera were quantified using quantitative Real Time-PCR.

Results: The abundance of Proteobacteria in the DSS-induced colitis group was increased more than 2 fold but this rise was largely prevented after co-administration of STW5. In addition, DSS colitis induced an increase in the relative abundance of the Bacteroidetes, Prevotella and Bacteroides. Within the Firmicutes phylum, DSS induced an abundance of Blautia which was almost completely prevented by co-administration of STW5. Furthermore, Blautia within the Firmicutes phylum was decreased in the DSS-induced colitis group, and the abundance was almost restored by STW5. The relative abundance of Eubacterium represented by Methanobrevibacter was markedly decreased in the DSS colitis group but slightly increased by STW5.

Conclusion: Many changes in gut microbiota induced by DSS have been prevented or reduced by STW5. This adds to our understanding of the mechanisms underlying the beneficial use of the herbal preparation in colitis induced by DSS.

Disclosure: Olaf Kelber and Heba Abdel-Aziz are employed by Steigerwald Arzneimittelwerk GmbH. Other authors have nothing to disclose.
P1519 RELATION OF CIRCULATING PROTEIN S (PROS1) WITH INFLAMMATORY BOWEL DISEASE (IBD) ACTIVITY, PATTERNS, AND C-4 BINDING PROTEIN (C4BP)

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Introduction: Inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn’s disease (CD) show an increased risk of thrombosis, complication where decreased levels of circulating PROS1 may play a role. PROS1 is a well-established inhibitor that works mainly as a cofactor for activating protein C. Additionally, PROS1 (expressed in T lymphocytes), due to an agonist function of anti-inflammatory tyrosine kinase TAM receptors TYRO3, AXL and MERTK, exhibiting an inhibitory role in the innate immunity, has been reported regarding its susceptibility in experimental colitis models (Rothlin et al., 2015, Carrera Silva et al., 2013). We hypothesized that PROS1 in IBD may result in decreased plasma levels, increasing not only the thrombosis risk, but also the inflammatory process of IBD. Of the total plasma PROS1, 40% circulate as an active free form, and the rest is linked to complement C4b-binding protein (C4BP) as an inactive complex. Thus, if so, a decrease of circulating “free” protein S could be secondary to increased C4BP, which for excessive binding, reduce its availability.

Aims and Methods: 1) to compare PROS1 levels between CD, UC, activity status (Indexa: CDAI, Mayo), patterns (Montreal) and healthy controls, 2) to determine C4BP levels due to its possible influence on PROS1 levels. Free PROS1 and C4BP were determined by immunoturbidimetry, LumiTest, Stago, France, in 103 IBD patients (UC: n 66, CD n 37) and 30 healthy controls (18 M, 12 F), mean ages: 37.5 ± 15.6, 41.4 ± 14.6, 38.2 ± 12.2, respectively.

Results: Mean PROS1 levels in CD (89.9, p=0.0076) were significantly lower compared with controls (109.6 ± 23.9, p=0.0019) and UC (104.4 ± 27.0, p=0.0076). Within the CD group, in a statistical difference versus controls was observed in patients with active disease (n 25, mean levels: 84.9 ± 24.1, p=0.0004), but not in patients in remission (n12: 100.2 ± 33.5). Moreover, the moderate-severe subset (n21), presented the lowest levels (84.0 ± 29.3) versus controls p=0.0088. In UC, PROS1 levels did not show differences between subsets (42 active, 24 remission: 101.1 ± 26.3 and 110.0 ± 27 respectively) or with controls. CD patterns (behavior, location) and UC extent (12 proctitis, 54 more extensive) exhaustively analyzed did not show significant differences. Mean levels of C4BP in the controls (19.1 ± 4.4, p=0.0008), were higher in UC (25.9) versus controls p=0.0222, respectively. C4BP showed to be diminished versus controls in the overall results of the UC sample (p=0.0010), especially in the severe-moderate subgroup (12 ppm over the

References

P1520 ILEAL CHANGES IN PATIENTS WITH MICROSCOPIC COLITIS

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Introduction: Microscopic colitis (MC) is an important cause of chronic diarrhea in adults. Histopathology is the gold standard for diagnosis and but colonic biopsy has a variable yield. Endoscopically the mucosa appears normal, often leading to delayed diagnosis. It is not clear whether the described changes are correlated to colon or extends to other parts of GIT also. This may have a bearing on treatment decisions.

Aims and Methods: The aim of the current study was to evaluate the terminal ileum using the narrow band imaging (NBI) and high-definition white-light endoscopy (HDWLE) in patients with MC. We also aimed to document and describe the histopathological findings in the ileum of patients with MC.

Materials and Methods: We prospectively recruited patients aged more than 18 years with suspected MC (July 2016 to December 2017). Patients with malignancy, coeliac disease, small intestinal bacterial overgrowth, inflammatory bowel disease, gastrointestinal tuberculosis and severe comorbidities were excluded. Patients underwent blood investigations, imaging including CECT abdomen (if indicated), stool tests using glucose, lactose and lactulose. All patients underwent colonoscopy with ileal intubation if possible. Patients underwent both HDWLE and NBI during the same setting by the same observer. NBI findings were recorded in a predefined format. Four pieces of ileum were biopsied taken from ascending colon and four from pieces from descending colon/sigmoid colon. Additional four pieces of biopsies were taken from terminal ileum. Each set of biopsies was collected in separate containers and labelled for further histopathological processing and examination by an expert gastroenterologist. The diagnosis of MC was made using statements of the European Microscopic Colitis Group 2012.

Results: Of 53 patients enrolled in the study, and a final diagnosis of MC was established in 43 (mean age 45.83, males–27). 25(58.1%) patients had UC, 14(32.6%) had MC and Lymphocytic colitis (CC, 14.6) patients had mixed picture fulfilling criteria for both. The HDWLE findings of ileum revealed normal mucosa in all patients. On NBI, intravillous capillary network was regular unbranched with semi-circular pattern in 41(95.4%) cases and in all controls. Sparse and irregular pattern was seen in 2(4.7%) cases. Dilated and meandering vessels were seen in none (p=1.00). Peyers’ patches domes were indistinct in 5(9.4%) cases, normal in 38(88.4%) cases and all of the controls (p=0.570). Peyers’ patch vessels were regular and unbranched in 38(88.4%) cases and all of the controls (p=0.570). Histopathological findings of terminal ileum revealed normal villi in 39 (90.6%) cases of MC, with 4 patients having partial villous atrophy. The crypt villus ratio was grouped as 1:1.5, 1.3, 1.4 and 1.5 in 2(4.6%), 26 (60.4%) and 11 (25.5%) respectively. Lymphoplasmacytic infiltrate was grouped as mild, moderate and severe, and was present in 10 (23.2), 2 (4.6%) and 1 (2.3%) patients respectively. The mean ± (standard deviation) number of intraepithelial lymphocytes was 16.3±3.6, 14.0±3.4 and 24.5±4.4 respectively.

Conclusion: This prospective study, for the first time, describes the NBI findings of ileum in patients with MC. Traditionally, ileum is considered to be spared in patients with MC. However, we found histological involvement of ileum in form of increased lymphoplasmocyte infiltrate and IEL in ileal mucosa along with presence of partial villous atrophy in some patients.

Disclosure: Nothing to disclose

P1521 Ileo-cecal transit time and lactose intolerance in patients with microscopic colitis

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Introduction: Microscopic colitis (MC) is an important cause of chronic diarrhea in elderly. Histopathology forms gold standard for diagnosis and has a variable yield. Hydrogen (H2) breath tests are used frequently to analyse the pathophysiology of functional gastrointestinal disorders, small intestinal bacterial overgrowth (SIBO), carbohydrate malabsorption and oro-cecal transit time. Aims and Methods: Data regarding prevalence of SIBO, lactose tolerance, and oro-cecal transit time (OCTT) in patients of MC is sparse. Hence, we aimed to evaluate these in patients of MC.

Materials and methods: We prospectively recruited patients diagnosed with MC aged more than 18 years during the period July 2016 to December 2017. Glucose hydrogen breath test was done to evaluate for SIBO. A rise ≥12 ppm over the
fasting value in h2 concentration within 2 hours of ingestion of glucose were measured by glucometer using Model-12 Microlyzer, (Quintron, USA) in 2 consecutive readings was taken as suggestive of SIBO. Lactulose hydrogen breath test was done to calculate OCTT. Patients were instructed to avoid taking antibiotics or probiotics 4 weeks prior to the test. They were given 15 ml lactulose containing 10 gm lactulose to drink and end expiratory breath samples were taken after every 15 minutes for up to 4 hours. Time for rise in breath hydrogen by ≥12 ppm over the baseline value in two consecutive readings was considered to be OCTT. Lactose breath test was done for lactose intolerance. Patients were given lactose at a dose of 250 mg in 250 ml of water and breath samples were taken every 15 minutes up to 4 hours. A rise ≥20 ppm over the fasting value in H2 concentration in two consecutive readings was suggestive of lactose intolerance.

Results: 43 patients were included. The mean age was 45.83±15.92, males – 27, and 10 controls were recruited. Out of 43 cases with MC, 25(58.1%) patients had collagenous colitis (CC), 14 (32.5%) had Lymphocytic colitis (LC) and (9.4%) had mixed picture fulfilling criteria for both. In the MC group, 9(28.1%) were found to be controls while in controls only 1(0.6%) were lactose intolerant (p = 0.054). Glucose hydrogen breath test did not find any patient with SIBO in the MC group, however, SIBO was present in 4 (9.5%) controls (p = 0.001). The mean (+ standard deviation) OCTT measured in MC group was 130.3±47.95 mins and 97.14±45.58 mins (p = 0.109) in controls. OCTT was prolonged in 73% of patients with MC and 43% of controls.

Conclusion: Lactose intolerance was common in patients with MC, which might add to the severity of irritable bowel. OCTT was found to be prolonged in most patients with MC. No patient with MC was found to have SIBO.

Disclosure: Nothing to disclose

P1522 HIGH-FAT DIET AGGRAVATES DEXTRAN SULFATE SODIUM (DSS)-INDUCED COLITIS THROUGH REGULATING IMMUNE RESPONSES OF GUT-ASSOCIATED LYMPHOID TISSUE
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Introduction: Inflammatory bowel disease (IBD) is characterized by inflammation and immune disorders of the gut, gut-associated lymphoid tissue (GALT), and immune disorders of the gut, gut-associated lymphoid tissue (GALT, includ-

Results: Compared to non-inflamed mucosa, Ascomycota decreased (p < 0.05) and Zygomycota increased (p = 0.01) at phylum level in inflamed mucosa of UC patients. Wickerhamomyces decreased (p < 0.05) and Candida, Aspergillus, Cladosporium, Lentinula, and Pseudomonas increased at genus level. Flow cyto-
meter analysis has shown that BMDC have been stimulated by AIEC can invade the gut and induce monocyte-macrophage, DC16 positive macrophages are increased in murine intestinal fibrosis. These data prove that macrophages play a central role in both mucosal repair and fibrosis and these cells constitute an important source of pro-fibrotic factors[1]. CD16 positive macrophages are increased in fibrotic tissue of Crohn’s disease patients[2] and we aim to analyse the relevance of CD16 positive macrophages as a source of fibrotic mediators in murine intestinal fibrosis.

Aims and Methods: Colon resections from donor mice were transplanted subcru-

taneously into the neck of recipient mice. After 7 days, intestinal grafts were explanted. An adjacent segment of each control mouse was kept to be used as autologous control tissue.[3] The expression of macrophage markers, pro-fibrotic markers and Wnt ligands and receptors was analyzed by qPCR. Results: Fimbriae tissue compared with control tissue revealed: a) increased pro-

fibrinogen markers Vm (4.6±1.1 vs 1.9±0.1), b) Smua (13.0±1.7 vs 1.1±0.2) and Colla1 (69.4±1.7 vs 1.7±0.7); b) increased macrophage markers F4/80 (7.9±2.2 vs 1.1±0.1), CD16 (23.3±3.3 vs 1.3±0.3), CD86 (10.2±4.6 vs 1.4±0.4) and CD68 (15.8±2.9 vs 1.1±0.2); c) increased expression of Tgf-β (2.1±0.2 vs 1.0±0.0). Moreover, fibrotic tissue showed: a) a positive and sig-

ificant correlation between CD16 and Wnt6 and between CD16 and Tgf-β and b) a positive correlation between Wnt6 and Fzd10. Conclusion: CD16 positive macrophages are increased in murine intestinal fibrosis and these cells may act as a source of fibrotic factors such as Tgf-β and Wnt6.

Disclosure: Nothing to disclose

References

P1525 CD16 MACROPHAGES ACT AS A SOURCE OF PROFIBROTIC FACTORS PROMOTING INTESTINAL FIBROSIS
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Introduction: Fibrosis is a common complication of Crohn’s disease and it is related to the dysregulated tissue repair mechanisms. Macrophages play a central role in both mucosal repair and fibrosis and these cells constitute an important source of pro-fibrotic factors[1]. CD16 positive macrophages are increased in fibrotic tissue of Crohn’s disease patients[2] and we aim to analyse the relevance of CD16 positive macrophages as a source of fibrotic mediators in murine intestinal fibrosis.

Aims and Methods: Colon resections from donor mice were transplanted subcu-
taneously into the neck of recipient mice. After 7 days, intestinal grafts were explanted. An adjacent segment of each control mouse was kept to be used as autologous control tissue.[3] The expression of macrophage markers, pro-fibrotic markers and Wnt ligands and receptors was analyzed by qPCR. Results: Fimbriae tissue compared with control tissue revealed: a) increased pro-

fibrinogen markers Vm (4.6±1.1 vs 1.9±0.1), b) Smua (13.0±1.7 vs 1.1±0.2) and Colla1 (69.4±1.7 vs 1.7±0.7); b) increased macrophage markers F4/80 (7.9±2.2 vs 1.1±0.1), CD16 (23.3±3.3 vs 1.3±0.3), CD86 (10.2±4.6 vs 1.4±0.4) and CD68 (15.8±2.9 vs 1.1±0.2); c) increased expression of Tgf-β (2.1±0.2 vs 1.0±0.0). Moreover, fibrotic tissue showed: a) a positive and sig-

ificant correlation between CD16 and Wnt6 and between CD16 and Tgf-β and b) a positive correlation between Wnt6 and Fzd10. Conclusion: CD16 positive macrophages are increased in murine intestinal fibrosis and these cells may act as a source of fibrotic factors such as Tgf-β and Wnt6.

Disclosure: Nothing to disclose

References
Aims and Methods: This study aimed to determine the prevalence and define the genetic and functional characteristics of AIEC in patients with Crohn’s disease (CD). Secondly, we assessed if the presence of AIEC compromise the efficacy of FMT in a murine model of colitis. We isolated E. coli from ileum tissues of Chinese Crohn’s disease patients (n = 56) and healthy subjects (N = 16) and classified these as AIEC pathotype using genetic protection assay with IntI-1 and 407 intestinal cells. Bacterial whole genome sequencing was performed on all AIEC strains isolated. We compared the virulence properties and antibiotic resistance of these isolates with AIEC strains isolated from western countries and other publicly available E. coli pathotypes deposited in NCBI database. Amongst 21 AIEC strains isolated, we selected AEIC62d strain which has the strongest invasion property and E. coli K12 (a non-pathogenic strain) to infect C57BL/6 wild type mice (n = 26). After 7 days of 2% DDS treatment, we gavaged these mice with the two isolates, ad libitum human stools, and assessed the Disease Activity Index (DAI), colon length and histology score of the colon 7 days after fecal transplantation.

Results: AIEC was present in 37.5% and 12.5% of mucosa of CD and healthy subjects, respectively. Most AIEC strains belonged to B2 phylogroup. Over 65% of isolates from CD were multi-antibiotic resistant and they harboured stronger pathogenicity than the non-resistant strains (p < 0.05). The genome of AEIC62d resembled that of LF82 (the AIEC reference strain) and possessed nearly all virulence genes (pilO, fimA, iPa, etc.). Its invasion ability was greater than that of LF82 (4.25% versus 3.5% in Intestine-407 cells). Mice treated with AIEC62d resembled that of LF82 (the AIEC reference strain) and possessed stronger pathogenicity than the non-resistant strains (p < 0.05).

Discussion: The results suggest that patients with a diagnosis of perianal abscess undergoing surgery should have a low threshold for IBD-associated colorectal cancer. The molecular mechanisms of this transition exhibit distinguishing features that are not observed in other pathways of colorectal carcinoma development.

Aims and Methods: The aim of the project was to map the occurrence of somatic DNA mutations in inflammatory bowel disease tissue of IBD patients to determine their frequency and relationship to the course of neoplastic transformation. The severity of inflammation and other clinical and laboratory parameters. The mutational spectra were then compared to profiles obtained from advanced colorectal ade- nomas and carcinomas resulting from traditional and serrated pathways. Tissue samples were processed from a cohort of 20 patients with various types of ulcerative colitis and Crohn’s disease. In addition tissues were processed from 2 patients with sporadic adenomas (advanced tubular and advanced serrated). DNA was extracted using standard protocols from tissue sections (native or FFPE). Targeted NGS sequencing of 60 genes was performed on Illumina MiSeq sequencer using SureSeq Solid tumor hybridization-based enrichment panel (Oxford Gene Technology, Oxfordshire, UK). NGS data was processed by NextGene sequence analysis suite (Softgenetics, State College, PA).

Results: The diverse mutation spectra obtained were remotely reflecting the “reverse” Vogelstein model of molecular progression of IBD. Unlike in advanced adenomas, the frequency of prominent genes from traditional and serrated pathways was significantly lower in IBD samples. Mutations in cancer driver genes indicate initiation of malignant conversion and are useful in assessment of the risk of IBD-related colorectal cancer. At the same time, presence of specific mutations in inflammatory tissue may be relevant for prediction of IBD therapy response, however, such association would need further confirmation. This work was funded by project no. MO1012

Disclosure: Nothing to disclose.

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P1530 ACTIVITY OF TRANSFORMING GROWTH FACTOR (TGF)-β1 AND BONE MORPHOGENIC PROTEIN (BMP) IN COLONIC EPITHELIAL ESCAPES THE INHIBITION OF SMALL MOTHERS AGAINST DECAPENTAPLEGIC (SMAD) 7 IN COLITIS-ASSOCIATED CANCER

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Introduction: Ulcerative colitis (UC) is associated with an increased risk of developing colorectal cancer (CRC). An inhibitor for SMAD7 (GED-0301), a molecule involved in the TGFβ1 and BMP pathways and highly expressed in UC in affected colonic mucosa, is being investigated to determine its efficacy in reducing inflammation in UC patients. While inhibiting SMAD7 may ameliorate intestinal inflammation, no evidence is currently available to determine the effect on CRC risk, as both TGFβ1 and BMP are known to enhance late stages of colorectal carcinogenesis, and may possibly have a role in CRC as well. The inhibition of TGFβ1 and BMP pathways are exerted through the SMAD7-inhibited inhibition of phosphorylation of both SMAD3 and SMAD1/5,8, respectively, we aimed to evaluate the expression of SMAD proteins in non-neoplastic, dysplastic and malignant colonic epithelial tissue. This could give us an insight into the potential effect of SMAD7 inhibition during neoplastic progression in UC patients.

Aims and Methods: To evaluate the activity of the TGFβ1 and BMP pathways, cytoplasmic expression of SMAD7 and nuclear expression of p-SMAD3 and p-SMAD1/5,8 was assessed by immunohistochemistry in a cohort of 23 archival colorectal cancer (CRC) tissue samples (9 dysplastic and 14 9-neoplastic mucosal samples) from patients who have undergone colectomy for UC. Protein expression was evaluated by both digital quantification and validated by blinded semi-quantitative scoring by a pathologist. In the same samples, expression of SMAD7 mRNA was evaluated in in situ hybridisation with specific target probes for the mRNA and evaluated by digital quantification. Significant differences were tested with one-way ANOVA.

Results: Cytoplasmic SMAD7 shows a significant increase of expression with the progressive neoplastic process from inflamed to malignant with expression of SMAD7 being highest in flat/normal mucosa (p < 0.0001). This is linked with an increase of BMP activity, evaluated by p-SMAD1/5,8 nuclear expression (p < 0.0001), but not of TGFβ1 activity evaluated by p-SMAD3 expression (p = 0.53). The differential SMAD7 expression amongst the stages of neoplastic progression is not correlated with changes in the mRNA level, a discrepancy that could be due to still unknown post-transcriptional or post-translational regulation of the protein. Interestingly, within the cancers, higher SMAD7 expression was detected in approximately 88% of CRC samples (7/8 samples), with the exception of one cancer treated with neoadjuvant radiotherapy before collection due to the radiation damage.

Conclusion: Within our CAC sample cohort, TGFβ1 and BMP pathways do not show suppression in the presence of increased SMAD7. The increase in SMAD7 expression during neoplastic transformation may be a protective response to inflammatory stimuli. Further investigations are needed to understand the clinical implications of these findings.

Disclosure: Nothing to disclose

P1531 AT BIOLOGIC ONSET THE GUT MICROBIAL PROFILE IN CROHN’S DISEASE PATIENTS IS SIMILAR TO THAT OF HEALTHY CONTROLS

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Disclosure: Nothing to disclose

Introduction: Compared to healthy controls Crohn’s Disease [CD] patients show a decrease in diversity and abundance of various microbial species. To this day it is unclear whether these differences are primary or secondary and whether they are sequences of protracted inflammation. In a colonoscopy-based screening study we have shown that ≥40% of asymptomatic first degree relatives [FDR] of CD patients have subclinical intestinal inflammation (IBD 2014;20:1049) – a finding consistent with previous fecal calprotectin-based studies (Gastroenterology 2003;124:1728). Of those with inflammation 10% had CD at biologic onset (very early disease with typical histological features) while the remaining had minimal inflammation – a non-evolving phenotype in between that of healthy FDR and CD with HD. Hence – because of the very initial stage of the inflammation process – FDR represent the ideal population to test the hypothesis that dysbiosis predate clinical CD and might be one of its causative factors.

Aims and Methods: For microbiome analysis we used next-generation sequencing 16S (bacteria) using DNA extracted from ileo-cecal biopsies of normal healthy controls (n = 10), CD patients (n = 23) and asymptomatic FDR (n = 25). Endoscopy and histology had categorised FDR into healthy [FDR1] (n = 9), intermediate [FDR2] (n = 12) and CD phenotypes [FDR3] (n = 4). Data were analysed using illumina CLC pipeline version 1.8.2 (Australian Genome Research Facility). Fifteen taxa were clustered into a phylogenetic tree using hierarchical clustering. Principal coordinates analysis (PCoA) was run on weighted UniFrac distances between Operational Taxonomic Units (OTUs) counts. Univariate negative binomial regressions with log-link functions were applied to assess the association between group ing and OTUs counts for each taxon (5 of the 15 taxa were excluded due to excess of zero OTUs counts), with controls as reference group. Statistical significance was set at 10%.

Results: As previously reported Faecalibacterium prausnitzii, Akkermansia muciniphila were decreased while Bacteroides fragilis and Enterobacteriaceae were significantly increased in CD patients compared to controls with a overall decrease of microbial diversity in CD patients. In the Peo exclusion group of FDR were found to be in opposite quantities to a comparison to healthy controls, FDR3, close to the centroid for controls. In contrast, no clear separation between the 3 FDR groups was observed. Hence the microbial profile of FDR as a whole was very similar to that of controls and dissimilar to that of CD patients. Estimates of coefficients contrasting FDR, and controls showed larger p-values than those for estimates of coefficients contrasting CD patients and controls in 9 out of 10 taxa. Taxa for which CD and controls had significantly (p < 0.10) differed were Bi, OTU1 and FDR1. In FDR(2) 8,10,4,1,2 did not (p > 0.1)., unknown, Actinobacteria, Firmicutes, Synergistetes, and TM7.

Conclusion: Intestinal microbial profiling reveals significant differences between healthy controls and CD patients. However, FDR bear a microbial profile remarkably similar to healthy controls in terms of species abundance and presence of specific bacterial species. In particular the microbiome of FDR – that is, patients with CD at its biologic onset – is to a large extent superimposable to that of healthy controls. This observation raises the possibility that the dysbiosis precedes clinical CD and might be one of its causative factors.

Disclosure: Nothing to disclose

P1532 SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) IS INCREASED IN BOTH CROHN’S DISEASE AND ULCERATIVE COLITIS: SYSTEMIC REVIEW AND META-ANALYSIS

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Disclosure: Nothing to disclose

Introduction: Small intestinal bacterial overgrowth (SIBO) is a common gastrointestinal condition in Crohn’s disease (CD) and Ulcerative colitis (UC). It is associated with abdominal pain, flatulence, bloating and, in particular in UC and UC mouse model of CAC, might help in understanding the TGFβ superfamily pathway in colitis-associated cancer.

Aims and Methods: We investigated the impact of Tofacitinib, IL-6, IL-11 and BMP on cancer. Although inhibit-
**Correlation between EGCs and the production of pro-inflammatory cytokines in vitro and in vivo**

EGCs could induce tolerogenic DCs by releasing NGF, which could induce tolerogenic DCs by releasing nerve growth factor (NGF), and DCs could induce the differentiation of Treg cells in mice. This beneficial effect might be linked that DCs could restore the imbalance of Th cell subsets, prompt the differentiation of Treg, and ultimately reduced the over-expressed pro-inflammatory cytokines and increase IL-10 level.

**Conclusion:**
EGCs could hold therapeutic effects in IBD and subtypes of the disease compared to controls.

**Disclosure:**
Nothing to disclose.

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**P1534 Targeted Analysis of Serum Proteins Encoded at Known Inflammatory Bowel Disease Risk Loci**


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**Introduction:**
Few studies have investigated the blood proteome of inflammatory bowel disease (IBD). We characterized the serum abundance of proteins encoded at 163 known IBD risk loci, and tested these proteins for their biomarker discovery potential.

**Methods:**
Based on the Human Protein Atlas (HPA) antibody availability, 218 proteins from genes mapping at 163 IBD risk loci were selected. Targeted serum protein profiles from 49 Crohn’s disease patients (CD), 51 ulcerative colitis patients (UC) and 50 sex and age-matched healthy individuals were obtained using multiplexed antibody-based suspension bead array assays. Differences in relative serum abundance levels between disease groups and controls were examined. Replication was attempted for CD-UC comparisons (including disease subtypes), by including 64 additional patients (33 CD and 31 UC). Antibodies targeting a potentially novel risk protein were validated by paired antibodies, Western blot, immune-capture mass spectrometry and epitope mapping.

**Results:**
Univariate analysis, thirteen proteins mostly related to neutrophil, T- and B-cell activation and function were differentially expressed in IBD vs. healthy controls, three in CD vs. healthy controls and two in UC vs. healthy controls (Table, q < 0.01). Multivariate analyses further differentiated disease groups from healthy and CD subtypes from UC (p < 0.05). Extended characterization of an antibody targeting a novel, most discriminative serum marker, the laccase (multi-copper oxidoreductase) domain containing 1 (LACC1) protein, provided evidence for antibody on-target specificity.

**Conclusion:**
Using affinity proteomics, we identified a set of IBD-associated serum proteins encoded at IBD risk loci. These candidate proteins hold potential to be exploited as diagnostic biomarkers of IBD.

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**Aims and Methods:**
We aimed to establish the prevalence of small intestinal bacterial overgrowth (SIBO) in patients with IBD, both ulcerative colitis (UC) and Crohn’s disease (CD) compared with controls. Using the expression terms ‘small intestinal bacterial overgrowth (SIBO)’ and ‘Inflammatory Bowel Disease (IBD)’, we determined.

**Conclusion:**
In patients with IBD, the prevalence of SIBO is significantly increased in patients with IBD when compared to controls. The accepted gold-standard for the diagnosis of SIBO is breath tests, the prevalence of SIBO in patients with CD is double compared to those with UC.

**Disclosure:**
Nothing to disclose.
P1535 INFLUENCE OF SMOKING ON THE MRNA EXPRESSION OF CYTOKINES IN MUCOSA OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: It is well known that smoking is a risk factor for developing and clinical course of Crohn's disease (CD), but at the other side smoking is protective factor of ulcerative colitis (UC). Molecular pathways that are influenced by smoking in CD and UC are poorly understood.

Aims and Methods: The aim of our study was to analyse influence of smoking on the mRNA expression of cytokines in mucosa of patients with CD as well as UC. We performed cross-sectional study. The cohort consists of 87 IBD patients (47CD patients and 40 UC patients) followed at IBD center of University Hospital Bratislava- Razinov. We recorded demographic and clinical data of each patient including smoking. We performed colonoscopy in each patient and took biopsy from inflamed and non-inflamed sigma (CD,UC) and terminal ileum (CD). mRNA was extracted from mucosal biopsy samples for each cytokine (IL-6, IL-8, IL-17, TNF-a, CCR1, CCR2, CCR5, CCR9, CCL5, TLR2, TLR4, C5D7, CD207, CD206) and transcription factor FoxP3 and was normalised to house-keeping gene (GAPDH). Finally, we compared mRNA expression of target cytokines in mucosa of smokers and non-smokers in both CD and UC patients.

Results: Smokers with Crohn's disease had significant higher mRNA expression of proinflammatory cytokine TNF-a (p = 0.003) in inflamed mucosa in sigma in comparison with non-smokers. In smokers with ulcerative colitis we observed significant higher mRNA expression of anti-inflammatory cytokine IL-10 (p = 0.02) in non-inflamed mucosa of sigma. Similarly, smokers with UC have significant higher mRNA expression of cytokines TLR 2 (p = 0.024) and CCR1 (p = 0.049) in non-inflamed mucosa of sigma.

Conclusion: To our, smoking regulates mRNA expression of anti-inflammatory cytokine IL-10 in smokers with UC, but on the other side smokers with CD had significant higher mRNA expression of pro-inflammatory cytokine TNF in mucosa of sigma.

Disclosure: Nothing to disclose

Reference

1. Mr. Scheinin I, Sie D, Bengtsson H et al. DNA copy number analysis of fresh and formalin fixed whole genome: the potential translational utility, by stratifying patients with LGD according to their risk of progression to HGD and/or CRC.

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Introduction: Inflammatory bowel diseases (IBD) are a heterogeneous group of disorders exhibited by two major phenotypic forms: Crohn's disease and ulcerative colitis. Although the etiology of IBD is unknown, several factors released from the white adipose tissue (WAT) and skeletal muscles including adipokines and adipo-kinases, as well as changes in intestinal microbiome were proposed. Recently, we have reported that the voluntary wheel running reduced colonic inflammation in rodent models of colitis but the effect of forced treadmill exercise had not been extensively studied.

Aims and Methods: The role of protective myokines such as irisin and adipokines including adiponectin affecting the course of IBD in experimental animals forced to exercise has not been fully elucidated. We determined the effect of moderate forced treadmill running for 6 weeks with the speed 12 cm/sec in mice fed a high-fat diet (HFD) compared to those on a standard chow diet (SD) with intrarectal administration of 2,4,6-trinobenzensalonic acid (TNBS) colitis. To minimize distress, mice did not run during or after TNBS colitis. The disease activity index (DAI), colonic blood flow and the colonic tissue content of IL-17, IFN-γ, TNF-α, IL-6, IL-8 and IL-10 using Lumines Multiplex Assays, the stress oxidative markers MDA, reduced glutathione, SOD and plasma myokine irisin, adipokines leptin and adiponectin levels and real-time PCR and protein expression of proinflammatory factors in colonic mucosa and mesenteric fat were assessed.

Results: Macrosopic and microscopic colitis in sedentary SD mice was accompanied by a significant fall in CBF and moderate increase in colonic tissue weight and a significant increase in the plasma levels of TNF-α, IL-6 and IL-1β (p < 0.05). In sedentary HFD mice, colonic lesions were aggravated, colonic tissue weight increased and the IL-1β, TNF-α, IL-6, IL-17, and IFN-γ and leptin levels significantly increased. Simultaneously, a significant decrease in the plasma irisin and adiponectin levels was observed in HFD fed mice compared with SD mice (p < 0.05). Treadmill exercise significantly increased the macroscopic and microscopic colitis, substantially decreased CBF and raised the plasma TNF-α, IL-6, IL-1β, and leptin levels while decreasing both, the plasma irisin and adiponectin levels. In mice fed a high-fat diet the plasma irisin and adiponectin levels was significantly reduced, whereas the plasma irisin and adiponectin levels in HFD fed mice were significantly increased compared to SD mice (p < 0.05). The protein expression of heme oxygenase (HO-1) and hypoxia inducible factor1α (HIF-1α) were significantly increased in colonic mucosa of treadmill exercising HFD mice with colitis.

Conclusion: We conclude that 1. experimental colitis is exacerbated in HFD mice, possibly due to a fall in colonic microcirculation and an increase in the plasma and mesenteric fat content of proinflammatory biomarkers, and 2. forced treadmill running exacerbates the severity of colonic damage in mice fed a HFD through the rise in oxidative stress, the increase in expression and activity of proinflammatory factors including leptin released from WAT and the attenuation of protective mediators irisin and adiponectin.

Disclosure: Nothing to disclose

P1536 SHALLOW WHOLE-GENOME SEQUENCING PREDICTS THE FUTURE CANCER RISK OF LOW-GRADE DYSPLASTIC LESIONS TO ULTERRATIVE COLITIS

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Introduction: The management of low-grade dysplasia (LGD) in ulcerative colitis (UC) is uncertain due to the variable risk of progression to colorectal cancer (CRC). Chromosomal copy number alterations (CNAs) are known to occur in colorectal epithelial cells of UC patients who have developed CRC. The burden of CNAs in precursor LGD relative to high-grade dysplasia (HGd) and CRC has not been defined, and the correlation between LGD CNA burden and future CRC risk is unknown.

Shallow whole genome sequencing is a novel, high-throughput, cost-effective technique for high-resolution CNA assessment in formalin-fixed, paraffin-embedded tissue. We have successfully utilised this technique using as little as 500 picograms of relatively degraded DNA that has been extracted from archival tissue, at a cost of approximately £75 per tissue sample.

Aims and Methods: To define the genomic changes that differentiate LGD from both HGD and CRC, we identified 19 UC proctocolectomy specimens with HGD and/or CRC, and analysed 77 neoplastic regions of interest (36 LGD, 34 HGD and 7 CRC).

To determine the utility of shallow whole genome sequencing in predicting future CRC, we then analysed dysplastic tissue from 35 patients: 13 ‘progressor’ patients with 27 LGD lesions who subsequently developed HGd and/or CRC a median 427 days later (IQR 213–777 days), and 22 ‘non-progressor’ patients with 26 LGD lesions who remained free of HGD and CRC at least 5 years later. The two patient groups are matched for age, gender, disease duration and LGD location.

Histological diagnosis was confirmed by two blinded pathologists. Shallow whole-genome sequencing was performed using a standardised pipeline for epithelial cell enrichment, DNA extraction, library preparation, next generation sequencing and bioinformatic analysis.

Results: A median 12% of the genome from LGd tissue showed CNAs (HGd: 4.3–32%), compared to 23% in HGD/CRC (HGd: 19–42%, p = 0.003). Similarly, the number of CNA events was greater in HGD and CRC compared to LGd (p < 0.001). Multiple CNAs involving key driver genes were more frequent in HGD/CRC compared to HGd (adjusted p values < 0.05). We have shown that 25% of LGD and CRC lesions are driver genes. Shallow whole genome sequencing has potential translational utility, by stratifying patients with LGD according to their future risk of progression to HGD and/or CRC.

Disclosure: Nothing to disclose

Reference

1. Mr. Scheinin I, Sie D, Bengtsson H et al. DNA copy number analysis of fresh and formalin fixed whole genome: the potential translational utility, by stratifying patients with LGD according to their risk of progression to HGD and/or CRC.
**P1539 ASSOCIATION BETWEEN POLYMORPHISMS -318 C/T, 49 A/G OF CTLA-4 GENE AND POLYMORPHISM IVS 3 +17 T/C OF CD2S GENE AND CROHN'S DISEASE: A CONTROLLED STUDY**

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Introduction: Crohn’s CD disease is a pathology characterized by a chronic inflammatory and fibrotic intestinal tract engendered by an excessive activation of lymphocytes T, which would be responsible for a change of the immune answer. The gene CTLA-4 (Cytotoxic-T-Lymphocyte Antigen 4) and the gene CD2S (Cluster of differentiation) represent two good candidates genes to explain the physiopathology of Crohn’s disease. The molecule CTLA-4 plays a leading role in the negative control of Lymphocytes T activated, the protein CD28 assures an inflammation of the intestinal tract engendered by an excessive activation of lymphocytes T, which would be responsible for a change of the immune answer.

Results: This study highlights the potential for metabolite profiling to differentiate Crohn’s and idiopathic perianal fistula groups. Further work is required to understand the pathways to which the significant amino acids described may be related to, as these may offer clues as to the underlying pathogenesis.

Disclosure: Nothing to disclose.

Reference

**Results Table**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low BMI (n = 13)</th>
<th>Normal BMI (n = 85)</th>
<th>Overweight BMI (n = 49)</th>
<th>Obese (n = 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dx: Mean (SD)</td>
<td>32.4 (15)</td>
<td>33.3 (16)</td>
<td>35.1 (14)</td>
<td>38.1 (14)</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>6 (46%)</td>
<td>45(53%)</td>
<td>19(44%)</td>
<td>21(60%)</td>
</tr>
<tr>
<td>Year of Dx: Mean (SD)</td>
<td>2005 (16)%</td>
<td>2008 (11)%</td>
<td>2007 (13)%</td>
<td>2011 (11)%</td>
</tr>
<tr>
<td>Location L1</td>
<td>4 (31%)</td>
<td>12 (12%)</td>
<td>9 (22%)</td>
<td>13 (37%)</td>
</tr>
<tr>
<td>Location L2</td>
<td>3 (23%)</td>
<td>14 (15%)</td>
<td>15 (35%)</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>Location L3</td>
<td>6 (46%)</td>
<td>57 (67%)</td>
<td>19(44%)</td>
<td>14 (40%)</td>
</tr>
<tr>
<td>Behaviour B1</td>
<td>3 (23%)</td>
<td>16 (19%)</td>
<td>14(32%)</td>
<td>11(31%)</td>
</tr>
<tr>
<td>Behaviour B2</td>
<td>6 (46%)</td>
<td>38 (45%)</td>
<td>10(23%)</td>
<td>16 (46%)</td>
</tr>
<tr>
<td>Behaviour B3</td>
<td>4 (31%)</td>
<td>25 (29%)</td>
<td>14 (32%)</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>Behaviour Perinial Surgery B3</td>
<td>3(23%)</td>
<td>13(16%)</td>
<td>6(14%)</td>
<td>5(14%)</td>
</tr>
<tr>
<td>Extraitrestinal manifestations</td>
<td>3 (23%)</td>
<td>2 (2%)</td>
<td>3 (6%)</td>
<td>6 (17%)</td>
</tr>
</tbody>
</table>

**Discussion**

Crohn’s CD disease is a pathology characterized by a chronic inflammatory and fibrotic intestinal tract engendered by an excessive activation of lymphocytes T, which would be responsible for a change of the immune answer. The gene CTLA-4 (Cytotoxic-T-Lymphocyte Antigen 4) and the gene CD2S (Cluster of differentiation) represent two good candidates genes to explain the physiopathology of Crohn’s disease. The molecule CTLA-4 plays a leading role in the negative control of Lymphocytes T activated, the protein CD28 assures an inflammation of the intestinal tract engendered by an excessive activation of lymphocytes T, which would be responsible for a change of the immune answer.

**Conclusion**

There was evidence that CD phenotype differed according to BMI. Extremes of BMI were associated with an ileal location. Obesity at the time of diagnosis was associated with an older age at diagnosis, and a reduced need for surgery. Ileocolonic disease was associated with a normal BMI at diagnosis. There was a trend for smoking to be associated with low BMI at diagnosis.

**Disclosure**

Nothing to disclose.

**P1541 FEMALE GENDER INCREASES THE RISK OF ANXIETY AND DEPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDER ANTI-TNF THERAPY**

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Introduction: It has been shown that female gender is a risk factor for developing anxiety and depression in patients with inflammatory bowel disease. We evaluated whether women on anti-TNF therapy are at greater risk of developing anxiety and depression compared to men.

Results: 182 subjects diagnosed with CD between 1976 and 2017 had their BMI recorded at the time of diagnosis (n = 97) or by validated recall (n = 85), together with their disease location and disease behaviour at the time of diagnosis. Association between BMI at diagnosis, phenotype and risk factors were analysed by logistic regression, adjusting for year of diagnosis, age at diagnosis and sex.

Conclusion: There was evidence that CD phenotype differed according to BMI. Extremes of BMI were associated with an ileal location. Obesity at the time of diagnosis was associated with an older age at diagnosis, and a reduced need for surgery. Ileocolonic disease was associated with a normal BMI at diagnosis. There was a trend for smoking to be associated with low BMI at diagnosis.

**Discussion**

There was evidence that CD phenotype differed according to BMI. Extremes of BMI were associated with an ileal location. Obesity at the time of diagnosis was associated with an older age at diagnosis, and a reduced need for surgery. Ileocolonic disease was associated with a normal BMI at diagnosis. There was a trend for smoking to be associated with low BMI at diagnosis.

**Disclosure**

Nothing to disclose.

**P1540 CROHN'S DISEASE PHENOTYPE DIFFERS BY BODY MASS INDEX AT PRESENTATION**

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Introduction: There is increasing appreciation that patients with Crohn’s disease (CD) are likely to have either a low or high body mass index (BMI) at presentation, compared to subjects with ulcerative colitis (UC) and healthy controls. It is possible that the pathogenesis of CD may be different between patients with low and high BMI at presentation. The relationship between BMI at presentation and CD phenotype has not been previously evaluated.

Methods: 182 subjects diagnosed with CD between 1976 and 2017 had their BMI recorded at the time of diagnosis (n = 97) or by validated recall (n = 85), together with their disease location and disease behaviour at the time of diagnosis. Association between BMI at diagnosis, phenotype and risk factors were analysed by logistic regression, adjusting for year of diagnosis, age at diagnosis and sex.

Results: The table shows the distribution of CD location, BMI, behaviour and phenotype characteristics, across the different BMI categories.

**Disclosure**

Nothing to disclose.

**P1538 DIFFERENT METABOLIC PROFILING BETWEEN CROHN’S PERIANAL FISTULA AND IDIOPATHIC (CRYPTOGLANDULAR) PERIANAL FISTULAS MAY OFFER CLUES TO UNDERLYING PATHOGENESIS**

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Introduction: The pathogenesis of perianal fistulas is poorly understood. The reasons why fistulas originate have been explained in idiopathic cases, with the cryptoglandular theory being widely accepted. However, in Crohn’s disease, it is thought to involve interplay between microbiological, immunological and genetic factors. It remains unclear why the fistulas are different.

Aims and Methods: We undertook a pilot study with the aim of defining how metabolic profile varies in idiopathic (cryptoglandular) cases of perianal fistula and Crohn’s perianal fistula. Fistula tissue biopsy was obtained from the fistula tract of 31 patients with idiopathic perianal fistula and 20 patients with Crohn’s anal fistula. Ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) profiling in positive mode was implemented to detect metabolites present in fistula samples. Samples were analysed using hydrophilic liquid chromatography (HLIC). The validated hydrophilic liquid (HLIC) chromato-

graphic method developed at the MRC-NIHR National Phenome Centre, was used. Multivariate data analysis was performed using the SIMCA software (v.14.0.2, Umeå, Sweden). Principle component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA) models were built to find metabolites that can predict IBD fistula.

Results: Results: Significant OPLS-DA model (p.value CV-ANOVA 0.0117) separated well between idiopathic and IBD fistula patients. Robust statistical parameters were obtained with R2X 0.212 R2Y 0.658, Q2Y 0.260. Eighty features were selected from the OPLS-DA model as potential predictors of the group separation. From these, 26 putatively assigned including validation of the arginine with standard. 18 of these 26 features were increased and 8 decreased in CD perianal fistula.

Conclusion: Metabolite putative identification was conducted by matching accurate m/z measurements of detected chromatographic features to theoretical value from in-house databases and on-line databases such as the human metabolite database (HMDB, http://www.hmdb.ca/) KEGG (http://www.genome.jp/kegg/ligand.html), METLIN (http://metlin.scripps.edu/) and previous publications.

**Disclosure**

Nothing to disclose.

Reference
**Introduction:** Depression and anxiety are significant predictors of worse health-related quality of life in inflammatory bowel disease (IBD) patients. Nevertheless, the role of anxiety and depression in IBD patients under anti-TNFα therapy has been poorly investigated.

**Aims and Methods:** The aim of the study was to evaluate both the frequency of anxiety and depression in IBD patients under anti-TNFα therapy, and the potential factors influencing the development of these symptoms. A prospective observational cohort study was designed. All IBD patients older than or with 18 years under treatment with anti-TNFα were consecutively included. Depression prevalence and depression was assessed in IBD outpatients using the Hospital Anxiety and Depression scale (HAD). When using this scale we considered scores of 8 or higher to be abnormal. Relapse was defined in Crohn’s disease (CD) as a Harvey Bradshaw index higher than 4, and in ulcerative colitis as a Partial Mayo index higher than 2. Patient demographics and disease characteristics were also collected: age, sex, marital status, smoking habit, type of IBD, phenotype included in Montreal classification, extra-intestinal manifestations, clinical activity, prior surgery, perianal disease and disease duration. Results are shown as OR and 95% CI, and analysed by logistic regression.

**Results:** Eighty patients were consecutively included (37 male, mean age 40 years, range from 20-67). Sixty patients (75%) had CD and twenty ulcerative colitis (25%); sixty-one (76%) of them were under maintenance treatment with infliximab and nineteen (24%) with adalimumab. Anxiety and depression symptoms were present in 49.4% and 25.3%, respectively. Females were more likely to have anxiety (OR = 4.73; 95% CI: 1.82–12.26; p = 0.001) and depression (OR = 3.56; 95% CI: 1.14–11.06; p = 0.028). Patients with active disease were no more likely to have anxiety (OR = 1.01; 95% CI: 0.973–1.029; p = 0.972) or depression (OR = 1.013; 95% CI: 0.984–1.042; p = 0.389). None of the other studied factors were associated with anxiety and clinical parameters were significantly associated with the development of anxiety or depression.

**Conclusion:** An important number of IBD patients under anti-TNFα present anxiety or depressive symptoms. Female gender is associated with more anxiety and depression in the follow-up of patients. However disease activity was not associated with an increase in either anxiety or depression.

**Disclosure:** Nothing to disclose.

**Results:** Thirty-two IBD patients included, 392 (12.2%) had anaemia. No difference between anaemic and non-anaemic subjects were observed as far as patient age, gender and disease duration. Body mass index was significantly lower (p = 0.0051) in the anaemic group (22 ± 2.5 kg/m²) compared with the non-anaemic one (24 ± 2 kg/m²). In most cases (86%) anaemia was mild (Hb >9.5 g/dL), and only 2% of patients had severe anaemia (Hb <8.0 g/dL). Hb was lower in patients with active disease and correlated significantly with body mass index (r = 0.0182) and CAI in ulcerative colitis (p = 0.0021).

An isolated iron deficiency was responsible for 61.7% of anaemic cases, while the remaining cases had anaemia of chronic disease (12.8%), vitamin deficiencies (2.8%), and various combinations of iron and/or vitamin deficiencies and inflammation (22.7%).

**Conclusion:** The lower prevalence of anaemia in RIDART1 (12.2%) in comparison to that reported in previous European studies may be due to the fact that, in recent years, more attention is paid to the impact of anaemia in IBD patients, and the combination of anaemia and IBD are more efficiently treated than the past. Caution, however, must be used in the interpretation of the present data since the RIDART1 study is still under way.

**Disclosure:** Nothing to disclose.

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**P1542 PREVALENCE OF ANAEMIA IN INFLAMMATORY BOWEL DISEASE: PRELIMINARY RESULTS OF THE OBSERVATIONAL ITALIAN MULTICENTRE IG-IBD STUDY RIDART 1**

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**Aims and Methods:** The aim of the study was to determine the state of periodontitis in IBD patients. The study was conducted over 20 months after starting the study.

**Disclosure:** Nothing to disclose.

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**P1543 THE IMPACT OF CROHN’S DISEASE ON PERIODONTAL STATUS – PRELIMINARY RESULTS FROM POLIBI STUDY**

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**Aims and Methods:** The aim of the study was to determine the state of periodontium based on CPITN index in correlation to smoking habits and type of treatment in patients suffering from Crohn’s disease (CD).

**Results:** In 110 subjects (80 with Crohn’s disease and 30 healthy controls) aged 18-65 (mean 34.9) were included to the study. Disease phenotype at diagnosis was included. Prevalence of anxiety and depression was assessed in IBD outpatients and their mobility leading consequently to the need for teeth extraction. Periodontal disease is the second cause (just after the dental caries) of premature loss of natural teeth. The course and severity of periodontitis are significantly influenced by the virulence of the plaque bacteria, as well as the immune defenses of the organism.

**Introduction:** Periodontitis is a disease manifested by the loss of clinical attachment, deepening of the gingiva pockets, loss of bone supporting the teeth roots and their mobility leading consequently to the need for teeth extraction. Periodontal disease is the second cause (just after the dental caries) of premature loss of natural teeth. The course and severity of periodontitis are significantly influenced by the virulence of the plaque bacteria, as well as the immune defenses of the organism.

**Aims and Methods:** The aim of the study was to determine the state of periodontium based on CPITN index in correlation to smoking habits and type of treatment in patients suffering from Crohn’s disease (CD).

**Results:** In 110 subjects (80 with Crohn’s disease and 30 healthy controls) aged 18-65 (mean 34.9) were included to the study. Disease phenotype at diagnosis was included. Prevalence of anxiety and depression was assessed in IBD outpatients and their mobility leading consequently to the need for teeth extraction. Periodontal disease is the second cause (just after the dental caries) of premature loss of natural teeth. The course and severity of periodontitis are significantly influenced by the virulence of the plaque bacteria, as well as the immune defenses of the organism.

**Disclosure:** Nothing to disclose.

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**P1544 PREDICTING FACTORS OF PROXIMAL DISEASE EXTENT IN ULCERATIVE COLITIS IN THE BIOLOGIC ERA**

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**Conclusion:** The disease proximal progression was observed in 19.7% of patients was a protective factor of proximal disease extent (HR: 0.19, 95% CI 0.04–0.82). There was no significant difference in Mayo score at diagnosis between the two groups.

**M. Sochal**

**P1545 THE ROLE OF SLEEP DISORDERS IN INFLAMMATORY BOWEL DISEASES (IBD) CLINICAL COURSE**

**Aims and Methods:** The aim of this study is to compare the baseline characteristics between the non-extent group and the extent group. The Cox logistic regression model was used to identify risk factors associated with proximal disease extent.

**Results:** We included 71 patients with distal UC: 36 E1 and 35 E2; 46.5% were male. Median follow-up of 7 (IQR 4–9) years. A total of 14 (19.7%) progressed to extensive colitis; median time to progression was 5 (IQR 1–8) years. 3 patients underwent colectomy during follow-up (2 in non-extent group). At diagnosis, 3 patients reported difficulty in falling asleep and the condition of patients with UC had extent disease progressed. Baseline patient characteristics including age, gender, smoking habit, hypertension, obesity, diabetes mellitus, history of appendectomy; family history of inflammatory bowel disease and initial laboratory data were not significantly different in the extent group compared with patients whose ulcerative colitis did not extend. However, extent group were more likely to suffer from primary sclerosing cholangitis (14.3% versus 0%, p = 0.016). Furthermore, there was no significant difference in Mayo score at diagnosis between the two groups. In the extent group, risk factors associated with disease progression were female sex (HR 6.7, 95% CI 1.4–32.5) and arthropathy at diagnosis (HR 3.7, 95% CI 1.1–12.8), whereas the use of oral 5-aminosalicylic acid since the diagnosis was a protective factor of proximal disease extent (HR: 0.19, 95% CI 0.04–0.82). Differences between quality of sleep and the type of IBD were not evident.

**Disclosure:** Nothing to disclose.

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**P1546 SELECTED CYTOKINES IN PERIODONTITIS IN PATIENTS WITH GORD ONE DISEASE – PRELIMINARY RESULTS FROM POIBD STUDY**

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**Introduction:** II-1β is a universal factor that stimulates the inflammatory reaction and can induce the secretion of other cytokines. Interleukin-6 (II-6) is secreted to stimulate immune response in the inflammatory and auto-immune processes. Pro-inflammatory cytokines mediate inflammation in both Crohn’s disease (CD) and periodontitis conditions. However, the influence of periodontitis overlapping CD on cytokine levels has not been elucidated up to the date. From clinical point of view, a characteristic pattern of inflammatory cytokines may be useful during the differentiation between common periodontitis and early stage of oral manifestation of CD.

**Aims and Methods:** The aim was to determine the serum levels of selected cytokines in patients with Crohn’s disease, according to the type of the disease and the state of periodontium as well as the habit of smoking, the type of treatment, the time elapsed from the diagnosis and disease phenotype according to the Montreal classification.

40 patients aged 18–65 years (mean 33.8) with Crohn’s disease were involved to the study. Patients completed self-report and dental examination with CEPIN index calculating according to WHO recommendations was performed. Following, the data on the II-1β and II-6 levels were assessed by MagPhx 13-plex bone panel.

**Results:** Overall cytokine levels were low. II-1β levels were 0.10–1.68 μg/mL and II-6 levels were 2.03–100.50 pg/mL (mean 11.73 pg/mL). Levels of both interleukins were significantly statistically positively correlated (R = 0.32, p = 0.039).

Suprisingly, II-1β was negatively correlated with state of periodontium related to CPITN (R = 0.10, p = 0.39).

We did not find any relationship between interleukin levels and smoking. The disease phenotype, type of treatment and time elapsed from diagnosis weren’t significantly correlated with II-1β or II-6 levels.

Conclusions: Since cytokine levels are known to influence both II-1β and II-6, are expected to be increased in the course of Crohn’s disease, our results differ from results obtained by other authors. We noticed differences in II-1β serum level of CD patients related to the state of periodontium. Some other findings reported changes (an increase) in periodontitis only in salivary or gingival fluid levels of II-1β and II-6 but not in serum.

**Disclosure:** Nothing to disclose.

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**P1547 PREDICTIVE FACTORS OF BONE LOSS IN INFLAMMATORY BOWEL DISEASE**

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**Introduction:** Patients with inflammatory bowel disease (IBD) have an increasing risk of developing bone and mineral metabolism disorders. Osteopenia and osteoporosis are a frequent but often underestimated complications in these patients. Several factors could contribute to osteopenia, while pathogenetic mechanisms are still ambiguous.

**Aims and Methods:** The aim of this study is to assess the prevalence and the risk factors associated with bone loss in IBD patients.

We conducted a prospective and descriptive study including 104 patients with IBD supervised within our department. Only patients who had bone densitometry and a phosphocapeutic biology analysis were included. Bone mineral density (BMD) was measured with diphotonic x-ray absorptiometry of the lumbar spine and the neck of the left femur. Results were expressed with T score (osteopenia: −2.5 standard deviation (SD)< T< −1 SD, osteoporosis: T< −2.5 SD) according to the World Health Organization (WHO) specifications.

**Results:** 104 patients included (55 men, 49 men), 55 had Crohn’s disease (CD) (52.88%), 40 had ulcerative colitis (UC) (38.46%), and 9 had indeterminate colitis (8.65%). The average age at diagnosis was 37.86 years [15–73]. BMD was normal in 47 patients (45.2%) and reduced in 57 patients (54.8%). Patients with CD had a reduced T-score (p = 0.001). In 22 cases osteoporosis was diagnosed (21.15%) and 35 patients had osteoporosis (33.65%). In patients with Crohn’s disease, 56% of cases (31.55) had a reduced BMD (osteoporosis in 13 cases and osteoporosis in 18 cases). 60% of patients with UC (24/40) had reduced BMD (osteoporosis in 8 cases and osteoporosis in 16 patients) and 22% of patients with indeterminate colitis (2/9) had a reduced BMD (osteopenia in 1 case and osteoporosis in 1 patient).

Rheumatologic manifestations were found in 19 patients with a reduced BMD. 27% of which had ankylosing spondylarthritiss. 29 patients received a full

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**P1548 THE ROLE OF SLEEP DISORDERS IN INFLAMMATORY BOWEL DISEASES (IBD) CLINICAL COURSE**

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**Introduction:** Etiology of Crohn’s disease (CD) and ulcerative colitis (UC) has not been entirely clear. Sleep disturbances in inflammatory bowel diseases (IBD) clinical course is multifactorial. Sleep may modulate the activity of the immunologic system. Mouse colitis model showed that sleep continuity disturbances exacerbated clinical and histopathological signs of the disease. The role of the sleep disturbances in inflammatory bowel diseases (IBD) clinical course is poorly understood.

**Aims and Methods:** The aim of the study was to evaluate the sleep patterns in patients with IBD whatever the disease activity. 25 individuals with IBD in exacerbation (age: 45 ± 13.5; 45% of men) and 25 in remission (age: 43 ± 14.5; 68% of men) were included in the study and completed questionnaires assessing sleep quality: Pittsburgh Sleep Quality Index (PSQI), Athens insomnia scale (AIS). The mood level (using Beck Depression Inventory (BDI)) and the level of pain (using Visual Analogue Scale (VAS)) for each patient. Spearman correlation were measured. The active disease will be defined as the Harvey-Bradshaw index score > 6 on the CD and the partial Mayo scale >3 in the UC. Information about the progress of the disease, methods of treatment and socio-demographic variables were also collected.

**Results:** Median quality of sleep and the type of IBD were not significant (CD: n = 24 ± 5.1 ± 1.5 and UC: n = 26 ± 2 ± 0.977 for PSQI; CD: 6 ± 0.25 and UC: 4 ± 0.4 ± 0.691 for AIS). Patients in exacerbation presented decreased quality of sleep in both PSQI (6 ± 0.2 ± 0.035) and AIS (6 ± 0.3 ± 0.035) compared to remission group (4 ± 0.5 ± 0.04 for PSQI and 4 ± 0.2 ± 0.016 for AIS). Additionally, exacerbation group score was higher in VAS (5 ± 2 ± 0.005, p = 0.006), LPS (5 ± 3 ± 0.004 and AIS (9 ± 5 ± 0.003) scale than in remission group (2 ± 1 ± 0.05 and AIS 5 ± 3 ± 0.5 and AIS). Subsequent ANCOVA analysis concluded there were no significant differences in exacerbation group and the type of IBD were not significant (CD: n = 24 ± 5 ± 1.5 and UC: n = 26 ± 5 ± 2 for AIS). Patients in exacerbation presented decreased quality of sleep in both PSQI (6 ± 2 ± 0.035) and AIS (6 ± 3 ± 0.035) compared to remission group (4 ± 1 ± 0.04 for PSQI and 4 ± 0.2 ± 0.016 for AIS).

**Conclusion:** Patients with IBD have similar sleep problems compared to those with CD. Decreased sleep quality may not depend on pain and depression, which are generally recognized as factors influencing sleep quality. The problem of sleep disturbances in IBD exacerbation should be considered in the disease treatment.

**Disclosure:** Nothing to disclose.
P1548 THE EPIDEMIOLOGICAL PROFILE OF INFLAMMATORY BOWEL DISEASE IN EASTERN REGION OF MOROCCO

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Introduction: Initially described in Northern Europe and the USA, inflammatory bowel disease (IBD) is now present worldwide. Africa is considered a continent of low incidence. However, the frequency of infectious colitis and the inadequacy of health systems in these countries explain the difficulty of assessing the actual incidence of these diseases.

Aims and Methods: The objective of our study was to describe the epidemiological and sociodemographic profile of IBD in the eastern region of Morocco. Descriptive and analytical retro-prospective study including 240 patients who were diagnosed with IBD at the Hepato-gastroenterology department of Mohamed VI University Hospital of Oujda over a course of 6 years and 3 months from January 2011 to April 2017. The data was collected using an exploitation sheet and the statistical analysis was done using Excel version 2010 and SPSS version 21.0.

Results: Among all eastern oriental inhabitants, the overall IBD prevalence was estimated at 10.3 / 100,000. The incidence of IBD progressively increased, especially for Crohn’s disease (CD), during the studied period. The average age was 13.2 ± 14.8 years, with a slight female predominance (sex ratio to 1.1). The majority of our patients came from an urban setting (93.3%). In this study 240 patients with established IBD diagnosis were included. among them, 132 patients were diagnosed with CD (55% of the total), 79 patients with ulcerative colitis (32.9% of the total), and 29 cases (12.1%) of indeterminate colitis (IC). In the CD group, patients were younger than those in ulcerative colitis, with average ages of 35.8 ± 12.6 and 41.6 ± 14.6 years, respectively. In our study, active smoking was noted in 3.8% of ulcerative colitis (UC) patients, and 7.5% of CD patients (p = 0.01). There was a personal history of appendectomy in 2 patients with UC (2.5%) compared with 19 patients (14.4%) in the CD group (p = 0.003). The presence of anorectal lesions was significantly associated with the male sex (p = 0.03). Ten (10) patients with CD (7.6%) and 12 patients with UC (15.2%) had a family history of IBD (p = 0.06).

Conclusion: Our study allows a better knowledge of the epidemiological profile of IBD in the eastern region of Morocco. These patients appear to be young with a female predominance and predominantly of urban origin. The creation of a national registry is necessary and not only allow the knowledge of the epidemiological and socio-demographic data but also an improvement of the subsequent care presented to these patients.

Disclosure: Nothing to disclose

P1549 PRESENCE OF GRANULOMAS IN INTESTINAL BIOPSY FROM PATIENTS WITH CROHN’S DISEASE CORRELATES WITH DISTINCT DISEASE CHARACTERISTICS

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Introduction: Detection of granulomas in intestinal biopsies is highly suggestive of a diagnosis of Crohn’s Disease (CD). The clinical significance of granulomas for the phenotype and natural history of CD has not been established yet, as previous studies produced conflicting results. Aims and Methods: We aimed to evaluate if granuloma detection correlated with specific characteristics and/or a particular disease course in a defined cohort of patients with CD. We retrieved all histological reports from an 8-yr period (2010–2017) that corresponded to the cohort of patients with CD with a regular and complete follow-up at our tertiary, reference IBD centers. Patients were classified according to the presence (or absence) of granulomas. The two groups were compared for various epidemiological, laboratory and clinical characteristics, as well as the clinical course and response to treatment.

Results: We identified biopsies from 220 patients with CD [male = 95, age range 18–76 (mean ± SD, range)] during the study period. Seventy-one patients (32.3%) were found to have epithelioid granulomas in at least one biopsy. The presence of granulomas was significantly associated with younger age at symptom initiation (37.2 ± 13.1 vs. 42.2 ± 15.3 years, P = 0.015), active smoking status (P = 0.032), weight loss and bloody stools at presentation (P = 0.001 and P = 0.012 respectively). Patients with granulomatous disease showed a trend towards colonic localization of the disease (non-L1 Montreal phenotype) (P = 0.097), and increased number of flares during follow-up (1.4 ± 2.4 vs. 2.6 ± 1.8 flares. P = 0.079). The latter trend persisted even when duration of follow was taken into account (0.6 ± 0.5 vs 0.5 ± 0.4 flares per year of follow-up, P = 0.071).

Conclusion: The presence of granulomas in biopsies from patients with CD was associated with specific disease characteristics and more frequent disease flares. Thus, granulomas may serve as a surrogate marker for a distinct subgroup of CD patients who may demonstrate more aggressive disease behavior.

Disclosure: Nothing to disclose

P1550 EPIDEMIOLOGY, INCIDENCE OF COLORECTAL CANCER, MORTALITY AND THE USE OF BIOLOGICAL THERAPY IN UC/CD PATIENTS BETWEEN 2007–2016 IN HUNGARY

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Introduction: Risk of colorectal cancer is increased among patients with ulcerative colitis.

Aims and Methods: Study design: Retrospective data analysis using the National Health Insurance Fund social security databases including inpatient- outpatient care, medications as well as the special drug reimbursement database of patients with the diagnosis of ulcerative colitis (UC) from 2007 to 2016. This is an observational, non-interventional, retrospective, epidemiological study.

Study population: All of the adult – over 18 years of age – UC patients between the examined period.

Eligibility criteria: Patients who have at least two events in all of relevant health care services or at least 1 inpatient event only with UC diagnosis (ICD codes: K51 – K50) between 2007–2016.

Primary endpoint: Analyze patient characteristics, epidemiology, CRC incidence and treatment patterns of UC patients in Hungary.

Results: The number of all UC patients between 2007–2016 was 27,850; 0.24% of total Hungarian population suffered from UC in 2016. The annual incidence of new patients with UC was between 1.51 to 2.92/100,000 with a declining tendency. The female/male ratio is 55/45. The median age of the patients with UC is 51 (male 49, female 53) in the examined period. Two thousand four hundred and fifty-two patients were diagnosed with CRC (8.8% of the total UC population). Ratio of mortality was 14.2% in the total group, 3941 of 27850 patients died. 24.8% of the total death was observed among patients with UC and CRC. Median survival of CRC was 64.7 months (95% CI 38.4–77.1). No significant difference can be observed between the different age groups, the confidence intervals are very wide due to the small sample size in the younger age groups. One thousand and ninety-five patients (2.89%) were treated with biological therapy between 2007–2016, while 2.1% of total UC population was treated with anti-TNF alpha therapy in 2016 that is more than 490 patients. The prevalence was 1.2% for ADA and 1.1% for IFX in the total UC population. The onset of biological therapy is between 20 and 39 years in the majority of the patients, average age is 37 years. This is 16 years less compared to the average age of total UC population.

Conclusion: Both the prevalence and incidence of UC are high in Hungary. While the ratio of co-existing CRC was 8.8%, 24.8% of these patients died during the examined decade. 2.89% of the UC population was treated with biological therapy in the examined period. Patients receiving biological therapy are typically from the younger part of the total UC population.

Disclosure: Nothing to disclose
P1551 NEXT-GENERATION SEQUENCING DERIVED MRNA SIGNATURES FOR ACTIVE ULCERATIVE COLITIS

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Introduction: MicroRNAs (miRNAs) are short non-coding RNAs that regulate gene expression. Growing number of studies have shown that miRNAs are highly involved in different inflammatory diseases including ulcerative colitis (UC). To date, miRNA deregulation profiles in active UC have not been fully explored. Aim of this study was to evaluate and compare miRNA profiles in tissues of active UC, UC in remission (inactive UC) and healthy controls. In the initial stage, miRNAs were sequenced in tissue samples of 32 healthy controls, 23 active UC and 21 sample of UC in remission using next generation sequencing platform. Most deregulated miRNAs were further validated in a second cohort of individuals with 38 healthy controls, 38 active UC and 36 inactive UC patients using RT-PCR based arrays. A multidimensional scaling analysis using Spearman’s correlation distance was performed to identify the similarities in miRNA expression profiles.

Results: Next-generation sequencing results of tissue samples from patients with active UC and healthy controls revealed 108 differentially expressed miRNAs, while miRNA profiles deregulated comparing active UC and UC in remission. Interestingly, only 31 deregulated miRNAs were found comparing healthy control and inactive UC tissues. In the validation phase, eight miRNAs (hsa-miR-223-3p, hsa-miR-155-5p, hsa-miR-146a-5p, hsa-miR-451-5p, hsa-miR-1180-3p and hsa-miR-424-3p) have been confirmed as consistently deregulated when comparing active UC and healthy controls. In parallel, only three miRNAs (hsa-miR-223-3p, hsa-miR-431-3p and hsa-miR-1180-3p) were confirmed as deregulated between healthy controls and inactive UC tissues.

Conclusion: Ulcerative colitis has unique miRNA signatures in colon tissues comparing active disease stage and disease in remission, which also differ from healthy controls. Furthermore, individuals with UC in remission have a more comparable miRNA expression profile with healthy controls than with active UC.

Disclosure: Nothing to disclose.

P1552 A COMPARISON OF CLINICAL, SEROLOGICAL AND GENETIC FACTORS PREDICTS COMPLICATED DISEASE COURSE IN PAEDIATRIC-ONSET CROHN’S DISEASE: RESULTS FROM A POPULATION-BASED STUDY

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Introduction: Identification of patients at high risk of disabling disease course would be invaluable to guide initial therapy in Crohn’s disease (CD). Clinical parameters at diagnosis are insufficient to predict a disabling course of CD (1). The objective of this study was to evaluate a combination of clinical, serological and genetic markers to predict complicated disease course in paediatric-onset CD.

Aims and Methods: Paediatric-onset CD patients, diagnosed before 17 years between 1988 and 2004 and followed more than 5 years were extracted from the French population-based Epidemiad registry. Complicated disease course was defined by the progression from an inflammatory (B1) to a complicated behavior (sticturing B2, or penetrating B3) or an intestinal resection within five years after diagnosis. Included are clinical data at diagnosis, serological markers at inclusion (ASCAP, ANCA, anti-OmpC, anti-Chib1, anti-Fla2, anti-Flax) and 370 candidate Single Nucleotide Polymorphisms (SNP) associated with CD or other immune-mediated diseases or having a role in inflammation pathways, interactions with microbiota, or modulation of innate immunity. A logistic regression model with stability selection was used to select variants associated with severe disease. After this selection step, a final lasso logistic model was performed including clinical, serological and selected variants.

Results: Two-hundred and nineteen patients were included, with a median age at CD diagnosis of 14.3 years (IQR [11.9–16.0]). Among the 156 patients with inflammatory disease (B1) at diagnosis, 35% (n = 54) progressed to a severe disease defined by a complicated behaviour or an intestinal resection during the five years following diagnosis. Final model included location at diagnosis (L1 or L3 at higher risk), ASCA (protective) and ANCA (protective) and 15 SNPs. Half of SNPs were known as susceptibility loci of IBD or CD including NOD2. This model showed good predictive measures with an AUC of 0.85, a sensitivity of 77%, a specificity of 80%, a positive predictive value of 68% and a negative predictive value of 87%.

Conclusion: In this population-based paediatric-onset CD cohort, a combination of clinical, serotypic and genotypic variables is able to predict disease progression with a high accuracy. After validation in an independent cohort, this prediction score will be helpful to identify patients needing early biological therapy.

Disclosure: Nothing to disclose.

Reference

P1553 THE ROLE AND EXPRESSION OF MIRNORNAS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Crohn’s disease (CD) and ulcerative colitis (UC) are the two major diseases that make up the inflammatory bowel disease (IBD). The major clinical challenge facing the clinician regarding inflammatory and chronic degenerative diseases, has indicated miRNAs as ideal candidates for diagnostic biomarkers, prognostics and potential therapeutic targets. An important feature of miRNAs is their stability and easy detection in body fluids.

We aimed to identify deregulated miRNAs in DII and to apply bioinformatic analysis strategies to identify target miRNAs and molecular pathways modulated by miRNAs through meta-analysis of literature data.

Aims and Methods: A meta-analysis was performed for the identification of miRNA expression data in IBD. An inclusion criteria was applied and 10 studies were selected, from which relevant miRNAs with increased or decreased and statistically significant expression were collected compared to controls, type and number of analyzed samples (serum, plasma or tissue) with CD and/or UC, platforms used for analysis of global miRNA expression and validation of data, author name and date of publication. Significantly deregulated miRNAs in DIIvs. Controls were used in bioinformatic analysis to predict the target miRNAs regulated by these miRNAs. Prediction analysis of miRNA target transcript enrichment of biological processes of the target genes were performed.

Results: The results showed 6 CD miRNAs with increased expression and 51 UC. On the other hand, miRNAs with decreased expression were found 51 CD and 26 UC. The miRNAs that showed the greatest number of interactions with DII deregulated genes were let-7a-5p, let-7b-5p and miR-19a-5p, miR-150-5p, miR-362-3p and miR-224-5p. In the RCU were -155p and miR-24-5p, miR-335-5p and let-7c-3p. Suggesting that they play an important role in the molecular mechanisms of disease. In addition, the results were used to identify gene interactions and biologic processes with inflammatory process and response to the immune system. We show that miRNAs and target genes may be useful biomarkers for the development of new therapeutic strategies for patients with IBD.

Conclusion: Several interrelated genes and miRNAs were identified as potential regulators of gene expression. Such miRNAs and genes may play important roles in the development and progression of inflammatory bowel disease. The miRNAs regulate several target genes and important molecular pathways, knowledge of these altered molecular pathways may be useful for the future development of more accurate treatment strategies for patients with DII.

Disclosure: Nothing to disclose.

P1554 BOWEL PREPARATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) should undergo multiple colonoscopies during their clinical history. Adequate bowel preparation is essential to high-quality colonoscopy but in our tertiary referral center for IBD it is not uncommon to find suboptimal bowel cleansing in these patients. In literature only few studies on bowel preparation in IBD patients can be found.

Aims and Methods: To assess bowel preparation in IBD patient, identify possible causes for suboptimal bowel cleansing and identify strategies for its optimization. Consecutive outpatients with IBD (ulcerative colitis [UC] and Crohn's disease [CD]) were prospectively enrolled before (ileo) colonoscopy at Gastroenterology and Endoscopy Unit of ASST Fatebenefratelli Sacco in Milan. Patients answered to a questionnaire with different items (type of bowel preparation, completeness of preparation, adherence to instructions given for preparation, palatability, side effects, Bristol Scale of stools in the previous week). Information about IBD type, duration of disease and treatment were also collected. Bowel preparation was evaluated by Boston Bowl Preparation Scale (BBPS); BBPS ≥ 6, at least 2 in every segment was considered adequate preparation. In a second part of the study, bowel preparation instructions were modified according to the last guidelines and patients received a telephone call to stress the importance of adherence to the suggested bowel preparation; the same questionnaire of the first part was administered to patients.

Results: In the first part we enrolled 120 patients (58 UC, 60 CD, 2 undetermined colitis) who had taken low volume PEG (lVP) in 57%, high-volume PEG (hVP) in 20%, stimulant laxatives (SL) in 16%, other (i.e., mix between PEG and stimulant laxatives) in 7% of patients. 53% of patients assessed correctly (i.e., respect of the timetable, completeness, correct diet) the preparation. 6% of patients presented the preparation with a split modality. Median time between preparation and colonoscopy was 15 (5–25) hours. 28% of patients fasted on the lunch before preparation. Adequate bowel preparation was observed in 67% of patients, with no differences with the type of IBD. In the second part of the study we enrolled 161 patients (80 UC, 80 CD, 1 undetermined colitis). lVP was used in 60%, hVP in 8%, SL in 24%, other in 8%. 70% of patients assessed correctly (i.e., respect of the timetable, completeness, correct diet) the preparation. 14% of patients assessed the preparation with a split modality. 6% of patients fasted on the lunch before preparation. Median time between preparation and colonoscopy was 14 (3–22) hours. Adequate bowel preparation was observed in 75% of patients, without differences with the type of IBD. In this second group of patients, independent predictors of adequate bowel preparation were age (OR 0.97, 95% CI 0.95–0.99), constipation (OR 0.98, 95% CI 0.96–1.00) and time between preparation and colonoscopy (OR 0.82, 95% CI 0.72–0.94).

Conclusion: Few studies are available on bowel preparation in IBD patients. The results of our study suggest that motivation of the patient to follow instructions for the preparation (including split preparation) may be of pivotal importance in stressing the importance of accurate execution of bowel preparation.

Disclosure: Nothing to disclose

P1556 THE EVALUATION OF IL-33/ST2 LEVELS CAN PREDICT MUCOSAL RESPONSE TO ANTI-TNF THERAPY IN ULCERATIVE COLITIS

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Introduction: Tumor necrosis factor (TNF) inhibitors (anti-TNF) are considered to be effective in inducing mucosal healing in patients with moderate-to-severe Ulcerative Colitis (UC). The role of IL-33 and its receptor, ST2, in intestinal inflammation is incompletely understood, with both pro-inflammatory and regulatory properties described. Recent evidence has shown that anti-TNF is able to modulate the IL-33/ST2 axis in inflammatory conditions.

Aims and Methods: The aim of our study was to explore the potential role of the IL-33/ST2 axis in the mucosal healing process mediated by anti-TNF therapy in UC.

Endoscopic Mayo score was calculated before the first anti-TNF infusion (T0) and after 6 weeks (T2). 26 UC patients (MAYO score at T0 ≤ 2) were enrolled. 14 responders with mucosal healing (MAYO score ≤ 1) and 12 non-responders to anti-TNF at T2 (MAYO score ≥ 2) were enrolled. 10 healthy controls undergoing routine colonoscopy for tumor screening were also enrolled. At each time point, serum samples were collected. ELISA and western blot were performed to assess IL-33/ST2 protein levels and to evaluate protein isoforms, respectively. Intestinal biopsies were also taken from the rectum and IHC was done to evaluate mucosal IL-33/ST2 expression and localization.

Results: IL-33 protein levels were significantly increased in responders vs. non-responders, both at T0 and T2. Among responders, IL-33 protein was slightly reduced at T2 vs. T0, while unchanged in non-responders. Interestingly, significantly higher levels of ST2 were found in responders vs. non-responders at T0, while no differences between groups were found at T2. Among responders, ST2 levels were dramatically reduced at T2 vs. T0. No significant differences were found.

Disclosure: Nothing to disclose
Introduction:

Change in PG and twice in SG. Patients on MG were assumed to be left on £123.50 (rectectin, colonoscopy, MRI, CT) were assessed to construct a global assessment of response group (SG)- reactive TDM on active patients with established primary group (MG)- proactive TDM on patients with quiescent IBD, secondary loss of and 89 ATI levels from 85 patients [54 male (64%), 32 females (36%); mean age: 39.13 years (±14.25); Crohn’s Disease (CD) n = 62, Ulcerative Colitis (UC) n = 23; 46 patients (54%) were on combination immunosuppressive therapy]. Patients were allocated to 3 groups based on the intent of TDM: Maintenance group (MG)- proactive TDM on patients with quiescent IBD, secondary loss of response group (SG)- reactive TDM on active patients with established primary response to IFX and post-induction group (PG)- TDM at week 14 post induction. In each sub-group, patient baseline characteristics (CRP, haemoglobin, calprotectin, coloscopy, MRI, CT) were assessed to construct a global assessment of patient state (active, remission or responding to drug) prior and after TDM led patient management for efficacy of IFX. Cost of IFX (INFLRECTA) was £123.50 (€VAIT) per 100mg while cost of TDM (IDKMONITOR ELISA KIT) was £45 per drug level assay and £45 per ATI assay. Calculations were done comparing TDM to empirical IFX dose escalation and switching of drug. Patients were compared to empirical dose escalation; once, before class drug change in PG and twice in SG. Patients on MG were assumed to be left on stable dose for one month with levels being measured twice a year.

Results: In MG (n = 51), 10 (20%) patients were de-escalated or stopped IFX and maintained in remission and 41 (80%) IFX was continued. The mean IFX level was 1.89mg/l vs 4.34, (p = 0.06) and mean ATI 85.10 vs 9.22, (p = 0.007) respectively. The two subgroups of 20% (n = 51) patients were maintained in remission till date for a mean of 12.2 months (Range 5-30 months) and were previously on IFX for a mean of 61.7 months (Range 20-132months). In the 80% of patients (n = 41), 2 became active after de-escalation, 2 became active despite having therapeutic IFX, 36 remained in remission and 1 patient’s status was unknown after stopping IFX (not included in cost savings calculation). Potential cost savings in MG was £669 per person per year (17% savings). In SG(n = 63), 21 (33%) patients switched drug or had surgery post TDM and in 42 (67%) IFX dose was escalated or maintained. The mean IFX levels was 2.24mg/ L vs 3.4mg/L and ATI 74.90IU vs 10.29IU (p = 0.0005) respectively in the two subgroups. 16 of 21 patients improved with change of drug, (remission = 8, 2 active, 3 unknowns) showing a 76–90% efficacy post TDM, 28 of 42 from IFX dose escalated SG subgroup improved (12 in remission), 12 patients were still active and 2 unknowns. Cost savings for SG group was £318.61 per person (13% savings). In PG, 2 of 8 achieved remission and 6 of 8 remained active and their mean IFX level were 2.2 vs 0.8 mg/L (p = 0.09) and mean ATI 0 IU vs 16.7 IU (p = 0.02) respectively. Cost saving of £607 per person in the PG group.

Conclusion: IFX TDM in IBD is clinically useful and has saved cost in all three patient groups with proactive TDM in post-induction and maintenance group benefitting the most.

Disclosure: Nothing to disclose.
therapy in PSC-IBD patients and represents a need for future studies regarding its role.

Disclosure: Nothing to disclose

P1559 PLATELET ACTIVATION BY ACTIVATED VON WILLEBRAND FACTOR IS A MARKER OF INTESTINAL WOUND HEALING IN PATIENTS WITH CROHN’S DISEASE

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Introduction: Crohn’s disease (CD) is a chronic inflammatory condition of the intestinal tract resulting in ongoing tissue damage and impaired wound healing. The reduced ability of CD patients to heal damaged tissue is reflected by the tendency of CD patients to develop fistula and fibrosis. ADAMTS13-processing of von Willebrand factor (VWF) reflects activated VWF, which is essential for initiation of primary haemostasis. Activated VWF is one of the rate-limiting factors in platelet activation and tethers to the damaged endothelium, and consequently is considered a surrogate biomarker for platelet activation. Any dysregulation in VWF processing could contribute to the development and progression of CD due to impaired and dysregulated wound healing, leading to a failure in the secondary hemostasis response.

Aims and Methods: The aim of the study was to investigate the processing of VWF, a marker of endothelial dysfunction, in patients with CD to assess primary hemostasis and platelet activation.

We developed two biomarkers specifically targeting the ADAMTS13-processed form of VWF (VWF-A), and formation/endothelial release of VWF by quantification of the pro-peptide (VWF-N). Serum samples from 13 irritable bowel syndrome (IBS) patients with high-grade inflammation and 51 CD patients and were included in the study together with 10 age-matched healthy subjects.

Results: Levels of VWF-N (p < 0.05; p < 0.0001) and VWF-A (p < 0.05; p < 0.01) and were significantly increased in CD and IBS patients compared to healthy subjects, respectively. VWF-N level (p < 0.0001) discriminated CD and IBS patients from healthy subjects with an area under the curve (AUC) of 0.94. No significant differences were observed in the ratio of VWF-N/VWF-A between IBS and healthy subjects.

Conclusions: CD patients showed an increased formation, but notably also an increase in activated VWF, indicating a sustained elevated primary wound healing response as compared to healthy subjects. Biomarkers of the dynamics of wound healing activation could serve as supplementary markers of intestinal healing in patients with inflammatory bowel diseases.

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Introduction: Patients with inflammatory bowel disease (IBD) have varying disease courses with phases of inactive disease and flares of active disease with impairment of the intestinal epithelial barrier leading to tissue damage. Due to the presence of an intact basement membrane, basement membrane is abundant in the intestine, and its constituents, such as laminins, play an important role in the intestinal epithelial homeostasis. The laminin gamma 1 chain is highly abundant along the entire crypt–villus axis in the basement membrane.

Aims and Methods: We investigated if a serum biomarker of the basement membrane (LG1M) could serve as surrogate biomarkers for disease activity in a rat in vivo colitis model and in IBD patients. Serum from male Sprague Dawley rats that received 5–6% dextran sulfate sodium (DSS) (n = 21) or regular drinking water (n = 9) for 5 days was included and scored for disease activity index (DAI). In addition, serum from 44 Crohn’s disease (CD) patients with inactive (n = 20) or active (n = 24) disease and healthy subjects (n = 20) was included in this study.

A competitive ELISA for matrix metalloproteinase (MMP) 9 mediated degradation of the laminin gamma 1 chain (LG1M) was used to estimate the level of laminin degradation in serum. Sections of the distal colon from the rats were assessed histologically for structural changes.

Results: LG1M were significantly elevated in CD patients serum compared to healthy subjects (p < 0.001), but with lower levels in inactive CD serum compared to active CD. The findings of LG1M were confirmed in the in vivo colitis model, in which the levels of LG1M in DSS rat serum with high DAI were significantly lower (p = 0.004) compared to controls. LG1M correlated negatively to DAI (r² = 0.2153; p < 0.01). The structure of the distal colonic tissue in DSS rats was disrupted compared to controls with loss of crypt architecture and total surface area.

Conclusion: Our data indicate that the basement membrane biomarker, LG1M, may be applied as non-invasive surrogate biomarker of disease activity in CD patients and thus aid in monitoring patients. We report lower serum levels of LG1M in active disease compared to inactive disease in both the in vivo model and patient samples. The decreased amount of LG1M during active disease corresponded to the apparent loss of surface area in the intestine, which results in a reduction of the total amount of laminins for MMP mediated degradation.


P1560 SERUM SIALIC-ACID-BINDING IMMUNOGLOBULIN-LIKE LECTIN (SIGLEC)-7 AS A FIBROGENIC BIOMARKER IN CROHN’S DISEASE

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Introduction: Currently, there are no serologic biomarkers useful in clinical practice for predicting the risk of developing strictures in Crohn’s disease (CD) and for identifying early stages of disease with the aim of optimizing the therapeutic management. Current biomarkers in CD are only predictors of a disabling disease course. Serum sialic-acid-binding immunoglobulin-like lectin (Siglec-7) is an inhibitory natural killer receptor, whose serum levels are associated with active liver fibrosis in hepatitis C virus infection. This study aimed at assessing serum Siglec-7 in CD patients with fibrosenosing phenotype.

Aims and Methods: Blood samples were collected from 30 CD patients (nine with fibrosenosing phenotype, eight with penetrating phenotype and 13 with inflammatory phenotype), 15 patients with ulcerative colitis (UC) and 26 control subjects. Serum concentrations of soluble Siglec-7 were measured by a commercially available quantitative ELISA kit.

Results: Among CD subgroups, serum Siglec-7 was significantly (p < 0.05) increased in CD patients with fibrosenosing phenotype (median 2071 pg/ml, range 1367–3292) in comparison to those with penetrating (median 1331 pg/ml, range 995–2132) or inflammatory (median 1356 pg/ml, range 846–1909) behaviour. No difference was found between penetrating and inflammatory phenotype. In addition, serum Siglec-7 was significantly (p < 0.05) up-regulated in patients with strictureting CD in comparison to both UC patients (median 1519 pg/ml, range 846–2090) and control subjects (median 1114 pg/ml, range 750–1386). Serum Siglec-7 was significantly (p < 0.001) higher in all the 30 CD patients (median 1411 pg/ml, range 846–3292) in comparison to control subjects.

Conclusion: Our study showed an increase of serum levels of Siglec-7 in CD patients with fibrosenosing behaviour in comparison to those with penetrating or inflammatory CD. These preliminary results support a role for serum Siglec-7 as a fibrogenic biomarker in CD.

Disclosure: Nothing to disclose

P1562 ASSOCIATION OF BODY COMPOSITION AND MUSCLE STRENGTH WITH DISEASE ACTIVITY IN PATIENTS WITH IBD

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Introduction: Inflammatory bowel disease (IBD) is commonly associated with alteration in fat and lean mass. The conventional indices for assessment of nutritional status such as body mass index (BMI) have been suboptimal and therefore require better modalities which can be assessed by bioimpedance analysis. In addition, correlation of body composition with disease activity has not been well studied. The aim of this study was to evaluate the association of body composition and muscle strength with disease activity in adult patients with Crohn’s disease (CD) and ulcerative colitis (UC).

Aims and Methods: All patients underwent the analysis of body composition measured by bioelectrical impedance analysis (TANITA body composition analyser, BC-420MA). Lean mass (LM), fat-free mass index (FFMI) and skeletal muscle index (SMI) were calculated using standard formulae. Muscle strength was obtained from handgrip strength values (HS) measured with Jamar Hydraulic Hand Dynamometer. Medical history data were obtained from clinical and electronic medical records. In order to evaluate disease activity, we used...
clinical indices: Crohn's Disease Activity Index (CDAI) for CD patients and Patrick Mayo Score for UC patients.

Results: In this study we have enrolled 75 patients (CD = 58, UC = 17; 50.7% male, 49.3% female). Clinically active disease (defined as CDAI > 150 or Patrick Mayo Score>5) was present in 25 patients (16.9% CD and 42.9% UC). There were no statistically significant differences among patients with active and inactive disease in FFMi [kg/m²] (17.7 (14.9–20.1) vs. 18.2 (15.3–26.2), SMI [kg/m²] 8.9 (7.1–10.7) vs. 9.3 (7.8–10.8), LM [kg] 50.4 (43–72.4) vs. 55 (43–93.0), and fat mass [%] 19.4 (14.9–45) vs. 23 (17.5–45), p > 0.05. Muscle strength was significantly lower in patients with active disease compared to inactive (32 ± 11.5 kg, p = 0.048). Underweight patients, defined as BMI < 18.5 kg/m², were significantly more prevalent in active group compared to inactive (27.8% vs 8.8%, p = 0.04,  χ² = 4.219).

Conclusion: Results of our study haven’t shown consistent association between body composition and disease activity. However, muscle strength was lower in group of patients with clinically active disease. Body composition analysis by BIA could be useful tool in evaluation of patients with inflammatory bowel diseases; however, there is a need to define age, gender and disease specific, percentile-based thresholds which can simplify the screening process in clinical practice.

Disclosure: Nothing to disclose

P1563 ASSOCIATION BETWEEN PROPOSED DEFINITIONS OF CLINICAL REMISSION/RESPONSE AND WELL-BEING IN PATIENTS WITH CROHN’S DISEASE


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Introduction: Recently, definitions of remission/response based on stool frequency (SF) and abdominal pain (AP) have evolved; however, data to support the validity of this approach are lacking. This analysis examined the association between the Inflammatory Bowel Disease Questionnaire (IBDQ) item 10 (Table), which can be considered a measurement of wellbeing, and clinical remission/response defined by SF and AP scores derived from the Crohn’s Disease Activity Index (CDAI).

Aims and Methods: Analyses included patients (pts) from 2 adalimumab (ADA) phase 3 and 1 upadacitinib (UPA) phase 2 Crohn’s disease trials with SF ≥ 4 and/ or AP score ≥ 2 at baseline. IBDQ item 10 response scores (ranging from 1–7) were categorized into 1/2 (feeling unwell all/most of the time), 3/4:5 (feeling unwell a bit/some/little of the time) and 6/7 (feeling unwell hardly any/none of the time) and analysed vs change from baseline to week 12/16 in SF and AP separately and clinical remission at week 12/16 defined as SF ≤ 2x, AP score ≤ 10 and neither worse than baseline.

Results: In the ADA trials, changes in IBDQ item 10 response categories were also grouped (≤2–0 ≥2-point-change from baseline) and analysed vs percentage change from baseline to week 12/16 and SF with AP with clinical response defined as ≥30% decrease in average daily SF and/or AP score; both not worse than baseline. Statistical differences were based on Mood’s two sample median test or chi-square test (2-sided alpha = 0.05).

Conclusion: 695 pts (40% with prior anti-tumour necrosis factor [TNF] exposure) from the ADA and 163 from the UPA (96% with prior anti-TNF exposure) trials were included. In the ADA trials, the median percentage changes from baseline to week 12 in SF (−62% vs 194) and AP scores (−83%; vs 193) were greater (both P < 0.001) in pts with IBDQ item 10 response scores 6/7 vs 1/2 (−13% [n = 127] and −3% [n = 128], respectively). In the UPA trial, changes in SF and AP (−76% and −73%, respectively [both n = 38]) were greater (both P < 0.001) in pts who responded 6/7 vs 1/2 (−14% [both n = 38]) at week 16. A significantly greater number of pts who responded 6/7 to item 10 in the ADA (62%) and the UPA (61%) trials met the definition of clinical remission compared with pts who responded 1–5 (both P < 0.01; Table). Pts in the ADA trials with ≥2-point-change in the IBDQ item 10 had greater median percentage reduction in SF (−50% [n = 339]) and AP scores (−64% [n = 338]) vs pts with +1-point (−32% and −31%, respectively [both n = 137]), 0-point (−17% [n = 139] and −14% [n = 138]), or −1-point change (−19% [n = 58] and 0% [n = 57]) from baseline. In the UPA trial, pts with ≥2-point-change in SF (n = 71) had greater change in SF (−68%) and AP scores (−55%) vs pts with +1-point (−35% and −25% [n = 33]), 0-point (−8% and −3% [n = 46]), or −1-point change (−22% and 0% [n = 13]).

Conclusion: The strong association demonstrated between SF and AP defined remission response and overall wellbeing support the validity of these measures in clinical trials.

IBDQ, Inflammatory Bowel Disease Questionnaire. *Defined as very soft/liquid SF ≤2x, AP score ≤10; and neither worse than baseline.

Table: Proportion of Patients Who Met the Clinical Remission Definition At Week 12 (Adalimumab) or Week 16 (Upadacitinib) by IBDQ Item Category

| Aims and Methods: The present study was aimed to compare the diagnostic performance of MRI and UCE. MRI was performed in the same day to minimize inter-scan variation. The results were analyzed using ImageJ software (version 1.53p, National Institutes of Health, Bethesda, MD). The images were reviewed by two experienced radiologists (SR and LR) who were blinded to the clinical data. The consensus agreement was used. The Cohen’s kappa coefficient was calculated to assess the inter-observer agreement. The results were analyzed using the Statistical Package for Social Sciences (SPSS) version 23.0. The significance level was set at p < 0.05.

Results: The study included 20 patients (12 male, 8 female; mean age 52 years) with Crohn’s disease. The inter-observer agreement for the measurement of lesion size on MRI and UCE was moderate (κ = 0.58). The mean lesion size measured on MRI was 2.6 cm ± 0.8 cm and on UCE was 2.5 cm ± 0.7 cm. The difference between the two modalities was not statistically significant (p = 0.76).

Conclusion: Our study demonstrates that UCE can be used as a non-invasive imaging tool for the evaluation of Crohn’s disease. Further studies with a larger sample size are needed to confirm these findings.
enlargement progression at 7m with respect to patients with low/moderate fibrosis (14.5% vs. 0.7%, p=0.001). By using UE as a gold standard, ROC curve analysis identified a cut-off value of 8.85% for MRI contrast enhancement progression at 7 min which was able to identify severe ileal fibrosis with a sensitivity of 87.5 and a specificity of 100%.

Conclusion: Results of this study demonstrate a good agreement between UE and MRI in identifying ileal fibrosis in patients with CD.

Disclosure: Nothing to disclose

P1565 PREDICTORS AT ADMISSION OF COLECTOMY WITHIN ONE YEAR IN PATIENTS WITH ACUTE SEVERE ULCERATIVE COLITIS

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Introduction: Definition criteria of acute severe ulcerative colitis (ASC) are well established, as well as the treatment strategy after hospital admission. In contrast, there are few data regarding predictors of colectomy at hospital admission. The aim of this study was to build a predictive score of colectomy based on clinical, biological and endoscopic parameters in patients with ASC.

Aims and Methods: All consecutive patients with ASC treated with intravenous corticosteroids, ciclosporin or tumor necrosis factor antagonists (anti-TNFs), and hospitalized in two French academic hospitals between January 2002 and January 2017 were included. Clinical, biological and endoscopic parameters at hospital admission were retrospectively collected. Treatment exposure was recorded and patients were followed until occurrence of colectomy or loss of follow-up. Predictors of colectomy within one year after admission were assessed by Cox survival analysis. The risk factors identified by multivariate analysis were used to build a predictive score of colectomy within one year after admission for ASC.

Results: A total of 270 patients with ASC were included with a median follow-up of 2.0 years (interquartile range [IQR] 0.5–4.8). Median age at occurrence of ASC was 32 years (IQR 24–47), 50% (n=81) and 12.6% (n=34) had a past or current exposure to thiopurines and anti-TNFs at admission, respectively. Median C-reactive protein (CRP) and albumin level at hospital admission were 53mg/L (IQR 18.6–110) and 30.7g/L (IQR 26.3–35.2), respectively. Crostidium difficile infection was diagnosed at hospital admission in 4.3% of patients (n=10) and 93.7% of patients (n=148) were exposed to thiopurines, anti-TNFs and corticosteroids, ciclosporin or tumor necrosis factor antagonists (anti-TNFs), and hospitalized in two French academic hospitals between January 2002 and January 2017 were included. Clinical, biological and endoscopic parameters at hospital admission were retrospectively collected. Treatment exposure was recorded and patients were followed until occurrence of colectomy or loss of follow-up. Predictors of colectomy within one year after admission were assessed by Cox survival analysis. The risk factors identified by multivariate analysis were used to build a predictive score of colectomy within one year after admission for ASC.

Score
3 24 24
2 113 6,5 10,7
1 91 7,1 9,6
0 41 0,0 0,0

<table>
<thead>
<tr>
<th>Score</th>
<th>N patients</th>
<th>Cumulative risk of colectomy at 3 months (%)</th>
<th>Cumulative risk of colectomy at 1 year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>24</td>
<td>24,1</td>
<td>53,0</td>
</tr>
<tr>
<td>2</td>
<td>113</td>
<td>6,5</td>
<td>10,7</td>
</tr>
<tr>
<td>1</td>
<td>91</td>
<td>7,1</td>
<td>9,6</td>
</tr>
<tr>
<td>0</td>
<td>41</td>
<td>0,0</td>
<td>0,0</td>
</tr>
</tbody>
</table>

[Table 1]

Conclusion: In this exploratory cohort of consecutive patients with ASC, we identified previous treatment by anti-TNFs or thiopurines, presence of Crostidium difficile infection, CRP level above 30mg/L and albumin level below 30 g/L as independent predictors of colectomy within one year. A score combining these predictors is highly predictive of the occurrence and risk magnitude of colectomy within one year after admission. These results need to be validated in a replicative cohort.

Disclosure: Nothing to disclose

P1566 ROLE OF SERUM TREFOIL FACTOR 3 AS A BIOMARKER OF INTESTINAL INFLAMMATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE


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Introduction: Several studies have shown the protective function of trefoil factors in the gastrointestinal tract and their up-regulated expression at the site of mucosal damage. However, the role of serum trefoil factor 3 (TFF3) in inflammatory bowel disease (IBD) still needs to be clarified.

Aims and Methods: The aim of the current study was to evaluate the role of TFF3 as a biomarker of intestinal inflammation in patients with IBD and to compare TFF3 values with those of fecal calprotectin (FCCP) in IBD patients. This prospective study enrolled 128 patients with IBD and 16 healthy controls. The patients were divided into four groups: with active ulcerative colitis (UC) (n=32), with active Crohn’s disease (CD) (n=32), and with CD in remission (n=32). Serum levels of TFF3 were measured by ELISA, FCCP levels were evaluated with quantitative immunochromato- graphic point-of-care test (Quantum Blue).

Results: The patients with active UC had the highest TFF3 levels. They were significantly higher than those of the controls (p<0.001), active CD patients (p<0.001), UC patients in remission (p=0.001) and CD patients in remission (p<0.001). UC patients in remission had really close mean values of TFF3 to healthy controls (p=0.593, p=0.015). In the control group, we found a significant difference (p=0.720). There was a significant moderate correlation between TFF3 and FCCP values in patients with active UC (r=0.516, p=0.041) and in UC patients in remission (r=0.593, p=0.015). In healthy controls and in CD patients correlation was not found.

Conclusion: Serum human TFF3 correlated well with FCCP levels and was able to identify patients with active UC. It has potential for being used as a marker for mucosal healing in UC patients. Further validation is needed to better establish the utility of TFF3 in IBD patients.

Disclosure: Nothing to disclose

P1567 DETERMINATION OF ANORECTAL FUNCTION WITH HIGH RESOLUTION ANORECTAL MANOMETRY IN ULCERATIVE COLITIS DURING DISEASE ACTIVITY AND AFTER REMISSION

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Introduction: Ulcerative colitis (UC) can impair anorectal function, resulting in distressing and disabling symptoms such as incontinence and increases in the stool frequency, urgency and tenesmus. Previous studies have linked rectal disorders during UC to an overactive rectum with an increased anorectal sensitivity and decreased rectal compliance. However, these results were based on conventional anorectal manometry, with the well-known limit provided by the use of less sensors, usually water perfused. Actually, there are no data reported on the rectal function in UC investigated with High-resolution anorectal manometry (HRAM).

Aims and Methods: The aim of this prospective study was to assess the anorectal function with HRAM in patients with mild-to-moderate UC at the first presentation. Secondary aims were to verify modifications after remission and to compare these data with those obtained in healthy volunteers (HVs).

Patients with UC satisfying the following inclusion criteria were included: an established diagnosis of UC, mild-to-moderate left-side colitis or proctitis (HRAM).

Results of this study demonstrate a good agreement between UE and MRI in identifying ileal fibrosis in patients with CD.

Disclosure: Nothing to disclose
All UC patients underwent HRAM before starting treatment and after remission. HRAM was performed with Sandhill InSight equipment, with a 7 cm long recording sites catheter. All recording sites were constituted by 4 recording pressure sensors arranged radially (28 pressure sensors). Two additional pressure sensors were located at the distal tip of the catheter in order to record intrarectal pressure and intra-balloon pressure. A disposable inflatable balloon was located at the tip of the catheter. The procedure was performed in left lateral (Sims) position after water enema irrigation. After accommodation time, the following parameters were assessed: anal resting pressure (ARP), length of anal canal, pushing endorectal pressure (PERP), recto-anal gradient pressure (RAPG, defined as the pressure difference between rectal pressure and lowest anal canal pressure during straining), rectal sensation and rectal compliance.

Results: Ten patients with UC (8 females) and 10 healthy volunteers (HV, 5 females) were prospectively enrolled. Before therapy, UC patients showed similar values for anorectal function to HVs, whereas rectal threshold volume for first sensation, desire to defecate, urgency to defecate and maximum discomfort were significantly lower than HVs values (p < 0.05). Rectal compliance was significantly impaired in UC than HVs (p < 0.001). After remission, rectal threshold volumes, as well as rectal compliance significantly increased (Table 1). An inverse linear correlation was found between regression of urgency and stool frequency and rectal compliance (r = 0.81).

Conclusion: HRAM can provide useful information about anorectal function in UC patients complaining urgency symptoms, in particular assessing the compliance of rectal wall that seems to be the responsible of the genesis of these symptoms.

Disclosure: Nothing to disclose

Table 1: Sociodemographic data of patients and healthy controls.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender</th>
<th>Marital Status</th>
<th>Status</th>
<th>Partner’s status</th>
<th>Divorced</th>
<th>Bachelor’s degree</th>
<th>Never married</th>
</tr>
</thead>
<tbody>
<tr>
<td>39.28 ± 12.75</td>
<td>Female: 58 (42.6%)</td>
<td>Married: 95/69 (69.9%)</td>
<td>Married</td>
<td>2 (1.5%)</td>
<td>Divorced: 2 (1.5%)</td>
<td>Married: 75 (44.6%)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>36.54 ± 14.14</td>
<td>Male: 78 (57.4%)</td>
<td>Never married: 37 (27.2%)</td>
<td>Married</td>
<td>2 (1.5%)</td>
<td>Divorced: 18 (10.7%)</td>
<td>Married: 80 (47.3%)</td>
<td>0.073</td>
</tr>
<tr>
<td>30.07</td>
<td>Female: 89 (52.7%)</td>
<td>Partner lost: 2 (1.5%)</td>
<td>Married</td>
<td>3 (1.8%)</td>
<td>Partner lost: 1 (0.6%)</td>
<td>Male: 80 (47.3%)</td>
<td>0.073</td>
</tr>
<tr>
<td>30</td>
<td>Never married: 71 (42.3%)</td>
<td>Male: 80 (47.3%)</td>
<td>Married</td>
<td>3 (1.8%)</td>
<td>Never married: 71 (42.3%)</td>
<td>Male: 80 (47.3%)</td>
<td>0.073</td>
</tr>
</tbody>
</table>

[Table 1:Sociodemographic data of patients and healthy controls.]
Results: Levels of vitamin D were measured among 83 patients with IBD (64 CD, receiving vitamin D supplementation, while undertreated group was defined as undertreated patients. Untreated patients were defined as those with vitamin D deficiency and not receiving treatment). Patients receiving treatment were defined as those with vitamin D insufficiency. Patients receiving treatment were defined as those with vitamin D insufficiency while undertreated vitamin D deficiency among IBD patients. Multivariate analysis showed that vitamin D deficiency was associated with increased collagen deposition. Intestinal fibroblasts and myofibroblasts are the main contributors of its strong connection with sexual function and satisfaction. Although the results show that SD is highly prevalent in IBD patients, with women to man ratio of almost 4 to 1. Erectile dysfunction is present in approximately 10% of IBD patients. In this cross-sectional study a random sample of patients with CD was included. None of the patients included in the study had HIV infection, vitamin D deficiency, endocrine dysfunction or neurological diseases. The results showed that SD is highly prevalent in IBD patients, with women to man ratio of almost 4 to 1. Erectile dysfunction is present in approximately 10% of IBD patients. In this cross-sectional study a random sample of patients with CD was included. None of the patients included in the study had HIV infection, vitamin D deficiency, endocrine dysfunction or neurological diseases.
Serum from CD patients (n = 44) and healthy subjects (n = 30) was included. The Mortensen’s criteria for endoscopic disease activity (non-stricturing, n = 20; B1: stricturing, n = 11; B3: penetrating n = 13) and disease location (L1, ileum: n = 14; L2, colon: n = 5; L3, ileum + colon: n = 25) was applied. The patients were classified as having inactive disease (n = 20) or active disease (n = 24) based on the Crohn’s Disease Activity Index (CDAI) score. Competitive ELISA was applied for the quantification of C16-C in serum from CD patients (total serum samples: n = 94).

Results: The biomarker C16-C was significantly elevated in patients with CD compared to healthy donors (P < 0.001, AUC = 0.81). CD patients with stricturing (B2) demonstrated significantly elevated serum levels of C16-C compared to CD patient without strictures (B1 and B3), and healthy donors. Furthermore, the diagnostic accuracy to separate CD patients with strictures (B2) from CD patient without (B1 and B3) was 76% (P < 0.001; AUC = 0.76) and healthy donors 96% (P < 0.001, AUC = 0.82). In addition, C16-C was also elevated in CD patients ilioum or ileum-colon disease involvement compared to only colon involvement and healthy donors (P < 0.05). There was no significant difference between active non-stricturing and inactive disease.

Conclusion: Our data demonstrates that type VI collagen can be quantified in serum from CD patients. The biomarker C16-C was significantly associated with stricturing disease phenotype, indicating that this biomarker might be a biomarker for intestinal fibrosis in CD, and may predict intestinal fibrosis developments in CD.

Disclosure: Joachim H. Mortensen, Majken Lindholm, Morten Asser Karsdal and Tina Manon-Jensen are fulltime employees at Nordic Bioscience.

PI154 PREVALENE AND PREDICTORS FACTORS FOR COMPLICATIONS IN ULCERATIVE COLITIS
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Introduction: Patients with ulcerative colitis may develop short-term or long-term complications such as malabsorption, arthropathies, erythema nodosum or primary sclerosing cholangitis, but the most serious complication is severe acute colitis.

Aims and Methods: The aim of this study was to assess the prevalence of complications in UC and to determine the risk factors related to the occurrence of these complications.

Our study included 76 patients with UC supervised within our department, we studied the following parameters in all these patients: age at the time of diagnosis, sex, smoking habits, extent of the disease, delayed diagnosis or therapy instaurment, therapeutic means and the occurrence of complications. The data was collected with an exploitation sheet.

Results: There were 48 women and 28 men. The average age at diagnosis was 39, 9 (7.74) years. The average age at disease progression was 38.7 months. No patient had a history of appendectomy. UC was classified as E3 in 50% of cases, E2 in 41% of cases and E1 in 9% of cases. The treatment was based on 5-ASA (5-aminosalicylic acid) in 45 patients (59.21%), Thiopurines in 23 patients (30.26%), Methotrexate in 4 patients (5.26%) and Anti-TNF in 4 patients. All the patients in our series had the following complications: malabsorption in 71 patients (93.4%), acute severe ulcerative colitis in 29 patients (38.15%) of which 8 presented a subtotal colectomy and one colonic stenosis in 2 patients (3.15%), ankylosing spondylarthropathy in 10 patients (13.5%), thromboembolic complications in 4 patients (5.26%) and a single case of anterior uveitis (1.31%). In a univariate analysis, anemia and the use of corticosteroid contributed significantly to the multivariate analysis model were statistically correlated to a delay of 5-AZA (5-aminosalicylic acid) in 45 patients (59.21%), Thiopurines in 23 patients (30.26%), Methotrexate in 4 patients (5.26%) and Anti-TNF in 4 patients. All the patients in our series had the following complications: malabsorption in 71 patients (93.4%), acute severe ulcerative colitis in 29 patients (38.15%) of which 8 presented a subtotal colectomy and one colonic stenosis in 2 patients (3.15%), ankylosing spondylarthropathy in 10 patients (13.5%), thromboembolic complications in 4 patients (5.26%) and a single case of anterior uveitis (1.31%). 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In a univariate analysis, anemia and the use of corticosteroid contributed significantly to the multivariate analysis model were statistically correlated to a delay of 5-AZA (5-aminosalicylic acid) in 45 patients (59.21%), Thiopurines in 23 patients (30.26%), Methotrexate in 4 patients (5.26%) and Anti-TNF in 4 patients.

Disclosure: Joachim H. Mortensen, Majken Lindholm, Morten Asser Karsdal and Tina Manon-Jensen are fulltime employees at Nordic Bioscience.
or mild UC compared with those with moderate to severe activity, with a sensi-
tivity of 88%; the positive predictive value (PPV) and negative predictive value (NPV) was 93 and 47% respectively. A CONUT score ≥6 points confers risk of moderate to severe activity by the TW score (OR:12.25 (2.46–60.91) p = 0.001). This same cut-off point (≥6 points) confers risk to pre-
sent elevated biochemical markers: ESR > 30 (OR: 5.0 (1.51–16.56) p = 0.005), with a sensitivity of 63% and specificity of 75, PPV 83% and NPV 50%; and CRP ≥5 (OR: 3.5 (1.2–10.19) p = 0.02), with a sensitivity of 67% and specificity of 64%, PPV 60% and NPV 70%.

Conclusion: CONUT score could be a predictor of clinical/biochemical severity in UC patients, as it is related to the severity measured by the TW score and with values of CRP:≥4 and ESR:≥30, the latter being independent predictors of coccidomy and severity in UC patients.

Disclosure: Nothing to disclose.

References

P1577 ANALYSIS OF COSTS, USE OF HEALTH RESOURCES AND IMPACT ON WORK PRODUCTIVITY AND QUALITY OF LIFE IN ULCERATIVE COLITIS: A PROSPECTIVE SINGLE-CENTER STUDY
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Introduction: Ulcerative colitis (UC) is a chronic condition with a heavy economic burden for the health system and the society. The need of lifelong treatments, hospitalizations and surgery causes significant direct costs and indirect costs due to sick leave, reduced employment opportunities and early retirements. Previous hospitalizations and surgery causes significant direct costs and indirect costs due to sick leave, reduced employment opportunities and early retirements. We aimed to assess the performances of Fcal to assess transmural healing in CD.

Aims and Methods: We included consecutively and prospectively all CD patients requiring MII. MII was associated with sustained clinical remission and lower risk of surgery. We aimed to assess the performances of Fcal to assess transmural healing in CD.

Aims and Methods: We included consecutively and prospectively all CD patients requiring MII. MII was associated with sustained clinical remission and lower risk of surgery. We aimed to assess the performances of Fcal to assess transmural healing in CD.

Fcal was moderately correlated with transmural healing in patients

 Conclusion: Fcal was moderately correlated with transmural healing in patients with CD. These two tools could be complementary to monitor patients with CD.

Disclosure: Nothing to disclose.

References

P1578 FAecal CALPROTECTIN AS SURROGATE MARKER OF TRANSMURAL HEALING ASSESSED USING MII IN PATIENTS WITH CROHN’S DISEASE
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Introduction: Mucosal healing (MH) is to date the most validated target in Crohn’s disease (CD). However, its use is limited by the low acceptability of repeated endoscopies. In this context, faecal calprotectin (Fcal) is a more convenient tool to monitor MH. Recently, transmural healing assessed using MII was associated with sustained clinical remission and lower risk of surgery. We aimed to assess the performances of Fcal to assess transmural healing in CD.

Aims and Methods: We included consecutively and prospectively all CD patients requiring MII. MII was associated with sustained clinical remission and lower risk of surgery. We aimed to assess the performances of Fcal to assess transmural healing in CD.

Fcal was moderately correlated with transmural healing in patients

 Conclusion: Fcal was moderately correlated with transmural healing in patients with CD. These two tools could be complementary to monitor patients with CD.

Disclosure: Nothing to disclose.

References
P1580 PATIENT-NEAR ADALIMUMAB TROUGH-LEVEL TESTING BY A NOVEL QUANTITATIVE RAPID TEST; THE QUANTUM BLUE ADALIMUMAB ASSAY

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Introduction: Therapeutic drug monitoring (TDM) has become standard clinical practice and overcoming clinical evidence indicates that dose-optimization improve clinical outcome by decreasing the risk for anti-drug-antibodies and improves the efficacy of the drug itself. Watanabe et al recently demonstrated that increasing trough levels were closely associated with endoscopic response in nesiritide, untreated Crohn’s disease were consecutively included in a cross-sectional study. The degree of barrier dysfunction impairment was higher in patients with IBD than in patients with IBD.

Disclosure: Nothing to disclose

P1582 THE ACCURACY OF THREE DIFFERENT METHODS ON THERAPEUTIC DRUG MONITORING OF SB2

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Introduction: Therapeutic Drug Monitoring is widely used in the adjustment of Infliximab (IFX) therapy and is expected to be used in the adjustment of biosimilars, SB2, a biosimilar of the originator IFX, has been recently approved by the European Medicines Agency (EMA) for the treatment of Inflammatory Bowel Disease (IBD).

Aims and Methods: The aim of this study was to evaluate the accuracy of three different methods for the quantification of biosimilar SB2. Moreover, the existence of IFX, CT-P13 and SB2 cross-immunogenicity was also evaluated. Three different IFX quantification assays were evaluated: an in-house built method, a commercially-available ELISA assay and a point-of-care device (POC-IFX). Spiking with known concentration of originator IFX, CT-P13 and SB2 were performed in donors’ samples and the percentage of recovery of each assay was evaluated. Reactivity of anti-IFX sera against anti-IFX and anti-CT-P13 antibodies was quantified using the in-house built method.

Results: The results show that all tested IFX-optimized assays are equally accurate in measuring SB2 levels: the intraclass correlation coefficient (ICC) between theoretical and measured concentrations varied from 0.945 to 0.983. Quantitative comparison showed an excellent ICC between the three assays when evaluating SB2, originator IFX and CT-P13. Regarding SB2, ICC was 0.986, 0.979 and 0.974 for POX IFX/in-house ELISA/in-house ELISA/POC IFX, respectively. Finally, the anti-IFX sera reacted almost to the same extent to SB2, originator IFX and CT-P13, with ICCs ranging from 0.986 to 0.993.

Conclusion: Our results suggest that either ELISA commercial assay, POC IFX or the in-house method can be used to measure IFX/biosimilar SB2 in an accurate fashion. Moreover, these drugs were shown to have a high cross-immunogenicity; this means that switching between them in a patient that has measurable levels of anti-drug antibodies will likely yield no clinical benefit.

Disclosure: FM served as speaker and received honoraria from Merck Sharp & Dohme, Abbvie, Vifor, Falk, Laboratorios Vitoria, Ferring, Hospira and Biogen.

0.05] (p < 0.001) and AILD – 0.101 [0.065; 0.257] (p < 0.001), which is the differences in the degree of barrier dysfunction – the ratio of lactulose/mannitol was in patients with AILD was higher – 0.101 [0.065; 0.257] than in patients with IBD – 0.024 [0.014; 0.05] (p < 0.001).

Conclusion: Patients with IBD and AILD decreased small intestine permeability by comparison to the control group. The degree of barrier function impairment was higher in patients with AILD than in patients with IBD.

Disclosure: Nothing to disclose

P1581 SERUM ALBUMIN CONCENTRATIONS ARE ASSOCIATED WITH ENDOSCOPIC DISEASE ACTIVITY IN NEWLY DIAGNOSED CROHN’S DISEASE PATIENTS

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Introduction: Serum albumin concentrations may be reduced in Crohn’s disease due to malnutrition and because albumin is an acute phase protein. The aim of this study was to investigate if serum albumin concentrations are associated with disease activity.

Aims and Methods: Seventy patients aged 16 years and above with newly diagnosed, untreated Crohn’s disease were consecutively included in a cross-sectional study between April 1, 2012 and December 1, 2016. Descriptive data, including age, gender and disease distribution were registered, as well as serum albumin concentrations. Disease activity was evaluated using the Simple Endoscopic Score for Crohn’s Disease (SES-CD), fecal (t)-calprotectin, CRP and the Harvey Bradshaw Index (HBI). Correlations were calculated by Spearman rank order test, and associations between albumin and disease activity markers were explored by linear regression analysis and measurements of albumin quartile concentrations vs. SES-CD.

A receiver operating characteristics (ROC) analysis was performed to determine a cut-off for s-albumin for severe vs. non-severe disease activity. SES-CD scores were categorized in non-severe (0–15) and severe disease activity (16 or above).

Conclusion: Patients with IBD and AILD had decreased small intestine permeability by comparison to the control group. The degree of barrier function impairment was higher in patients with AILD than in patients with IBD.

Disclosure: Nothing to disclose

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P1583 QUANTIFIED TERMINAL ILEAL MOTILITY DURING MR ENTEROGRAPHY AS A BIOMARKER OF CROHN’S DISEASE: A PROSPECTIVE STUDY

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Introduction: Previously, quantified MRI small bowel motility has been demonstrated as a non-invasive, objective biomarker of Crohn’s Disease (CD) inflammatory activity in retrospective investigations (1,2). In this study we prospectively evaluate the accuracy of quantified small bowel motility for CD activity against endoscopic and histopathological standards of reference. We also include the MaRIA score (validated MRI index of CD severity) to provide context (3).

Aims and Methods: 82 subjects (42 male, median age 32.5 years) recruited from two centres, underwent colonoscopy and MR enterography separated by median 5 days (range 0 to 14). The Crohn’s Disease Endoscopic Activity Index (CDEIS) was measured using endoscopy, and a histopathological activity index (eAIS) derived. Motility was quantified using a validated motility algorithm based on image registration and the magnetic resonance index of severity (MaRIA) score calculated. Sensitivity and specificity of Motility (> 0.3 AU ) and MaRIA (≥1) for disease activity (CDEIS ≥4 or eAIS ≥1) was compared using McNemar’s test, and Receiver Operating Characteristic (ROC) area under the curves constructed. Motility was correlated with reference standards using Spearman’s rank.

Results: Against CDEIS, motility had sensitivity and specificity of 92.7% and 66.7%, which was significantly higher & lower respectively than MaRIA (78.1% P = 0.03 and 80.5% P = 0.05). Against eAIS, motility had sensitivity and specificity of 91.7% and 73.5% for inflammatory activity. Sensitivity, but not specificity, was significantly higher than MaRIA (75.0% P = 0.03 and 80.5% P = 0.05). Using ROC curves, we determined the most relevant thresholds to detect endoscopic activity defined as no ulcer (cut-off value = 75.0; AUC = 0.65, Se = 54.9, Sp = 75.0, NPV = 64.0; PPV = 71.8%, NPV = 58.9%, CDEIS = 0–2 (cut-off value = 75.0; AUC = 0.65, Sp = 55.9%, Se = 81.5%, PPV = 88.4%, NPV = 42.3%). CDEIS > 3 (cut-off value = 77.0; AUC = 0.64, Se = 60.0%, Sp = 67.0%, PPV = 46.2%, NPV = 78.6%), SES-CD = 0 (cut-off value = 75.0; AUC = 0.68, Se = 57.7%, PPV = 76.9%, NPV = 60.7%) and SES-CD = 2 (cut-off value = 87.0; AUC = 0.62, Se = 60.0%, Sp = 64.0%, PPV = 30.8%, NPV = 85.7%).

Overall, 25 patients were monitored with serum CHI3L1 testing every 3 months (83 measurements). Serum CHI3L1 was significantly increased in the patients with clinical relapse within 3 months (p = 0.001). Using a ROC curve, we identified CHI3L1 > 64.0 as the best threshold to predict clinical relapse in patients with CD (AUC = 0.70, Se = 82.4%, Sp = 56.1%, PPV = 32.6%, and NPV = 92.5%).

Conclusion: Serum CHI3L1 is a promising surrogate marker of mucosal healing and may be a highly acceptable tool to predict the risk of relapse (high NPV).

Disclosure: This study was granted by Lesaffre company.

References


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Introduction: In recent years a proactive attitude is getting more common in treating inflammatory bowel disease (IBD) patients. We now look beyond symptoms and imaging, biomarkers and drug monitoring help guide the treatment changes. This strategy that is based on regular assessment of disease activity by using objective clinical, imagistic and biological outcome markers and the subsequent adjustment of treatment is called “treat to target approach”.

Aims and Methods: Capsule endoscopy has a well-defined role in Crohn’s disease patients’ diagnosis and monitoring. We present our experience of capsule endoscopy use in Crohn’s disease patients followed in a treat to target manner. We prospectively evaluated 17 Crohn’s disease patients followed in proactive manner using fecal calprotectin in a single center.

Results: Seventeen patients with known Crohn’s disease had a pan-enteric endoscopy. All patients had high levels of fecal calprotectin, but only 13 of them had symptoms. We had an incidence of endoscopy due to symptoms in the ileum for 9 hours. Active lesions were found in 15 patients: two of them had ileocolic ulceraions, one had gastro-duodenal and ileal lesions, one had peri-anastomotic fistula and 11 patients had ileal disease. Two patients had no lesions. Pan-enteric endoscopy examination identified lesions in 88% of patients with raised fecal calprotectin (even in asymptomatic patients).

Conclusion: In selected Crohn’s disease patients (inflammatory pattern) without known/suspected stenosis the pan-enteric endoscopy using capsule might
be used in conjunction with biomarkers to actively monitor the patients in a treat to target approach. This helps to stratify disease activity (due to well known limitations of clinical assessment) and can be paramount to guide therapeutic modifications.

The addition of FICE 1 and blue mode can detect even subtle lesions and therefore the risk of recurrence in this patients.

Disclosure: Nothing to disclose

PIS86 PERSONALISED CARE WITH THE TELEMEDICINE TOOL MYIBDCOACH IS COST-EFFECTIVE. A COST-UTILITY ANALYSIS OF THE MYIBDCOACH TRIAL


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Introduction: Value-based care is a promising strategy to improve quality of care and control costs, but warrants systematic measurement of patient-reported outcomes. Telemedicine is a powerful tool to enable continuous monitoring of outcomes in chronic diseases. For inflammatory bowel diseases (IBD), implementation of telemedicine previously showed to reduce outpatient visits and hospital admissions.1 However, cost-utility analyses are lacking. We therefore evaluated the incremental cost-utility of telemedicine versus standard care for IBD patients.

Aims and Methods: We used data from the 12-month myIBDcoach trial in which 904 IBD patients were randomized to teledicine (n=465) or standard care (n=444). Direct healthcare costs were estimated based on resource use multiplied by the appropriate unit prices, indirect or productivity costs were calculated using the friction-cost method, a license fee of €40 was calculated for patients using telemedicine, and utilities were assessed using EQ-5D (Dutch tariff). Cost-utility and uncertainty were estimated using the non-parametric bootstrapping method.

Results: Telemedicine resulted in a mean yearly cost saving of €554 per patient (95%CI, [-697, €2,094]; mean costs of €9495 for standard care and €8941 for telemedicine) and was associated with a small mean gain in quality adjusted life years (QALY) of 0.002 (95%CI, [-0.022, 0.018]). As myIBDcoach results on average in lower costs and somewhat better health, overall this innovative intervention dominates usual care. Telemedicine was cost-saving in 76% of the replications. However, there is still uncertainty, as dominance occurs only in 57% of the replications (figure 1).

Conclusion: MyIBDcoach is on average cost-reducing compared to standard care with maintained quality of life. However, there is large uncertainty and it might be of interest to detect whether a subgroup can be identified in which use of myIBDcoach results in higher QALY without higher cost. A cost-utility analysis is required to determine whether telemedicine can improve quality of life and disease outcomes on the long term.

Disclosure: Nothing to disclose

Reference
1. de Jong MJ, van der Meulen-de Jong AE, Romberg-Camps MJ, et al. Telemedicine with myIBDcoach is on average cost-reducing compared to standard care with maintained quality of life. However, there is large uncertainty, as dominance occurs only in 57% of the replications. However, there is still uncertainty, as dominance occurs only in 57% of the replications (figure 1).

PIS87 WHAT DO IBD PATIENTS KNOW ABOUT DIET AND PREVENTIVE PRACTICES IN IBD?

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Introduction: The IBD patients’ understanding of their disease is of extreme importance for its long-term management.

Aims and Methods: We aim to evaluate the knowledge of IBD patients about the role of diet, sun exposure, vaccination and smoking habits on their disease.

A cross-sectional observational study was performed through the application of a questionnaire (by e-mail using google forms platform) to patients of our outpatient clinic and members of the national association of IBD patients.

Results: We received 412 valid questionnaires (66.3% females, mean age ± SD of 37 ± 13years, 63.6% patients with Crohn’s Disease and 57.8% patients under immunosuppression/biologic therapy). The majority of participants acknowledged diet as an exacerbation factor for IBD (76.7%) and have modified their diet after the diagnosis of their disease (83%). The majority have never received advice on sun exposure (68%), thus being unaware of the risk of skin cancer associated with IBD and/or IBD therapy (66.5%). Most patients have never done skin cancer screening (88.9%), nor have they adjusted their lifestyles with reference to sun exposure (65.3%). The majority of patients (54.6%) discussed the vaccination plan with their gastroenterologist before starting an update of their biological plan (92.7%). Only 46.8% of the participants take influenza vaccine yearly. The anti-pneumococcal vaccine had been prescribed in 43.4% of patients. The majority never smoked (56.8%), nor did they discuss the topic of smoking with their gastroenterologist (62.9%). Only 13% of patients have changed their smoking habits after diagnosis: 54 out of 60 quit smoking and 8 out of 234 began smoking.

Conclusion: The participants in this study revealed limited knowledge about the role of diet, sun exposure, vaccination and smoking in IBD. It is absolutely necessary to invest in IBD education and prevention in order to provide them with an active role in the treatment of their disease and prevention of its complications.

Disclosure: Nothing to disclose

References

PIS88 DOES FECAL CALPROTECTIN BASED MONITORING HAVE AN IMPACT ON LONG-TERM OUTCOMES IN FINNISH ADULT PATIENTS WITH CROHN’S DISEASE: RETROSPECTIVE MULTI-CENTRE CHART REVIEW STUDY

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1. de Jong MJ, van der Meulen-de Jong AE, Romberg-Camps MJ, et al. Telemedicine with myIBDcoach is on average cost-reducing compared to standard care with maintained quality of life. However, there is large uncertainty, as dominance occurs only in 57% of the replications (figure 1).

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Introduction: To assess descriptively, whether Crohn’s disease (CD) patients with fCal testing one year after biological treatment initiation have different characteristics and outcomes compared to patients without such testing in real-life treatment setting.

Aims and Methods: A non-interventional, retrospective patient chart review study was carried out in 4 Finnish gastro clinics (EUPAS179190 registration). The study included patients with confirmed CD diagnosis, who had initiated a biological therapy for CD at any time between January 2010 – June 2016 (N = 186). The collected data included patient characteristics, CD characteristics, drug treatments, laboratory test results, health care resource use and outcomes. fCal had been assessed one year after biological treatment initiation in 46.8% of the patients who formed the fCal-group (n=87) whereas the remaining patients formed the non-fCal-group (n=99). For the purposes of the analysis, only patients with follow-up period of at least 14 months were considered (fCal-group, n = 80; non-fCal, n = 70).

Results: The study cohort consisted of patients aged on average 44.2 years, 58.0% males, median duration of 10.0 years (sd 9.7) and follow-up period of 1249.5 days (range 429-2369) with no significant differences between fCal and non-fCal groups. The patients with and without fCal testing at 1 year had relatively similar disease location: ileal (20.0% vs 18.6%; p = 0.83), ileocolonic (58.5% vs 51.4%; p = 0.37) and colon (21.3% vs 30.0%; p = 0.22). There were no differences in prior biological exposure (33.8% vs 35.7%, p = 0.80) or number of previous biological treatments (0.38 vs 0.49; p = 0.29) in the compared groups. During the study period 45 (55.0%) and 37 (52.9%) composite events (surgical procedure, new treatment initiation, disease relevant failure or unexpected occurrence of fCal and non-fCal groups, respectively (p = 0.79) with no statistically significant differences in mean time to composite event from the biologic initiation (414.2 vs 368.8 days; p = 0.64) between groups. Nine surgical procedures were performed in four patients during the follow-up period (1.1). There were no statistically significant differences in mean time to surgery from biological initiation in patients with and without fCal-testing (526.1 vs 531.3 days). Patients with fCal testing at 1 year had overall more fCal-testing during the follow-up period (5.3 vs 3.7, p < 0.001). The difference remained significant also when the fCal test at 1 year was excluded for the fCal-group (p < 0.05). However, there were no differences in the proportion of patients with imaging (colonoscopy, ileal or perianal MRI, abdominal CT, esogastroduodenoscopy) 12.6 months after biological initiation (25.0%
and 33.4% of patients in fCal and non-fCal groups, p = 0.213). Treatment-site-specific adverse events were observed for both treatments. In the total VDZ group, proportionally more patients in non-fCal group underwent imaging at 1 year (39.6% vs 26.2%; p = 0.14; n = 109) even though the difference did not reach statistical significance, whereas the opposite was true for one site (22.7% vs 7.8%; p = 0.09; n = 35). Non-fCal patients had significantly lower leucocyte levels at baseline (6.89 vs 8.47, p = 0.004) and at 1 year (5.88 vs 6.78, p = 0.030) and higher haemoglobin values at 1 year (141.16 vs 135.13, p = 0.04).

Conclusion: This study showed only minor differences in long-term outcomes of CD patients with and without fCal measurements 2 months after biological initiation in Finland. However, measuring fCal potentially decreases the use of imaging for assessing response to biological treatment in real-life setting.

Disclosure: Nothing to disclose
Disclosure: Nothing to disclose

Conclusion: Clinical response rates to VDZ in elderly IBD patients are similar to previous reports in younger patients. Anti-TNF naïve IBD patients may have greater response rates. VDZ has a favorable safety profile and is a valid and attractive option for this age group.

Reference


Disclosure: Nothing to disclose

References

One-hundred and twenty-three Japanese patients with UC and CD treated with thiopurines were enrolled. Genotyping for total seven SNPs of the NUDT15 gene was performed using Custom TaqMan SNP genotyping assays or Sanger sequencing. The changes in WBC count, mean corpuscular volume (MCV), platelet count, hemoglobin, CRP, amylase, albumin, AST, ALT, and ESR were evaluated.

The rates of protocolektomies, ileocolonic resections, and open laparotomies were similar in all 3 groups, as well as disease duration and severity, age and sex distribution, the CD/UC ratio, median days of hospital stay, and reoperation rates.

One hundred and three patients were included (52 female (50.5%), UC 47.7% were operated laparoscopically (in UC 77.5%) and in 7.3%, surgeons converted to open laparotomy (in UC 2.5%).

Minor complications* 10.8% 12.8% 20.3%
Major plus minor complications* 3.6% 7.7% 5.6%

Rates of postoperative complications * differences significantly not significant
Late complications occurred more frequent in group 3 as compared to group 1 (14.9 vs. 3.5%, p < 0.01), early complications occurred similarly in all groups.

Conclusion: Independently from the preoperative time interval, the use of TNF-inhibitors before surgery did not increase the risk of postoperative complications, reoperations or prolonged hospital stays as compared to patients without such preoperative therapy. Long disease duration was a risk factor for a complicated postoperative course.

Based on these data, the preoperative use of TNF-inhibitors might even exert a protective function. The introduction of infliximab and adalimumab biosimilars provides a chance to perform large prospective trials on strategies how we could best use TNF-inhibitors before surgery.

Disclosure: Thomas Ochsenkühn has received lecture fees, unrestricted travel grants and honoraria for advice from Abbvie, Biogen, Celltrion, Janssen, MSD, Mundipharma, R-Biopharm, Sandoz, Shields, Shire, Stada, and Takeda.

Fabian Schmitzer has received honoraria from Abbvie and MSD.

Disclosure: Nothing to disclose
P1596  LOWER RELAPSE RATES FOLLOWING A THERAPEUTIC Dosing Strategy of Infliximab Inadequate CRP De-escalation: A Single-Center Experience of a Real-Life Setting

Introduction: Infliximab is the first anti-TNF antibody approved for the treatment of IBD. However, the risk of relapse following infliximab dose de-escalation remains unclear.

Methods: We performed a single-center study on 96 patients with IBD who were receiving infliximab therapy. The primary objective was to assess the rate of relapse following inadequate CRP de-escalation in IBD patient in remission as well as predictors of the relapse including infliximab trough level prior to de-escalation.

Results: A total of 146 de-escalations were performed in the 96 patients. There were 57 (35%) males with a median age of 36 at infliximab de-escalation. The cumulative probabilities of relapse following anti-TNF de-escalation were 16% and 47% at 1 and 2 years respectively. By multivariate analysis, smoking (HR = 2.2, IC95%[1.07–4.6], p = 0.03), diagnosis of ulcerative colitis (HR = 2.9, IC95%[4.5–9.9], p = 0.0028), absence of combination therapy at infliximab initiation (HR = 3.4, IC95%[1.51–7.1]) increased the risk of relapse. The risk de-escalation was achieved with a strategy based on therapeutic drug monitoring decreased the risk of relapse (HR = 0.48, IC95%[0.24–0.96], p = 0.03). Infleximab trough level above 3 mg/L following infliximab de-escalation was associated with less relapse. Pre- and post- infliximab trough levels were well correlated (Spearman correlation coefficient p = 0.67, p < 0.0001).

Conclusion: Infleximab dose de-escalation increase the risk of IBD relapse. The use of infliximab trough level to assess the feasibility of dose de-escalation seems a prerequisite to decrease the risk of relapse. Infleximab trough level post de-escalation may be predictable.

Disclosure: Gu. Bouguen declares COI with Abbvie, MSD, Takeda, Janssen, Ferring, Pfizer, Hospira, Diasorin

P1597  LONG-TERM EFFICACY OF VEDOLIZUMAB THERAPY ON CLINICAL AND ENDOSCOPIC ACTIVITY IN PATIENTS WITH ANTI-TUMOUR NECROSIS FACTOR ALPHA RESISTANT INFLAMMATORY BOWEL DISEASE

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Introduction: Vedolizumab (VDZ) is the first gut-specific monoclonal antibody alternative to anti-tumor necrosis factor alpha (anti-TNF-alpha) therapy in patients with moderate-to-severe inflammatory bowel disease (IBD). It has been registered since 2016 in Hungary, but currently the high treatment costs are considerably limiting the availability of VDZ. All newly initiated VDZ therapy was individualized, it should be approved by the steering committee of five Hungarian IBD-specialist. The aim of our non-interventional retrospective study was to assess the efficacy of induction VDZ therapy on clinical and endoscopic activity in moderate or severe active IBD with previous anti-TNF failure or intolerable. The main objective was to evaluate the efficacy of induction VDZ therapy on clinical and endoscopic activity in moderate or severe active IBD with previous anti-TNF failure or intolerable.

Aims and Methods: Anti-TNF-alpha therapy intolerant IBD patients who received VDZ therapy were enrolled between July 2016 and January 2017 in Hungary. The therapeutic response was assessed based on the changes of clinical indexes (CDAI, POUCH, Mayo score) and Endoscopic Score for Crohn Disease (SES-CD), endoscopic Mayo score). Clinical response was defined as >3 points decrease in the total Mayo score or >100 decrease in CDAI score from baseline. Remission was defined as Mayo score <2 and CDAI score <150. Mucosal healing was defined as Mayo endoscopic subscore ≤1 or as SES CD score ≤5.

Results: 49 Crohn’s disease (CD) and 73 ulcerative colitis (UC) patients received VDZ induction therapy after anti-TNF failure or intolerance. The mean age was 46 years (range 18–85; median 39) and the average disease duration was 10.3 years (range 1–36; median 9). Extraintestinal manifestations occurred in 32 patients (26.2%), and in 10 cases (8.2%) IBD was associated with primary sclerosing cholangitis (PSC). At the baseline the mean CDAI and SES-CD were 303 (range 27–1295) and 5.7 (range 0–6) respectively. In the UC group mean Mayo and EMD score were 9.5 (range 5–12; median 10) and 2.72 (range 2–3; median 3) in the UC group, respectively. Clinical response during the VDZ induction therapy was seen in 30 (61.2%) CD and 61 (83.6%) UC patients. The remission of clinical disease in the UC group was seen in 9 patients (18%) with CD group (47.9% and 30.1% vs. 48.9% and 38.8%, respectively). In 51 cases the first-year VDZ treatment could have been completed during the study period, however in 15 cases due to lack of response therapy was observed. 31 patients received maintenance VDZ therapy. The rate of response, clinical remission and steroid-free remission were substantially higher in UC (55.0%, 41.4% and 41.4%) compared with CD (34.6%, 26.5% and 26.5%) (p < 0.0001). The difference between CD and UC subgroups was not statistically significant. There were 6 patients (37.5%) in CLD group who had pouchitis and / or fistulae. The response rate in CD patients without pouchitis and / or fistulae was more than 90%.

Conclusion: Our results suggest that both induction and the one-year long maintenance VDZ therapy is effective and it is a safe therapeutic option in anti-TNF-alpha failure or intolerant IBD patients with moderate or severe disease activity, however significant difference was observed between the UC and CD subgroups. The induction therapy in the second UC and CD subgroups is more effective in UC patients both by the end of induction and by the end of first-year therapy (48.3% and 51.7% vs. 9.1% and 13.6%).

Disclosure: Nothing to disclose
18.7% (3/16) of patients with CLD had ulcer morphology suggesting CD in the present study. Any of patients in this diseased control and the control group had endoscopic findings suggesting CD.

Conclusion: CLD is more common in patients who had an inadequate preoperative investigation of terminal ileum. To detect ulcers on colonoscopy before surgical aspects suggesting CD is a risk factor for CLD, even if the ileum is normal. In CLD mucosal remission could not be achieved in any patient despite combined immunosuppressive therapy. Fistula rate was about 40% in CLD patients, and 3 of 6 patients with fistula in our series required permanent stoma.

Disclosure: Nothing to disclose

P1500 AN INTRODUCTION TO LUCID: LIVING WITH ULCERATIVE COLITIS; IDENTIFYING THE SOCIOECONOMIC BURDEN IN EUROPE

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Introduction: The need for newer therapies remains an important challenge to properly manage patients with Ulcerative Colitis (UC). Colectomy still remains the last resort faced by patients who are non-responsive to current medical therapies. The increasing incidence of UC and the advent of biological drugs ultimately generated a new economic burden associated with UC that remains to be explored. To date there is little evidence about direct and indirect medical and societal costs across Europe. Although Health-related quality of life (HRQoL) outcomes are crucial to assess UC treatment benefits, it is still poorly reported in the literature.

HCD Economics in conjunction with the University of Chester (UoC) UK, are undertaking a pan-European burden of illness study (LUCID) across 10 countries (Denmark, France, Germany, Italy, Norway, Poland, Romania, Spain, the United Kingdom of Great Britain and the UK) including 377 physicians and 3,582 patients. LUCID is governed by an expert review group consisting of charity, academic, medical and health economist representatives.

Aims and Methods: The primary objective is to quantify UC-related costs from a societal perspective. The secondary objective is to determine the impact on patient’s HRQoL. The study population includes adult patients diagnosed with UC at least 24 months prior to the index date (date of clinical consultation). The study cohort comprises two arms: Arm 1: patients with moderate to severely active UC at the initiation of a treatment period. Arm 2: patients with prior moderate or severely active UC who had achieved mild UC or remission.

Data are to be collected by means of two questionnaires: physician on-line clinical record form (CRF), and written public and patient involvement engagement form (PIIF). The CRFs collect information on direct medical resource utilisation over the 12 month documentation period. The PIIF form captures out-of-pocket expenses and work loss direct (non-medical and indirect costs), as well as quality of life (disability and work-related activity (EQ-5D-5L, IBD-DI and Work Productivity and Activity Impairment Questionnaire, WPAI).

Full ethical approval is being sought from the UoC Faculty of Health and Social Care Research Ethics Committee. This study will enable the generation of a granular database comprehensively detailing the wide variety of costs that accompany living with UC. Per-patient costs are calculated by multiplying the quantities of the resource use collected in the study with the national unit price of each resource. Costs are valued using the traditional human capital approach.

Disclosure: Nothing to disclose
Disclosure: (particularly advanced endoscopic lesions), still one-third of patients develop this setting, although anti-TNFs prevent POR in a large proportion of patients. In markedly different from RCTs: they are more frequently used in combination. Use of anti-TNF agents for the prevention of POR in real practice is Conclusion: exposure to anti-TNF, concomitant immunosuppressant therapy and penetrating ADM. Endoscopic or clinical POR were the main reason to dose-escalate ADM. Treatment was dose-escalated in 24% of patients, being similar for IFX and 30% presented clinical POR as considered by the treating physician. Surgical POR was defined by the need of the new intestinal resection during follow-up. Results: A total of 152 patients were included, 55 treated with IFX and 97 with ADM. Concomitant use of immunosuppressants was prescribed in 39%, of which 83% thiopurines and 17% methotrexate. 44% received an additional 3-month course of metronidazole after surgery. Anti-TNF was started after a median time of 32 days (IQR3–44) from surgery. Regarding risk factors for POR (i.e., pre-surgery dose increase of 5 mg/kg or more, prior resection, 44% had penetrating CD behaviour, and 28% had a history of perianal disease). In total, 27 (18%) had none, 59 (39%) had only 1, and 66 (43%) had >1 risk factor for POR. 82% had been exposed to anti-TNF prior to the index surgery (73% within the last 6 months). Median time of follow-up on anti-TNF was 29 months (IQR 13–48). 121 patients (80%) had one endoscopic assessment within 18 months after surgery were included. Clinical and endoscopic features were collected before and within 18 months after surgery. Endoscopic POR was defined by Rutgeerts score >11 and >15 in patients with exposed to anti-TNF and >8 in patients with thiopurine therapy. Clinical POR relied on the criteria of the treating physician. Surgical POR was defined by a Rutgeerts score 4. Further, 44% of patients reported a low adherence to their oral medications. Ulcerative colitis patients had a lower risk of low adherence when compared to Crohn's disease subjects [OR 0.57 (0.37–0.87)]. Low adherence was more prevalent when considering aminosalicylate consumption (52.2% had a score compatible with low adherence). Independent variables significantly associated with low aminosalicylate adherence were use of other chronic medications [OR 1.49 (1.01–2.25)] and the lack of perception of easy communication with the gastroenterologist [OR 1.67 (1.2–2.2)]. Low adherence to thiopurines was reported in 40.25% of patients under that treatment. Endoscopic POR was associated with low adherence to thiopurine therapy [OR 1.2 (1–5.8)] and smoking [OR 3.75 (1.53–9.17)] were significantly associated with thiopurine low adherence. When considering biologic treatment, 21.8% reported low adherence; subsequent administration instead of intravenous was significantly associated with low adherence to biologics [OR 4.8 (1.57–14.60)]. Conclusion: Low treatment adherence is common among IBD patients, especially among aminosalicylate consumers. Clinical features were found to be associated with adherence to medical treatment, and they are potentially modifiable and thus efforts should be directed towards that aim. Disclosure: Nothing to disclose.

P1602 EVALUATION OF TREATMENT ADEQUACIE INFLAMMATORY BOWEL DISEASE PATIENTS FROM ARGENTINA: A MULTICENTER STUDY

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Introduction: The aim of this study was to evaluate the effect of Inflammasome dose-reduction on clinical remission in IBD patients in deep remission. In this retrospective single-centre study, patients treated with IFX monotherapy every 8 weeks and in composite deep remission for at least 1 year had a dose reduction to their infusion from 5 mg/kg to 3 mg/kg. Patients were followed up every 3 months and relapse was defined by composite markers of clinical, biological and endoscopic remission. IFX was increased at 5 mg/kg in patients with relapse and infusion reaction or intolerance to IFX was recorded. Statistical analysis was performed by Student t test and a p value of 0.05 was considered significant.

Results: Fifty-seven patients (17F, 40M) were included (33 Crohn’s disease [CD] and 24 ulcerative colitis [UC]) with a mean follow-up after dose reduction of 12.7±8.3 months. Mean duration of IFX before dose reduction was 45.8±28.4 months. Overall, 14 (24.5%, 6 UC and 8 CD) patients relapsed during the follow-up. Cumulative probability of relapse free survival was 74.9%±0.06% at 1 year and 69.2±0.08% at 2 years. Patients relapse with an IFX re-escalation to 5 mg/kg dose with clinical response in 11/14 (78.5%). None of the patients
reported adverse events during maintenance with dose reduction whereas one patient (1/14) reported an infusion reaction after re-escalation to 5 mg/kg. No difference in the mean duration of IFX before dose reduction was observed in patients with relapse compared to patients maintaining remission (45.2 ± 26.4 months vs. 44.8 ± 28.2 months, p = 0.1). In CD patients there was a trend of association between duration of IFX before dose reduction < 36 months and the risk of relapse, although not statistically significant (OR = 2.07; CI 95% 0.3–12.4, p = 0.4).

Conclusion: In a real-life clinical setting, IFX dose reduction is feasible and safe in IBD patients and can achieve deep remission with a relatively low risk of relapse at 2 years. More than three-quarters of patients who relapsed regained remission after IFX re-escalation. In CD patients an IFX use > 36 months seems to be associated with a lower risk of relapse after dose reduction.

Disclosure: Nothing to disclose.

P1604 RESCUE THERAPY WITH ANTI-TNF AGENTS FOR ESTABLISHED POST-OPERATIVE RECURRENCE OF CROHN’S DISEASE. A MULTICENTRE, RETROSPECTIVE, NATIONWIDE STUDY

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Introduction: Thiopurines are the treatment of choice for the prevention of post-operative recurrence (POR) in Crohn’s disease (CD) in high-risk patients, whereas those at low risk should be monitored and treated only in case POR occurs. Endoscopic assessment of POR is recommended within the first year following surgery in all patients. With this strategy, up to 50% of patients will develop POR within 6–12 months after surgery. In patients with established POR, anti-TNF agents may be of benefit, but scarce data on this are available.

Aims and Method: Our aim was to evaluate the rate of endoscopic remission and improvement of mucosal lesions under rescue therapy with anti-TNF for established POR. Retrospective, multicentre, nationwide study in CD patients who received therapy with anti-TNF agents because of established POR as defined by a Rutgeerts’ endoscopic score >11. Epidemiological, clinical, biological and endoscopic features were collected before and after starting anti-TNF.

Endoscopic improvement and remission were defined by a reduction in the baseline Rutgeerts’ score and by a score <12, respectively. Clinical POR was defined by the presence of 2 out of the following 3 criteria: weight loss, increase in stool frequency, and new onset of abdominal pain, in the setting of POR at endoscopy or MRI enterography.

Results: 287 CD patients treated with infliximab (n = 126) or adalimumab (n = 161), 70% in combination with immunosuppressants, because of established POR were included. Table 1 summarizes the baseline characteristics of the patients. Endoscopic assessment was available in 190 patients (66%) after a median time of anti-TNF treatment of 16 months (IQR 11–31). Among these patients, 114/190 (60%) had endoscopic improvement and 82/190 (43%) achieved endoscopic remission (Rutgeerts 0–1). Of the 82 patients with clinical POR at anti-TNF start, 60 patients (73%) achieved clinical remission. Median time of follow-up on anti-TNF treatment was 45 months (IQR 20–75). During this time, 44 patients (15%) developed clinical POR and 17 patients (7%) developed surgical POR. Univariable and multivariable logistic regression model showed that combination therapy with thiopurines and treatment with infliximab were the only factors associated with a higher rate of both endoscopic improvement (OR 2.97; 95% CI 1.6–5.7, and OR 2.23; 95% CI 1.2–4.2, respectively), and endoscopic remission (OR 2.28; 95% CI 1.2–4.3, and OR 2.65; 95% CI 1.5–4.8, respectively).

Conclusion: Rescue therapy with anti-TNF is efficient for the treatment of established POR, even in patients in whom endoscopic POR occurs while on azathioprine.

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Disclosure: Nothing to disclose.

P1605 STOPPING 5-AMINOSALICYLATES IN ULCERATIVE COLITIS PATIENTS STARTING BIOLOGIC THERAPY DOES NOT INCREASE THE RISK OF ADVERSE CLINICAL OUTCOMES

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Introduction: 5-aminosalicylates (5-ASA) are commonly used in the treatment of ulcerative colitis (UC). The benefit of continuing 5-ASA in UC patients who initiated anti-tumor necrosis factor alpha (anti-TNF) biologics is unknown.

Aims and Methods: We aimed to compare clinical outcomes in UC patients already on 5-ASA who started anti-TNF and then either continued or stopped 5-ASA. Our primary outcome was any adverse clinical event defined as a composite of new corticosteroid use, hospital admission, or colectomy. We utilized two national databases: the United States (U.S.) Truven MarketScan health claims database and the Danish National Patient Register linked with the Danish National Prescription Register. Patients with UC who started anti-TNF after having been on oral 5-ASA for at least 90 days were included. Patients were classified as stopping 5-ASA if therapy was discontinued within 90 days of starting anti-TNF. Analyses were performed using multivariable Cox regression models controlling for age, sex, disease duration, 5-ASA treatment duration, and baseline healthcare utilization. Hazard ratios (HR) with 95% confidence intervals (95% CI) are reported comparing stopping 5-ASA with continuing 5-ASA (reference group).

<table>
<thead>
<tr>
<th>[Table 1.]</th>
<th>Female sex</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n = 287)</td>
<td>135 (47)</td>
<td>0.01</td>
</tr>
<tr>
<td>Infliximab (n = 126)</td>
<td>66 (40)</td>
<td></td>
</tr>
<tr>
<td>Adalimumab (n = 161)</td>
<td>66 (40)</td>
<td></td>
</tr>
</tbody>
</table>

>1 known risk factor for POR

| Anti-TNF exposure prior to surgery | 102 (36) | 0.10 |

Preventive thiopurines for POR

| Advanced POR (Rutgeerts score i3–i4) at anti-TNF start | 173 (60) | 0.99 |

Clinical POR at anti-TNF start

| Concomitant thiopurines with anti-TNF | 182 (63) | 0.08 |

[Table 1.]

Disclosure: Nothing to disclose.
G. Dijkstra1, R.K. Weersma1, E.A.M. Festen1,2

observed on a specific subset of gut directed CD4+ peripheral blood and intestinal mucosa. Indeed, the highest level of binding was Vedolizumab binds to a large variety of immune cells in both per-
capillaries and to only 5% (IQR 2%-10%) of monocytes, at intermediate levels.

Vedolizumab binds to 37% (IQR 21–50) of leukocytes from the vasculature into the gut. It leads to sustained steroid-free remission in about 30% of Crohn’s disease (CD) and ulcerative colitis (UC). The new biological vedolizumab (anti-a4b7) blocks the migration of Surgery 6.2 (4.4–8.7) 10.2 (6.7–15.5) 1.36 (0.75–2.46) 0.3

Hospitalization 13.0 (10.2–16.6) 22.2 (16.4–30.1) 1.35 (0.88–2.08) 0.2

Composite 44.7 (41.6–48.1) 51.2 (46.3–56.7) 1.04 (0.90–1.21) 0.6

Denmark Cohort New Steroid Use 22.9 (19.0–27.6) 21.7 (16.1–29.3) 1.05 (0.71–1.55) 0.8

Hospitalization 13.0 (10.2–16.6) 22.2 (16.4–30.1) 1.35 (0.88–2.08) 0.2

Surgery 6.2 (4.4–8.7) 10.2 (6.7–15.5) 1.36 (0.75–2.46) 0.3

Composite 37.5 (32.0–43.8) 42.9 (33.2–55.1) 1.09 (0.90–1.48) 0.6

Table 1. Risk of Adverse Outcomes in Patients Who Continue or Stop 5-ASA

Disclosure: Nothing to disclose

P1608 TARGET CELLS OF VEDOLIZUMAB IN PERIPHERAL BLOOD AND GUT MUCOSAL CELLS FROM IBD PATIENTS

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2University Medical Center Groningen, Genetics, Groningen, Netherlands

Introduction: The new biological vedolizumab (anti-a4b7) blocks the migration of leukocytes from the vasculature into the gut. It leads to sustained steroid-free remission in about 30% of Crohn’s disease (CD) and ulcerative colitis (UC) patients. In UC, this remission is reached much faster (47% after 6 weeks) than in CD (15% after 6 weeks), rendering treatment with vedolizumab much more cost-efficient in UC than in CD. Deeper insight into the immunological effects of vedolizumab is necessary to explain differences between the mechanistic impact of vedolizumab therapy in CD and UC.

Aims and Methods: The aim of this study was to determine the binding capacity of vedolizumab to both immune cells in blood and to isolated mucosal cells from the inflamed ileal and colonic mucosa. We collected peripheral blood and intestinal biopsies from patients with CD and UC prior to vedolizumab treatment, and peripheral blood from healthy controls. Intestinal biopsies were dissociated into cell suspensions from the epithelial layer and lamina propria separately. We engineered fluorescent-labeled vedolizumab and assessed the percentage of vedolizumab-bound cells as well as the level of vedolizumab binding per cell type, using flow cytometry.

Results: Vedolizumab binds a large variety peripheral blood immune cells (i.e. CD4+ T cells, CD8+ T cells, B cells, eosinophils, NK cells and monocytes). Vedolizumab binds nearly all eosinophils (median 91% [IQR 83–94]) and gut mucosa directed CD4+CD38+CD62L−/− T cells (median 82% [IQR 68–91]), at high levels. Vedolizumab also binds the majority of B cells (median 84% [IQR 75–92]), CD8+ T cells (median 70% [IQR 60–80]) and CD4+ T cells (median 55% [IQR 48–61), at intermediate levels. Vedolizumab binds to 37% (IQR 21–50) of NK cells and to only 5% (IQR 2–10%) of monocytes, at intermediate levels. The adverse outcomes observed in this study were associated with the gut directed CD4+CD38+CD62L−/− T cells, which was significantly higher than on CD4+ T cells, CD8+ T cells and B cells (P < 0.0001). Before vedolizumab treatment, no significant differences in percentage of vedolizumab-bound cells or levels of vedolizumab binding were observed between patients with CD, UC, and similar to healthy controls. Within the intestinal mucosa, vedolizumab preferably binds lamina propria cells, at moderate levels, and in particular CD8+ T cells from the terminal ileum (median 64% [IQR 28–94]). These lamina propria CD8+ T cells from the terminal ileum also showed the highest levels of vedolizumab binding.

Conclusion: Vedolizumab binds to a large variety of immune cells in both peripheral blood and intestinal mucosa. Indeed, the highest level of binding was observed on a specific subset of gut directed CD4+ T cells. Pretreatment percentages of vedolizumab-bound cells or levels of vedolizumab binding do not explain differences between mechanistic impact of vedolizumab therapy in CD and UC. These results provide baseline data for correlating vedolizumab binding capacities to clinical response in IBD patients.

Disclosure: Nothing to disclose

References:


Abstract No: P1610

Table 1: Clinical and Radiological Outcomes

<table>
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<tr>
<th>Study</th>
<th>Number of p/C patients</th>
<th>Induction with anti-TNFa</th>
<th>Maintenance with anti-TNFa</th>
<th>Short-term clinical remission</th>
<th>Long-term clinical remission</th>
<th>Short-term MRI healing</th>
<th>Long-term MRI healing</th>
<th>Short-term Odds Ratio</th>
<th>Long-term Odds Ratio</th>
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<tr>
<td>Bell et al</td>
<td>7</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.01</td>
<td>-</td>
</tr>
<tr>
<td>Van Assche et al (Part 1)</td>
<td>7</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.01</td>
<td>-</td>
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<tr>
<td>Van Assche et al (Part 2)</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>0.01</td>
<td>-</td>
</tr>
<tr>
<td>Tugeron et al</td>
<td>26</td>
<td>26</td>
<td>16</td>
<td>13/26 (50%)</td>
<td>11/16 (69%)</td>
<td>2/14 (14%)</td>
<td>0.08</td>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Savoije-Collet et al</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>1/20 (5%)</td>
<td>2/20 (10%)</td>
<td>0.21</td>
<td>0.04</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Karmiris et al</td>
<td>59</td>
<td>59</td>
<td>-</td>
<td>24/59 (41%)</td>
<td>3/29 (10%)</td>
<td>5/38 (12%)</td>
<td>0.22</td>
<td>0.08</td>
<td>0.05</td>
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<tr>
<td>Horstius et al</td>
<td>16</td>
<td>16</td>
<td>-</td>
<td>1/6 (16%)</td>
<td>1/6 (16%)</td>
<td>0.11</td>
<td>0.01</td>
<td>0.07</td>
<td>-</td>
</tr>
<tr>
<td>Tozer et al</td>
<td>41</td>
<td>41</td>
<td>41</td>
<td>4/19 (21%)</td>
<td>6/19 (32%)</td>
<td>1.73</td>
<td>0.40</td>
<td>0.71</td>
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</tr>
<tr>
<td>Thomassin et al</td>
<td>49</td>
<td>49</td>
<td>-</td>
<td>26/49 (53%)</td>
<td>16/49 (33%)</td>
<td>0.43</td>
<td>0.19</td>
<td>0.97</td>
<td>-</td>
</tr>
<tr>
<td>Totals</td>
<td>253</td>
<td>184</td>
<td>192</td>
<td>72/163 (44%)</td>
<td>6/67 (9%)</td>
<td>33/146 (23%)</td>
<td>0.14</td>
<td>0.03</td>
<td>0.54</td>
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</table>
P1611 GOLIMUIM IMPROVES PATIENT-REPORTED WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH ULCERATIVE COLITIS: INTERIM RESULTS FROM A NON-INTERVENTIONAL TRIAL IN GERMANY
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2Praxis Grümmert, Potsdam, Germany
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5Gastroenterologische Gemeinschaftspraxis am Germany-Campus, Münster, Germany
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7MSD Sharp & Dohme GmbH, Haar, Germany
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Introduction: No prospective data evaluating work productivity and activity in real world practice are available in patients with moderate to severe ulcerative colitis (UC) treated with Golimumab (GLM) for more than 3 months. The aim of this study is to assess the change of work productivity, activity and quality of life (QoL) in UC patients treated with GLM for 1 year in an observational real-world setting in Germany.

Aims and Methods: The validated WPAI-questionnaire (Work Productivity Activity Impact Questionnaire) was used for the primary analysis. The change of work productivity and activity for daily activities at 3 months and 12 months versus baseline was evaluated. The 4 subscores of WPAI were assessed: disease-related absence from work (absenteeism), working while sick (presenteeism), total work productivity impairment (TPWI) and activity impairment. TPWI was the primary endpoint. To assess disease-specific quality of life the IBDOQ (Inflammatory Bowel Disease Questionnaire) was used. Analysis population included all treated pts (N = 287) and patients who completed the WPAI and were employed at baseline (N = 203).

Results: 287 UC patients were included in the study. At baseline, 61% had moderate UC, 18% had severe UC by global physician’s assessment. Slightly less than half of the population were male (48%). 75% of the subjects were either employed full-time or part-time. 269 patients completed the WPAI and 203 were analyzed for the primary endpoint, as these were employed at baseline. 12 months after start of all WPAI subscores showed significant improvements compared to baseline. Similarly significant improvements were detected in the IBDOQ.

<table>
<thead>
<tr>
<th>Change from</th>
<th>Change from</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL Mo 3 (%)</td>
<td>BL Mo 12 (%)</td>
</tr>
<tr>
<td>WPAI</td>
<td></td>
</tr>
<tr>
<td>TPWI [mean ± SD]</td>
<td>−16.6 ± 32.1 (N = 99)*</td>
</tr>
<tr>
<td>Absenteeism [mean ± SD]</td>
<td>−14.9 ± 38.6 (N = 132)*</td>
</tr>
<tr>
<td>Presenteeism [mean ± SD]</td>
<td>−14.1 ± 28.6 (N = 100)*</td>
</tr>
<tr>
<td>Activity impairment [mean ± SD]</td>
<td>−13.5 ± 28.2 (N = 149)*</td>
</tr>
<tr>
<td>IBDOQ</td>
<td></td>
</tr>
<tr>
<td>Change from BL Mo 3</td>
<td>Change from BL Mo 12</td>
</tr>
<tr>
<td>26.0 ± 35.7 (N = 191)*</td>
<td>41.2 ± 38.7 (N = 121)*</td>
</tr>
</tbody>
</table>

[1] Comparison vs baseline: p < 0.001

Conclusion: GLM treatment results in significant improvement of work productivity and daily activities in patients with UC up to 12 months after start of treatment. Patients also experience a significant improvement in their QoL in terms of IBDOQ.


P1612 DRUG-INDUCED TOXICITY AND IMMUNE-INFLAMMATORY DISORDERS OF HEPATO-PANCREATO-BILIARY SYSTEM IN IBD PATIENTS: A DIAGNOSTIC CHALLENGE
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2Clinical Center of Serbia, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia
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Introduction: Drug-induced toxicity by commonly used therapeutics, aminosalyciates (ASA) and azathioprine (AZA), in patients with inflammatory bowel disease (IBD) have been described in a literature, with AZA-induced pancreatitis occurring more frequently in IBD patients than in other AZA-treated patients. IBD are also often accompanied by extraintestinal immune-inflammatory diseases, frequently involving hepatopancreato-biliary system.

Aims and Methods: To investigate frequency and clinical presentation of drug-induced toxicity and its association with extraintestinal diseases in IBD patients treated with common therapeutic protocols.

Patients with verified IBD (endoscopy and histopathology) were included in the retrospective study. For each subject we collected general and anamnestic data, laboratory and other diagnostic findings, data regarding application of therapeutic protocols, clinical response to applied therapy and the presence of extraintestinal immune-mediated diseases, drug-induced toxicity and disease complications.

Drug-induced toxicity was confirmed empirically (symptom withdrawal after drug cancellation).

Results: Out of 258 IBD patients (male 55%, female 45%, mean age 40.8 yrs, 51.6% had ulcerative colitis and 48.4% had Crohn’s disease. Extrapancreato-biliary system was present in 21.3% of IBD patients. Drug-induced toxicity occurred in 16.3% IBD patients, AZA-induced more frequently than ASA-induced (69% and 31%). The incidence of AZA-induced toxicity was 18%, while ASA-induced toxicity was 5%. Drug-induced toxicity manifested as hepatitis in 42 (patients 52%), includ- ing: toxic pancreatitis (43%), more frequently ASA-induced than AZA-induced (66.7% vs. 33.3%, p < 0.05) and toxic hepatitis (7%) presented only in ASA-treated patients. The incidence of toxic pancreatitis was 7.3% among AZA treated IBD patients. The second most frequent drug-induced toxicity were hematopoietic disorders (11/42, 26%), which were all AZA-induced, with the incidence of 6.7% in IBD patients. Patients with extraintestinal autoimmune disease more often developed drug-induced toxicity (p < 0.05).

Conclusion: Susception of drug-induced toxicity in IBD patients requires multidisciplinary diagnostic approach in order to differentiate drug-induced toxicity from immune-inflammatory extraintestinal manifestations, especially when they are presented as hepatopancreato-biliary disorders.

Disclosure: Nothing to disclose

P1613 EFFICACY AND SAFETY OF BIOSIMILAR INFlixIMAB CT-P13 IN PATIENTS WITH CROHN’S DISEASE WHO WERE NAı¨ VE TO ANTI-TNF THERAPY: PRELIMINARY RESULTS FROM POLIBD STUDY
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Introduction: CT-P13 biosimilar monoclonal antibody to infliximab (IFX) approved for the same indications as its IFX counterpart in Poland.

Aims and Methods: The primary study was to evaluate the efficacy and safety of biosimilar infliximab in Crohn’s disease (CD) in patients from Subcarpathian Region (South- Eastern Poland). 93 patients with CD naïve to anti-TNF therapy were enrolled (30 females/63 males), aged from 18 to 69 years, treated with CT-P13 in the Department of Gastroenterology of University Hospital in Rzeszow in 2010 and 2017. 7 (7.5%), 43 (46.2%) and another 43 (46.2%) of patients had ileal, ileo-colonic and colonic CD respectively. All patients received standard immunosuppression with no additional steroid or antibiotic therapy.

Results: In 56% of the patients clinical remission was achieved (CDAI score <150). Response to treatment (CDAI score reduction of ≥70 points) was noticed in 31% patients, and 13% patients worsen. Secondary loss of treatment in 5 patients (5.4%) was observed. Among those with ileal CD, clinical remission
was achieved in 3 patients (45%), 2 patients responded to the therapy (28.5%) and 2 patients did not respond. Among those with colonic CD, clinical remission was achieved in 25 patients (58%), 13 responded to the therapy (30%) and 5 patients did not respond (12%) Among those with ileo-colic CD, clinical remission was achieved in 24 patients (56%), 14 responded to the therapy (32%) and 5 patients did not respond (11%). 11 out of 70 patients (12%) had adverse events (AEs); 8 of them (8.5%) had serious adverse events (SAEs) that forced the withdrawal of treatment: sepsis (1 patient 1%), allergic reactions (6 patients 6.5%), perianal abscesss (1 patient 1%) Other AEs were perianal abscesses (3 patients 3.2%).

Conclusion: In analysed population, biosimilar I邢 CT-P13 seems to be effective and safe in patients with CD who are naive to anti-TNF therapy.

References: not applied

Disclosure: nothing to disclose

P1614 DE-ESCALATING THERAPY IN PATIENTS WITH CROHN’S DISEASE RECEIVING ADALIMUMAB: A SUBGROUP ANALYSIS OF THE CALM STUDY

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4University of California San Diego, La Jolla, United States
5Medical University of Vienna, Vienna, Austria
6Oxford University Hospitals, Oxford, United Kingdom
7University Hospital Schlewig-Holstein, Kiel, Germany
8Fondazione Policlinico Gemelli Universita, Rome, Italy
9Humanitas University, Rozzano, Italy
10AbbVie, Solna, Sweden
11AbbVie Inc, North Chicago, United States
12Incahn School of Medicine at Mount Sinai, New York, United States

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Introduction: This analysis evaluated the impact of de-escalating therapy on mucosal healing 48 weeks (wks) after randomisation in patients with Crohn’s disease (CD) in the CALM.

Aims and Methods: In CALM, adult patients with moderate to severe CD naive to immunomodulators and biologics were randomized 1:1 to a tight control (TC) or clinical management (CM) group after ≤ 8 wks of prednisone therapy. Treatment was withdrawn for no treatment (NT), ADA induction+40 mg every other (EO) wks to 40 mg ADA EOW (EO) to 40 mg ADA EOW+2.5 mg/kg azathioprine (AZA)/day at 12, 24, and 36 wks after randomisation based on specific failure criteria (CD Activity Index [CDAI] ≥200 or decrease <70% (1 wk prior to randomisation) or <100 points compared with baseline (at wk 11, 23, 35) and prednisone use for the CM group, and CDAI ≥150, C-reactive protein ≥5 mg/L, faecal calprotectin ≥250 μg/g, and prednisone use for the TC group). At 24 and 36 wks, if failure criteria were not met, patients de-escalated to ADA EOW (ADA induction+40 mg every other week [EO]) to 40 mg ADA EOW if the failure criteria were met at the following visit. In this subgroup analysis, the primary endpoint (mucosal healing [CD Endoscopic Index of Disease <3] and no deep ulcers at 48 wks after randomisation) was evaluated in patients who de-escalated and/or re-escalated treatment.

Results: 15 patients in the CM group and 31 patients in the TC group de-escalated treatment during the study (CM, n = 15 from 40 mg ADA EW to 40 mg ADA EOW; TC, n = 21 from 40 mg ADA EW to 40 mg ADA EOW; TC, n = 10 from 40 mg ADA EOW+2.5 mg/kg AZA/day to 40 mg ADA EOW+2.5 mg/kg AZA/day). Of those, 2 patients in the CM group and 8 patients in the TC group re-escalated to 40 mg ADA EOW. Overall, 54% (7/13) of patients in the CM group and 61% (14/23) of patients in the TC group who de-escalated to 40 mg ADA EOW ± AZA achieved the primary endpoint (Table). Of the patients who re-escalated to ADA EW, 0% in the CM group, and 75% (6/8) in the TC group achieved the primary endpoint (Table). The overall adverse event rates in CALM have been previously reported.

Conclusion: Our data suggest that repeated dose optimization (ADA de-escalation to ADA EOW [re-escalation based on tight control is a more refined approach] or re-escalation in mucosal healing compared with CM. Larger data sets are needed to confirm our observation on repeated dose optimization.

Disclosure: Mrs. Bossuyt, D’Haens, Sandborn, and Travis have received research support from AbbVie and other commercial entities. Mrs. Bossuyt, D’Haens, Panaccione, Sandborn, Reinisch, Travis, Schreiber, Armuzzi, Danese, and Colombel have received speaker’s fees from AbbVie and other commercial entities. Mrs. D’Haens, Panaccione, Travis, Sandborn, Schreiber, Armuzzi, Danese, and Colombel have received consulting fees from AbbVie and other commercial entities. Drs. Reinisch, Armuzzi, Danese, and Colombel are advisory board members of AbbVie or other commercial entities. Sofie Berg, Joel Petersson, Jen-Fue Maa, and Ezequiel Neimark are AbbVie employees and may own stock or options. AbbVie funded the study, contributed to the design, and was involved in the collection, analysis, and interpretation of the data, and in the writing, review, and approval of the publication. Medical writing support was provided by Catherine DeBrosse, PhD. Complete Publication Solutions, LLC (North Wales, PA), which was funded by AbbVie.

Reference

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P1615 ATTITUDES TOWARDS TREATMENT WITHDRAWAL IN IBD

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Introduction: A recently published ECCO topical review on exit strategies in inflammatory bowel disease (IBD) has underlined the role of treatment withdrawal in selected cohorts with stable disease. As the disease course in IBD varies greatly, certain patients may well be over-treated with immunosuppressive agents. Identifying which patients can safely stop their treatment remains a challenge. Little is known regarding patients’ own attitudes towards stopping long-term immunosuppressive treatment.

Aims and Methods: We invited patients undergoing immunosuppressive therapy, attending either out-patients or the infusion suite, during a 6-week period in March-April 2018, to participate in this prospective observational study. Participants were asked a series of questions regarding their disease and treatment history, compliance with treatment, awareness of risks of immunosuppression, concerns regarding long term treatment, concerns regarding treatment withdrawal and willingness to switch to generic medication.

Results: In total, 151 (female = 77, 51%) patients participated. The mean age was 41.5 years, with a range of 19–82 years. The majority of patients had a diagnosis of Crohn’s disease (n = 117, 77%). The mean duration of disease was 12.2 years, with a range of 0.5–46 years. The breakdown of current treatments was as follows: 28% Adalimumab, 26% Infliximab, 22% combination therapy, 14% Infliximab, 14% Ustekinumab, 4% Vedolizumab. The mean duration of therapy was 4.67 years, with a range of 0.4–18 years. At least one course of glucocorticoids had been taken by 35% (n = 43) in the previous 12 months. Amongst the cohort there were 32 active smokers (21%) and 52 (34%) former smokers. Missed doses were reported most frequently for oral medications (80% IMM) and subcutaneous injections (78%). There were less missed doses in the intravenous treatment group (35%). Overall for the group the mean HBI was 6.3, with a range of 1–26, and the mean Mayo score was 1. There was very good awareness of the effect of therapy on the immune system (n = 147, 97%), with 100 (65%) expressing concern regarding same. There was general acceptance of life-long therapy (n = 115, 77%), however many (n = 91, 60%) would be happy to stop treatment if advised so by their Physician, particularly if the decision were based on suboptimal drug levels (n = 142, 93%). In terms of switching to a biosimilar drug, the majority (n = 111, 73%) had no objection. The main concerns expressed regarding treatment withdrawal included the risk of relapse (68%), loss of response (16%) or none (16%).

Conclusion: There is a good understanding amongst patients regarding the risks of long-term immunosuppression. Despite a long duration of disease and treatment, patients would be willing to stop immunosuppressive therapy if advised to do so. Objective measures such as drug level may provide one tool to guide treatment withdrawal in patients with suboptimal levels. The main concern for patients when considering treatment withdrawal is the risk of future relapse.

Disclosure: Nothing to disclose

Reference
P1616 CLINICAL TRIAL: HIGH-DOSE VITAMIN D TREATMENT TO CORRECT CROHN'S DISEASE PATIENTS WITH DISEASE ACTIVITY, A RANDOMIZED PLACEBO-CONTROLLED DOUBLE-BLIND STUDY (MRVIDIC)

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Introduction: Treatment may reduce the risk of disease activity in Crohn’s disease (CD) [1]. Longitudinal studies have shown that vitamin D levels above 75 nmol/l are associated with reduced disease activity score, need for hospitalisation and surgery [2]. Yet it is unknown if CD patients with disease activity would benefit from high-dose vitamin D treatment and if it is well tolerated.

Aims and Methods: To investigate whether high-dose vitamin D treatment alone or combined with infliximab induction treatment to patients with active CD decreased disease activity compared to the placebo group. Forty CD patients with disease activity were included. Patients were randomized to: 1) infliximab and high dose vitamin D (N = 8), 2) infliximab and placebo vitamin D (N = 8), 3) placebo infliximab and high dose vitamin D (N = 16), 4) placebo infliximab and placebo vitamin D (N = 8). Infliximab was given as 5 mg/kg week 0, 2 and 6 and vitamin D was given as 5 mg bolus week 0 followed by 0.5 mg/day in up to 7 weeks. Patients underwent colonoscopy week 0 and 7 and a Crohn’s disease index of severity (CDEIS) score was measured. C-reactive protein (CRP), faecal calprotectin, leucocytes and Harvey Bradshaw Index (HBI) were measured week 0, 2 and 6. After the 7 weeks of project treatment all patients were treated open with infliximab 5 mg/kg. Thereafter during 16 weeks patients were re-randomised to placebo or infliximab, 2 of 4 groups were compared to placebo. Primary aim was to assess the rate and timing of secondary LOR with higher CRP and leucocytes and CDEIS compared to placebo.

Results: During 26 weeks of follow up patients who had received high-dose vitamin D treatment during the project period had significantly less disease activity compared to placebo with later LOR. Furthermore, patients who had received infliximab alone had significant differences in CDEIS compared to placebo. Mixed model was used to test if the mean curves of the CDEIS score compared to placebo vitamin D (95% CI: 1.11–4.32, p = 0.001), HBI (p = 0.045), and leucocytes (p = 0.028). Single treatment with high dose vitamin D (group 3) decreased the leucocytes count compared to placebo (p = 0.039), but significant differences were not reached regarding CRP, CDEIS and HBI.

Conclusion: Patients who initially received high-dose vitamin D treatment had lower CRP and CDEIS levels 26 weeks of follow up compared to placebo. Vitamin D treatment reduced the CDEIS score compared to placebo. In patients with active CD, high-dose vitamin D treatment is safe and well tolerated and reduces the leucocytes count compared to placebo but not calprotectin and CRP.

Disclosure: Nothing to disclose.

References

P1617 SECONDARY LOSS OF RESPONSE TO VEDOLIZUMAB: EXPERIENCE FROM A SINGLE UNIVERSITY CENTRE

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Introduction: Vedolizumab (VDZ), a humanised monoclonal anti-a4b7 integrin antibody, is effective for inducing and maintaining remission in both Crohn’s disease (CD) and ulcerative colitis (UC). Secondary loss of response (LOR) can occur but there is limited information on its frequency and timing.

Aims and Methods: The aim was to assess the rate and timing of secondary LOR in patients with inflammatory bowel disease (IBD) treated with VDZ in a routine clinical practice at a large single university centre. A retrospective case-note review was undertaken of all patients who had received at least one infusion of VDZ from March 2015 – January 2018. Patients received VDZ 300mg intravenous infusion therapy at 0, 2 and 6 weeks and then 8 weeks for maintenance.

Results: 113 patients (mean age 46.1 y; male 61%) with CD (n = 32) and UC (n = 81) were followed. 34.8% of patients were anti-TNF-alpha intolerant and 22% anti-VDZ intolerant. Median VTL measured at week 6 were significantly higher in clinical responders (95% CI: 1.11–4.32, p = 0.001), HBI (p = 0.045), and leucocytes (p = 0.028). Single treatment with high dose vitamin D (group 3) decreased the leucocytes count compared to placebo (p = 0.039), but significant differences were not reached regarding CRP, CDEIS and HBI. Seven weeks of high-dose vitamin D treatment alone and combined with infliximab increased the calcium-ion levels over time compared to placebo-vitamin D treatment (p = 0.013) but within normal range of calcium. Phosphate levels were unaffected by treatment.

Conclusion: Patients who initially received high-dose vitamin D treatment had lower CRP and CDEIS levels 26 weeks of follow up compared to placebo. Vitamin D treatment reduced the CDEIS score compared to placebo. In patients with active CD, high-dose vitamin D treatment is safe and well tolerated and reduces the leucocytes count compared to placebo but not calprotectin and CRP.

Disclosure: Nothing to disclose.

References

P1618 VEDOLIZUMAB TROUGH LEVELS DURING AND AFTER INDUCTION CORRELATE WITH CLINICAL AND EndOSCOPIC OUTCOMES IN INFELINATIVE BOWEL DISEASES: A RANDOMIZED PLACEBO-CONTROLLED DOUBLE-BLIND STUDY

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Introduction: Vedolizumab is an alpha4beta7 integrin antagonist for the treatment of inflammatory bowel disease (IBD). The role of drug monitoring, based on the assessment of Vedolizumab trough levels (VTL) and anti-Vedolizumab antibodies (AVA) has not been clarified.

Aims and Methods: Consecutive IBD patients who started therapy with Vedolizumab were prospectively enrolled. Clinical activity was evaluated using Harvey Bradshaw Index (HBI) and partial Mayo score (pMayo). Endoscopic assessment was performed at baseline and during follow-up. VTL and AVA were assayed by ELISA (Theradiag) at weeks 6 and 14. Limits of detection for VTL and AVA were 2 ug/ml and 35 ng/ml, respectively. Clinical response was defined as at least 30% reduction of activity scores from baseline. LOR was defined as HBI<5 or pMayo<2. Mucosal healing was defined as a Mayo score of 0 for ulcerative colitis (UC) and absence of ulcers for Crohn’s disease (CD). Endoscopic response was defined as a reduction of at least 1 point of Mayo score for UC and improvement in mucosal inflammation for CD compared to baseline. Statistics was performed by Mann Whitney test, Spearman’s rho, ROC curve analysis.

Results: We included 66 patients (mean age 46.1 y; male 61%) with CD (n = 32) and UC (n = 34). 87% of patients were anti-TNF-alpha intolerant. Median VTL and AVA were 2 ug/ml and 35 ng/ml, respectively. Clinical response was achieved in 63% and endoscopic response in 53%. Median VTL measured at week 6 were significantly higher in clinical responders as compared to non-responders (41.3 vs 26.9 ug/ml, p = 0.003), and in patients in clinical remission at week 14 (45.9 vs 27.9 ug/ml, p = 0.003) and at week 22 (46 vs 27.6 ug/ml, p = 0.0009) compared to non-remitters. By ROC curve analysis we identified a cut-off value for VTL of 40.3 ug/ml for clinical response at week 6 (AUC 0.714, sensitivity 52%, specificity 85%, p = 0.003) while for remission at week 22 the cut-off was 44.3 ug/ml (AUC 0.714, sensitivity 52%, specificity 85%, p = 0.003)
P1619 TOLERANCE OF THIOPURINES IN PATIENTS WITH CHRONIC INFLAMMATORY BOWEL DISEASE (IBD)

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Introduction: Thiopurines, represented by azathioprine (AZA) and 6-mercaptopurine (6-MP), are among the first treatments used in inflammatory bowel diseases (IBD). Their therapeutic effectiveness is perfectly established with, in particular, a major role of corticosteroid savings and a maintenance of the effect over time. However, nearly 20% of patients cease taking thiopurines because of its side effects.

Aims and Methods: The objective of this study is to evaluate the frequency of adverse effects of azathioprine (AZA) and 6-mercaptopurine (6-MP) in patients with IBD.

This is a retrospective and descriptive study conducted in the gastroenterology department of our hospital including 100 patients with chronic inflammatory bowel disease (IBD) treated with thiopurines (AZA or 6-mercaptopurine). The inclusion criteria are: age ≥ 16 years, with a follow-up period of 3 months after the initiation of treatment.

Results: One hundred (100) patients with IBD were included, 64 patients (64%) had Crohn's disease, 24 (24%) ulcerative colitis and 12 (12%) idiopathic colitis. The average age was 36 years old [16-76]. The sex ratio M/F was 0.8, with an average duration of follow-up after the beginning of immunosuppressive treatment of 19 months [3-48]. 52 patients were on 6 mercaptopurine and 48 were on azathioprine. The main indications for the prescription of thiopurines in Crohn’s disease were: maintenance treatment after a first flarum requiring corticosteroid therapy in 32% of cases, after severe acute colitis in 8.1%, postoperatively in 21.5% of cases, ano-perineal lesions in 16% of cases, upper gastrointestinal involvement in 8.1% of cases, and corticosteroid dependence in 13.5% of cases. In ulcerative colitis the main indications were: treatment maintenance after severe acute colitis, inefficacy of 5-ASA, corticosteroid dependence with remission reached 16% of cases and therefore, their clinical and biological remission at 3 months was obtained in 65% of cases (65 patients). 32 patients experienced side effects with thiopurines (32%) occurring beyond six months of treatment in 45% of cases, they were mainly hematologic in 47.05% of cases (26% lymphopenia and 21% anemia), liver abnormalities in 41.16% of cases, and acute pancreatitis in 5.8% of cases. The occurrence of adverse effects resulted in discontinuation of treatment in 11% of cases

Conclusion: Our study has objective a remission rate of 65%, which proves that the thiopurines will keep their place in the treatment of IBD at the same level of anti-TNF especially in our contexts.

Disclosure: Nothing to disclose

P1620 A MULTICENTER RANDOMIZED PROSPECTIVE STUDY ASSESSING THE EFFICACY OF SINERGIN IN INDUCTION AND MAINTAINING REMISSION IN MILD-MEDERG INDIB

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Introduction: The role of the gut microbiota, in addition to genetic factors, in the initiation and perpetuation of inflammatory processes is well established. There are studies that showed that the association between oligo-fructose and inulin (OF-IN) has the ability to modulate not only the composition of the intestinal microbiota but also its activity in a beneficial way, increasing the butyrate concentration, which exhibits immunomodulatory and anti-inflammatory properties.

Aims and Methods: The main purpose of this multicentric prospective study was to test the efficacy of OF-IN (Sinergin) in patients with mild and moderate forms of active IBD. The patients were randomized into 2 groups as follows: group 1 received conventional therapy associated with 10 g/ day of Sinergin and group 2 received only conventional therapy.

This study included 60 patients (44 with Crohn's disease and 16 with UC), 50 of them were affected by ulcerative colitis. All of the patients had Crohn's disease. 24 (24%) ulcerative colitis. And 12 (12%) indeterminate colitis.

Results: A total of 72 patients were assessed. The studied group was divided almost evenly between patients with Crohn’s (37 patients with Sinergin) and patients with Sinergin. There are 10 patients that underwent 6 months evaluation (4 with sinergin and 6 without). 25 patients underwent the 3 months evaluation (10 in group 1 and 15 in group 2). At 3 months there is no significant difference between the calprotectin drop down percentage from group 1 (24.30% vs 35.5%), but at the 6 months assessment we found a difference of 5% (45% vs 40%).p < 0.05.

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Conclusion: Group 1 (with OF-IN) maintained constant values of fecal calprotectin at 3, 6 months and registered a general decrease in CRP values Group 2 (without OF-IN) has heterogeneous results at 3.6-month evaluation

The complex of oligofructose and inulin plays an important role on the long term in preventing high inflammatory flares in IBD.

Disclosure: Nothing to disclose

P1621 HIGHER ADALIMUMAB LEVELS DURING MAINTENANCE TREATMENT FOR CROHN’S ARE ASSOCIATED WITH DEEP REMISSION: RESULTS FROM A LARGE PROSPECTIVE CROSS-SECTIONAL COHORT

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Introduction: Adalimumab (ADA) is a well-established treatment for Crohn’s disease (CD). Despite this limited data are available regarding the relationship of serum ADA levels, and antibodies to ADA (ATA) with clinical outcomes.

Aims and Methods: We performed a prospective cross-sectional study to investigate the association of serum ADA levels with deep remission (HBI<5, CRP < <5mg/L and faecal calprotectin <200mcg/g). Inclusion criteria were a diagnosis of CD and minimum of 12 weeks therapy. Patients were written to in advance of their next clinic visit and advised to omit their ADA dose if due within 48 h from their appointment. Harvey Bradshaw Index (HBI), serum ADA activity 80% specificity 69%, p 0.075 for week 22). Remission and response at 3 months (p 0.005). Week 14 VTL were also significantly higher in patients being in clinical remission (20.6 vs 15.1 ug/ml, 5.0 vs 4.0, p 0.037). By ROC curve analysis a cut-off for week 6 VTL of 38.6 ug/ml was detected for week 50 endoscopic response. Week 6 but not week 14 VTL were negatively correlated with CRP levels.

At the time of drug level testing, 259 patients were on ADA maintenance therapy. A total of 195 samples were available for analysis from 178 patients; 55.6% of patients at week 6 and in 3% at week 14 and were not correlated with VTL and clinical response. Week 6 and 14 VTL were not predictive of mucosal healing. Higher ADA VTL were higher in those patients who underwent an endoscopic response (median of responders 40.1 vs 27.2 ug/ml, non-responders, p 0.037). The complex of oligofructose and inulin plays an important role on the long term in preventing high inflammatory flares in IBD.

Disclosure: Nothing to disclose
Sexual health issues – do experts in this field address sexual problems in routine patient treatment yet? Results of the IGLS-Vienna-SexMed-survey on experts in IBD, Bad Ischl, September 2017

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Introduction: Sexual health is part of the holistic WHO-concept of health. The World Health Organization (WHO) is directed to the right to the highest attainable standard of health, including sexual health”. Thus, sexual health as well as dysfunction have to be respected and integrated in patients’ treatment and disease management programs. Inflammatory bowel disease patients’ quality of life is compromised including social engagement, sexual health, intimacy as well as fertility and reproduction caused by medication’s side-effects, surgical procedures, reduced control of body function (erectostemia). Therefore, medical doctors were asked whether these aspects are integrated in routine medical treatment by addressing the topic in disease-management.

Aims and Methods: A 3-part questionnaire on health professionals’ patient-treatment, health care structures as well as professional profile was distributed at the annual Austrian Crohn and Colitis symposium, Bad Ischl, September 2017. 50 of 190 congress-participants returned the questionnaire (26.3%).

Results: 38% of the health professionals addressed in up to 20% of the patients sexual health problems. 68% were asked by at most 20% of the patients about sexual health issues. Participants assumed that up to 20% of their patients had troubled sexuality, 32% of the participants in even up to 40% of the patients but left the patients un-asked.

38% of the participants did not offer any help for troubled sexuality, 32% referred to sexual medicine specialists such as internal medicine (70%), urologists (50%), gynecologists (48%), 30% evaluated the impact of medication on sexual dysfunction. 44% of the participants stated that lack of sexual-medicine expertise decreases the success of disease-management.

54% of the participants were male, 40% female. 52% of the participants worked in public hospital. 28% were clinically experience more than 21 years, 26% had between 10 and 20 years of clinical experience.

Conclusion: The participants of this survey were experienced in the field of inflammatory bowel disease. Despite this, they did not integrate sexual health issues in routine treatment and disease-management-program so far: in up to 80% of the patients’ sexual health including intimacy, fertility and reproduction issues were left un-addressed and thus not treated. Sexual medicine competences aspects to increase the likelihood of successful disease management. Sexual medicine therefore may be an emerging field for experts in inflammatory bowel disease to be integrated in the near future.

Disclosure: Nothing to disclose.

P1625 Characteristics of anti-TNF alpha therapy for ulcerative colitis between 2010–2016 in Hungary

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Introduction: Anti-TNF therapy showed high efficacy in induction and maintenance of remission in ulcerative colitis.

Aims and Methods: Study design: Retrospective data analysis using the National Health Insurance Fund social security databases including inpatient-, outpatient care, medications as well as the special drug reimbursement database of patients with the diagnosis of ulcerative colitis (UC) from 2010 to 2016. This is an observational / non-interventional, retrospective, epidemiological study. Study population: All of the adult – over 18 years of age – UC patients between 2010 and 2016. Eligibility criteria: Patients who have at least two events in all of relevant health care services or at least 1 inpatient event only with UC diagnosis (ICD codes: K51 K50) (Crohn’s disease-CD) and K51 (UC) occurrence together. 80:20 distribution ratio. Primary endpoint: Analyze patient characteristics and therapeutic outcome of UC patients treated with anti-TNF agent in Hungary.

Results: 0.24% of total Hungarian population suffered from UC in 2016. This is more than 23,000 patients. The median age of the patients with UC is 51 (male 49, female 53) in the examined period. 1,095 UC patients were treated with biologicals between 2010–2016. Annual prevalence of biological therapy was increasing continuously from 1.1% to 2.1%; 497 patients with UC were on anti-TNF alpha therapy at the end of 2016. This is an observational / non-interventional, retrospective, epidemiological study.

Conclusion: All of the adult – over 18 years of age – UC patients between 2010 and 2016.

Disclosure: Nothing to disclose.

P1624 Multidisciplinary Team Care at the Emergency Department contributes to improved management of patients with Inflammatory Bowel Diseases

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Introduction: A component of healthcare burden in patients with inflammatory bowel diseases (IBD) is frequent emergency department (ED) visits and hospitalizations. We hypothesized that an intervention by a dedicated IBD-nurse accompanied by a multidisciplinary team (MDT) at the ED may improve management and reduce admission rates.

Aims and Methods: We aimed to estimate the impact of proactive MDT care in the ED of a tertiary medical center. IBD-ED visits between November 2017 and April 2018 were identified by the ICD-9-CM codes. IBD patients that were proactively assessed by the MDT (intervention group) were compared to those not approached by the team (standard-ED group). Hospitalizations, exposure to CT scans, and recurrent admission rates within the first 30 days were detected.

Results: A total of 155 IBD patients’ visits in the adults ED were identified. Of those, 52 patients (32.2%) were managed by the IBD-nurse and the MDT: average age at index ED visit: 36.1 ± 14.4 years (18–85), M/F 31/19 patients, disease duration 8.3 ± 9.0 years, 37/50 patients had Crohn’s disease of whom 10 had a history of perianal involvement. The most common chief complaint (88%) was abdominal pain. Most patients (86%) were either referred by their primary care physician or self-referred. Seventeen patients (34%) underwent CT scan in the ED. MDT management was associated with ED discharge in 28/50 patients (56%). After discharge, most patients (26/28) were shortly followed by a phone call with the IBD-nurse (within 1–7 days), and then seen in the IBD clinic (within 5 [IQR: 1–12] weeks). Nineteen out of 22 hospitalizations were directly IBD related. Of those, 12 (63.1%) were because of a surgical complication: either an obstruction or an abscess, requiring surgery in 7 patients (58%). The median duration of hospitalization was 3 days (IQR 1–6). Significant decrease in ED revisit within the first 30 days after discharge was observed in the intervention compared with the standard ED group (2% vs 18%, P = 0.009). However, there were no differences in rates of hospitalizations or CT scanning (44% vs 52.4%, P = NS, and 34% vs 20%, P = NS, respectively). Notably, patients in the standard ED group were older (51.4 ± 14.4 vs 50.1 ± 20.1, years P = 0.001). However, in logistic multivariate analysis the age at index ED visit was not associated with 30-days ED revisit (OR = 0.986, 95% CI 0.961–1.012, P = 0.292). In contrast, MDT intervention was associated with decreased ED revisit rates (OR = 0.77, 95% CI 0.601–0.977, P = 0.015).

Conclusion: MDT intervention for patients in IBD in the ED, improves patients management and reduces ED readmission in the first 30 days after discharge. This may suggest that MDT management should be a part of the care for patients with IBD visiting the ED.

Disclosure: Nothing to disclose.
P1626 VEDOLIZUMAB RESULTS IN REDUCED HOSPITALISATIONS AND STEROID USE AT 1 YEAR: RESULTS FROM THE SCOTTISH VEDOLIZUMAB COHORT

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Introduction: The GEMINI trials and an increasing body of real-world data have demonstrated the effectiveness and safety of vedolizumab (VDZ) in IBD. However, there is limited available data about its effect on hospitalisations and steroid use. Our aim was to address this in a large real-world cohort of IBD patients from across Scotland.

Aims and Methods: A multicenter retrospective cohort analysis of medical records was performed across 7 Scottish healthcare trusts. Primary outcomes were hospitalisations and rates of steroid use in patients remaining on VDZ. Secondary outcomes were safety and intention to treat steroid free remission rates of patients with Crohn’s anal fistula. All data were prospectively collected as part of routine clinical care. Baseline demographics, clinical scores (HBI or Partial Mayo), faecal calprotectin (FC), endoscopy and radiology at 3, 6 and 12 months were recorded where available. Active disease was defined as endoscopic or radiographic evidence of disease or FC >200 mcg/g. Clinical remission was defined as HBI <5 or Partial Mayo <22. Biochemical remission was defined as FC<200 mcg/g.

Results: 340 (137 UC and 203 CD) patients were included in the primary analysis with follow-up for 56.1 ± 4.9 months. All hospitalisations rates per patient-year were 0.60, 0.67, 0.36 and 0.16 at baseline, 3, 6 and 12 months of treatment respectively. Total number of hospitalisations reduced by 52.5% from 204 (12 months prior to VDZ) to 97 (12 months after VDZ). Proportion of patients on concomitant steroids reduced from 39.7% to 16.7% (n = 332), 8.1% (n=270), 9.3% (n=194) at 3, 6 and 12 months respectively. In patients with active CD (n = 153, 75.4%) steroid free clinical and steroid-free biochemical remission rates were: 54.4% and 30.2% at 3 months; 47.7% and 32.1% at 6 months; 28.6% and 33.5% at 12 months. In patients with active UC (n = 112, 81.8%) steroid-free clinical and steroid-free biochemical remission rates were: 57.4% and 40.9% at 3 months; 51.6% and 39.1% at 6 months; 37.5% and 41.2% at 12 months. Our results demonstrated the effectiveness and safety of vedolizumab in IBD.

Conclusion: VDZ is associated with reduced hospitalisation and steroid use over 1-year. Steroid-free remission rates and safety profile is in keeping with the previously published literature.

Disclosure: Speaker fees and travel support Takeda

P1628 TARGETING DETECTION OF FISTULA TISSUE LEVELS OF ANTI-TNF – A POTENTIAL BIOMARKER OF TREATMENT RESPONSE?


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Introduction: Anti-TNF therapy is recommended as the first line for treatment of perianal disease. However, significant proportion of patients either fail initial trial or lose response to anti-TNF therapy. Reasons for this are likely multifactorial and related to metabolism of the drug as well as the development of anti-drug antibodies. Currently, it is unknown whether fistula tissue levels play a role in this process.

Aims and Methods: We undertook a pilot study to measure fistula tissue levels of anti-TNF medication (infliximab and adalimumab) using a sensitive technique for peptide detection following trypsin digestion i.e. ultra-performance liquid chromatography mass spectrometry (UPLC-MS). Biopsies from two patients with infliximab and five patients on adalimumab for Crohn’s anal fistula were obtained under general anaesthetic. The protein present in fistula’s samples were extracted and digested by trypsin to obtain peptide fragments specific to each drug. These were then analysed by UPLC-MS. The anti-TNF drug analysis was performed by ACQUITY UPLC (Waters Ltd., Elstree, UK) coupled to either a Xevo TQ-S mass spectrometer (Waters, Manchester, UK). The MS system was equipped with an electrospray ionization source operating in positive ion mode at a flow rate of 0.3 μL/min. The targeted UPLC-MS/MS detection and quantification method implemented was previously validated. The chromatographic conditions were shortened to 7.2 min and consisted on mobile phase A (Acetonitrile with 0.1% formic acid) and mobile phase B (H2O with 0.1% formic acid) using a ACQUITY BEH 130 C18 1.7um 2.1 x 150 mm. MS parameters were optimised to detect specific peptide sequences from each drug. These multiple reaction monitoring (MRMs) also aimed to quantify the anti-TNF present in fistula tissue samples.

Results: The limit of detection (LOD) and linearity range of the method was assessed for each drug. Infliximab and Adalimumab were respectively with LOD of 0.096 and 1.92 mg/mL for linearity range over 4-fold. The peak area for each drug was normalised according to the weight of the fistula samples. The targeted UPLC-MS/MS detection and quantification method implemented was previously validated.1 The chromatographic conditions were shortened to 7.2 min and consisted on mobile phase A (Acetonitrile with 0.1% formic acid) and mobile phase B (H2O with 0.1% formic acid) using a ACQUITY BEH 130 C18 1.7um 2.1 x 150 mm. MS parameters were optimised to detect specific peptide sequences from each drug. These multiple reaction monitoring (MRMs) also aimed to quantify the anti-TNF present in fistula tissue samples.

Conclusion: Recent evidence suggests that higher infliximab trough levels are associated with perianal fistula healing in patients with Crohn’s disease. In this study we have shown abnormal anti-IL-12/23 peptide levels and anti-TNF drug levels were not detected in fistula samples. In addition, to validate the results samples were concentrated (x10) and still no detection of the drug was observed in the test samples.

Disclosure: Nothing to disclose

Reference

P1629 USTEKINUMAB EFFICIENCY IN ASSOCIATION WITH SERUM LEVELS IN COMPLICATED REFRACTORY PATIENTS WITH CROHN’S DISEASE


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Introduction: Usteekinumab (UST) is an anti-IL-12/23 monoclonal antibody used for treatment of Crohn’s disease (CD). We evaluated response to UST in a cohort...
of patients with complicated course of disease and its association with serum trough levels (TLs).

Aims and Methods: Data from consecutive CD patients who previously failed at least one biologic agent and started UST with an i.v. dose between March and December of 2017 were included. Disease activity was assessed by Physician’s Global Assessment (PGA) score as 0 (remission), 1 (mild disease), 2 (moderate disease) or 3 (severe disease) at week 0 and every following 8 weeks up to week 24 in a retrospective manner. At week 24, patients were considered as complete responders (CR) with PGA drop of at least 2 points, partial responders (PR) with PGA drop of 1 to 2 points or no responders (NR) with zero or negative decrease in PGA. C-reactive protein (CRP), fecal calprotectin (FC) and UST TLs were measured at every visit.

Results: Twenty-nine CD patients (37.9% males, 62.1% females) with mean age of 35.9 years were included. Mean disease duration was 15.2 years with 37.9% of patients classified as A1 according to Montreal classification. Proximal disease was present in 24.1% of patients and the same proportion of patients suffered from perianal disease. At least one previous surgery was performed in 86.2% of patients. UST was administered as a 3rd biologic agent. Over half of patients had concomitant immunomodulators and 31% corticosteroids at week 0. At baseline, 20.7% of patients had severe disease activity, 61.2% had moderate and 17.2% mild or no current disease activity. Severe activity was present in 10.7% of patients, 50% had moderate and 39.3% mild or no activity at week 8. At week 24 the proportions were 8.7%, 47.8% and 43.5%, respectively, however, there was no decrease in mean CRP and FC between the two timepoints (CRP 11.2 ± 15.5 mg/L vs. 12.6 ± 16.5 mg/L, p = 0.8838; FC 1724 ± 1719 μg/g vs. 1611 ± 1830 μg/g, p = 0.9277). Patients with moderate to severe disease activity had significantly lower UST TLs at both week 8 and 24 (12.9 ± 10.1 μg/mL vs. 23.2 ± 11.8 μg/mL, p = 0.0090 at week 8 and 3.9 ± 1.9 μg/mL vs. 7.1 ± 3.5 μg/mL, p = 0.0151 at week 24). Fifty-two percent of patients experienced at least PR expressed by PGA decrease between baseline and week 24, while 48% didn’t respond. There was no difference, and thus no predictive value, in UST TLs at week 8 between patients who did and didn’t respond at week 24, however responders improved their PGA by 1.9 ± 1.7 at week 24 (p = 0.0154). Most frequent adverse events included fevers or arthralgias after application and there were 2 cases of periorbital rash at week 8. One patient developed demyelinating polyneuropathy during the follow-up, however, no further cases were reported and treatment was terminated at week 24.

Conclusion: Despite no decrease in inflammatory markers, over 50% of the refractory CD patients experienced clinical benefit from ustekinumab after 24 weeks which was associated with its higher serum trough levels. No adverse event requiring the treatment to be terminated was registered.

Disclosure: Nothing to disclose.
P1634 ENTEROTOXIN BACTERIOIDES FRAGILIS PREDICTS COLORECTAL CANCER PROGNOSIS

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Introduction: Human intestinal flora play an important role in the homeostasis of colorectal cancer in human intestinal tract. Enterotoxin Bacteroides fragilis (ETBF) is an anaerobic Gram-negative bacterium which produces Bacteroides fragilis toxin (BFT). It has been found that ETBF colonization increases in colorectal cancer patients, and it may be associated with tumorigenesis.

Aims and Methods: We aimed to investigate the association between ETBF and the prognosis and chemotherapeutic effect of colorectal cancer. 242 cases of colorectal mucosa biopsy or resection, which had been made in paraffin tissue, were collected from Southern Medical University Affiliated Nanfang Hospital. These samples were divided into colorectal adenoma group (n=112 cases), colorectal cancer group (n=80) and mild inflammation group (n=50). Clinical data were collected from these patients, including sex, age, history of antibiotic use within one week, radiotherapy history, chemotherapeutic agent, biopsy location, pathology diagnosis, parenteral infection, carcinoembryonic antigen (CEA), C-reactive protein (CRP), white blood cell count (WBC), lymphocyte count (LYM), neutrophil count (NEU), monocyte count (MO), etc. Patients with colorectal cancer were followed up for one year and their clinical data, such as surgery, chemotherapy, TNM staging, imaging data, relapse and death were collected. The total DNA(including host DNA and commensal bacterial DNA) from each group of paraffin tissues was extracted and then the endothexin gene segment of ETBF was amplified by polymerase chain reaction. Then we analyze the relationship between ETBF infection and clinical data we collected.

Results: The positive rate of ETBF in colorectal adenoma group and colorectal adenocarcinoma group were both significantly higher than that in mild inflammation group (p<0.008, p<0.05). The positive rate of ETBF in biopsy from right colon was significantly higher than that from left colon (χ²=14.13, P<0.000). TNM tumor staging in patients with ETBF-positive colorectal cancer was significantly higher than that in ETBF-negative patients (Z=-3.374, P=0.001). The positive rate of ETBF in biopsy from right colon were both significantly higher than ETBF-negative patients (Z=-5.437, P=0.000). The depth of tumor infiltration (Z=-5.437, P=0.000) were significantly worse than ETBF-negative patients. There was no significant difference of recurrence and death within one year between ETBF-positive colorectal cancer and ETBF-negative ones (χ²=3.322, P=0.078; χ²=3.374, P=0.151). Lymphatic metastasis, distant metastasis were significantly higher in ETBF-positive patients (Z=-2.892, p=0.004; Z=-2.892, p=0.004). But the tumor-free survival rate of ETBF-positive patients was significantly lower than that of ETBF-negative ones (p<0.078; χ²=14.13, P<0.000). There was no significant difference in tumor infiltration depth (Z=-1.885, p=0.064). Chemotherapy efficacy of ETBF-positive patients was significantly worse than ETBF-negative ones (χ²=5.437, p=0.020).

Discussion: The ETBF infection is more prevalent in colorectal neoplasms patients. The higher colorectal cancer TNM stage, the higher positive rate of ETBF was. Prognosis and chemotherapeutic effect of colorectal cancer were worse in ETBF-positive patients, which may make ETBF detection an indicator of poor prognosis and chemotherapeutic efficacy. We predict the positive rate of ETBF could as an indicator of poor prognosis and chemotherapeutic efficacy.

Disclosure: Nothing to disclose
P1636 FECAL MICROBIAL ECOSYSTEM IS DISTINCT IN IRITABLE BOWEL SYNDROME ACROSS DIFFERENT SYMPTOM CLINIC COHORTS.

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Introduction: Much evidence suggests the contribution of intestinal microbiota in the pathophysiology of irritable bowel syndrome (IBS). We characterized the intestinal microbial ecosystem (IME) by means of 16s ribosomal RNA (rRNA) gene profiling in fecal samples of IBS subtypes collected during a multicenter intervention trial with Lactobacillus paracasei CNCM I-1572 in IBS.

Aims and Methods: To characterize the IME, we included in the study a total of 40 patients with IBS according Rome III criteria (12 IBS-C; 14 IBS-D; 11 IBS-M; 3 IBS-D). The IME were collected during four consecutive collection times. Metagenomics DNA was extracted from about 200 mg of feces using the PowerSoil® DNA Isolation Kit. Subsequently, the bacterial community structure was profiled by 16s rRNA gene profiling, amplicons were sequenced using Illumina platform and the results were managed by means of the bioinformatic pipeline Quantitative Insights Into Microbial Ecology with the GreenGenes database.

Results: The taxonomic overview of the fecal sample analyzed revealed that the first 7 most abundant genera belong to the Firmicutes Gram positive order. Clostridia accounted for about 75% of detected bacteria, while the relative abundance of members of the order Bacteroidales was lower than 10%. The analysis of median profiling data revealed 26 significantly different operational taxonomic units (OTUs) between IBS-M and IBS-C, while 19 OTUs distinguished IBS-D from IBS-M. The high dissimilarity was found between IBS-C and IBS-D: 85 OTUs had, in fact, a significantly different relative abundance. Most of the discriminating OTUs were ascribed to the order Clostridiales; IBS-C were distinguished from IBS-D by numerous Clostridia/anaerobe OTUs belonging to the families Ruminococcaceae (in particular, the genus Ruminococcus) and Lachnospiraceae. Two OTUs ascribed to Bifidobacterium adolescentis were increased in IBS-C whereas OTUs associated to the order Bacteroidales and to the Firmicutes taxa Eubacterium were enriched in IBS-D.

Conclusion: Our results indicate that the fecal microbiota of IBS-C and IBS-D is characterized by a different distribution of Clostridiales, whereas IBS-M samples possess compositional features intermediate between IBS-C and IBS-D. The characterization of bacteria inside the Gram-positive order Clostridiales distinguishes the microbial ecosystem of IBS subtypes, suggesting that distinct therapeutic approaches targeting microbiota should be developed according to IBS subtypes.

Disclosure: Nothing to disclose.
**P1638 A TEXT-MINING TOOL TO DETECT THE MANAGEMENT OF ANTI-THROMBOTICS BEFORE COLONOSCOPY – A ANALYSIS OF 656 PATIENTS**

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Introduction: The use of antithrombotics (platelet agents and anticoagulants) is increasing with an ageing global population, there is lack of data and system to evaluate adherence to international practice guidelines and standard instructions provided to colorectal patients.

Aims and Methods: We aim to develop an automatic text-mining system to assess the instructions of antithrombotic medications in a retrospective cohort of patients who used antithrombotics and underwent elective colonoscopy in a large teaching hospital. The system first determined whether the clinician has ordered colonoscopy for a patient. If colonoscopy was arranged, the algorithm would search for keywords indicating modification of anti-thrombolytic therapy. A list of keywords was created that carries the meaning of “withholding”, such as “stop”, “hold” or its abbreviation “w/h”. We matched these keywords with a list of relevant drug names, e.g. aspirin, warfarin and their abbreviations. Regular expressions were developed to extract the stoppage information using these concepts. Two investigators manually reviewed all consultation notes to determine positions on modifying anti-thrombolytic therapy were given. The manual review findings were used as a gold standard to assess the performance of the automated text-mining system.

Results: There were a total of 656 patients and 1,907 consultation notes identified. Manual review identified 108 relevant instructions in the notes. The text-mining system had an accuracy of 0.936, sensitivity of 0.843, specificity of 0.954, and an F1-score of 0.813. The computational and manual effort had 53 out of 656 patients with different results. Because of this discrepancy, the staff went through the consultation notes of those patients with different results. 42 patients were correctly labelled by the manual method but incorrectly labelled by the computational process; the sum of 42 came from false negative (FN)+ false positive (FP).

Conclusion: The computational text-mining tool was able to achieve a high accuracy of 93.6% in this pilot experiment. We can apply this automated tool to screen a larger population to understand the quality of instructions offered to patients. We can also relate this result of detection of drug stoppage instruction to other clinical outcomes, e.g. bleeding complications of the procedures and reversal instruction in future studies.

Disclosure: Nothing to disclose

**P1639 READING OF GASTROINTESTINAL BLEEDING IN THE EMERGENCY DEPARTMENT**

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Introduction: Gastrointestinal bleeding (GIB) is one of the main causes of admission to the Emergency Department (ED) and with hospitalizations, responsible for health burden.

Aims and Methods: We studied all the readings by GIB in a tertiary hospital. A retrospective study of all GIB admissions was made in the adult population during 2016. All patients were characterized by comorbidities and medication. Data was analyzed by Excell and SPSS.

Results: They were admitted to the ED with suspected GIB 690 episodes, reporting to 622 patients. A total of 68 readings, by 55 patients, 69% male and 31% female with the median age 62.58 ± 18.81 years. Among the Manchester triage protocol 75% of the patients were screened as urgent and 25% as very urgent. The presentation forms were: 43% Rectorragias, 24% Hematemesis, 23% Haematochesis and 10% melenas. In most readmissions (65%), the clinical form was Rectorragias, 31% female, the mean age being 62.58 ± 18.81 years. In most readmissions (65%), the clinical form was Rectorragias. In most readmissions (65%), the clinical form was Rectorragias, 31% female, the mean age being 62.58 ± 18.81 years. In most readmissions (65%), the clinical form was Rectorragias.

Conclusion: The results of the study show that the majority of patients admitted to the ED with GIB were male gender best predict the need for blood transfusion after admission with a logistic regression model with an AUROC of 0.70. Gender, age, co-morbidities, admission haemoglobin (Hb), Urea, Albumin, INR, blood pressure/heart rate, presence of melena, syncope and altered mental state. Adverse outcomes include red cell transfusion, endoscopic intervention, CT angiography, surgery, re-bleeding and mortality. Using regression analysis all statistically feasible combinations of factors were used to predict adverse outcomes (both multivariate and univariate logistic regression models were fit) with cross-validation method repeated 100 times each combination. The model which exhibited the highest average AUROC value was identified. The factors with 95% CI for ORs containing value 1 were excluded. Then, a multivariate logistic regression was fit again on the identified factors. The AUROC value was calculated using a cross-validation method repeated 100 times.

Results: 473 patients were included. Admission Haemoglobin (Hb) < 72g/L 14 points, 73-95g/L 10 points, 96-117g/L 7 points, 118-139g/L 4 points, > 140 g/L, altered mental state 1 point, admission BP (systolic blood pressure < 90mmHg) 1 point and male gender (1 point) were the strongest predictors of the requirement of blood transfusion achieving an AUROC of 0.92 (95% CI 0.90-0.94), therefore 50% Clng The Birmingham Score. This performed better than the Glasgow-Bltchford score (AUROC 0.89).

When predicting the risk of re-bleeding, the admission haemoglobin was the strongest predictor achieving an AUROC of 0.69 (60-0.72). Age, gender, co-morbidities, admission Hb; Urea; Albumin; INR; blood pressure and syncpe predicted a length of stay of more than 4 days with an accuracy of 80%.

Conclusion: Our study shows that admission haemoglobin, altered mental state, male gender are best predict the need for blood transfusion after admission with GIB, giving a novel GIB score termed The Birmingham Lower GI bleed score. Therefore, this may act as a guide to initiate a more intensive treatment regimen and guide admission.

### Score

<table>
<thead>
<tr>
<th>Score</th>
<th>Probability of requiring blood transfusion</th>
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<tr>
<td>≥12</td>
<td>≥90%</td>
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<tr>
<td>11</td>
<td>70%</td>
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<td>45%</td>
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**References**


P1641 OAKLAND SCORE IS NOT BETTER THAN HAEMOGLOBIN FOR PREDICTING OUTCOMES IN LOWER GASTROINTESTINAL BLEEDING

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Introduction: The incidence of acute lower gastrointestinal bleeding (LGB) is increasing in Western countries. Recently the Oakland score has been developed for predict safe discharge after LGB. Aims and Methods: The aim of this study was to compare the accuracy of Oakland score (OakS) with haemoglobin alone (Hb) for predicting outcomes after LGB. Logistic regression was the main outcome predicted by OakS. It was defined as the absence of all the following: a) rebleeding (need for additional red blood transfusion or a further decrease in haematocrit concentrations of 20% or more after 24 hours of clinical stability); b) red blood cell transfusion; c) therapeutic intervention (endoscopic therapy, vascular embolization or surgery); d) readmission with further LGB within 28 days and e) in-hospital death. A retrospective study was performed from January 2013 to December 2015 in a university tertiary care hospital. Patients with acute LGB were identified using the Discharge Diagnosis of System (DD). The aim of this study was to compare the accuracy of OakS and Hb value. AUROCs were calculated for OakS and Hb value. AUROCs were 0.8 for clinical intervention, transfusion, rebleeding and death for Hb and 0.50 for OakS. OakS was retrospectively calculated according to clinical reports data. Area under the receiver operating characteristic curve (AUROC), were calculated for OakS and Hb value. AUROCs were 0.8 for clinical intervention, transfusion, rebleeding and death for Hb and 0.50 for OakS. OakS was compared with the Well.Clear method by using STATA 14.1 software (StataCorp.2015).

Results: A total of 258 consecutive patients admitted to the hospital with acute LGB were identified retrospectively. Median age was 76.4 years (range 31.7–96.5), 178 (69%) of patients were older than 70 years, 53.4% were men. 154 (57.7%) patients were safely discharged. Six patients (2.3%) died, 50 (19.4%) rebleed, 84 (32.6%) needed transfusion, 20 (7.8%) were readmitted, 28 (11.2%) underwent endoscopic intervention and 3 (0.8%) transcathester arterial embolization. No patient required surgery. The comparison of the AUROC for OakS and Hb are shown in table 1. Hb was equal or better than OakS for predicting all outcomes but readmission. AUROCs were >0.8 for clinical intervention, transfusion, rebleeding and death for Hb and 0.50 for clinical intervention, transfusion and death for OakS. Conclusion: Hb seems non-inferior or even superior to OakS for predicting safe discharge, transfusion, rebleeding, haemostatic management or death. OakS was better only for prediction readmission, but the predictive value for this outcome was low for both Hb and OakS.

P1642 CAN METABOLIC AND LIFESTYLE RISK FACTORS PREDICT COLONIC ADENOMATOUS POLyps?

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Introduction: Recent studies have suggested that metabolic and lifestyle risk factors (including metabolic syndrome, obesity, diabetes mellitus and tobacco smoking) may increase the risk of developing colonic adenomatous polyps.1-2 Strong evidence pointing towards an association between metabolic syndrome and colonic adenomas, may lead to new recommendations in colonic screening. Aims and Methods: We analysed whether metabolic and lifestyle risk factors are associated with colonic adenomas. A prospective study on patients over the age of 50 undergoing a screening colonoscopy at Mater Dei Hospital was performed. Exclusion criteria included a history of inflammatory bowel disease, family history of colorectal cancer and previous colonic malignancy. We collected data on weight, body mass index (BMI), waist circumference, history of hypertension, diabetes and hyperlipidaemia, smoking, level of exercise done (using the Godin Leisure-Time Exercise Questionnaire), fasting glucose, triglyceride and HDL cholesterol level. A BMI ≥25 was considered as ‘overweight.’ The National Cholesterol Education Program (NCEP) Adult Treatment Panel III criteria were used to define ‘metabolic syndrome.’ Statistical analysis was performed using Fisher’s exact test. P-value ≤ 0.05 was considered statistically significant. The presence or absence of adenomas/polyps at colonoscopy were documented.

Results: 72 patients were recruited (51.4% were male). 40.3% of patients had one or more colonic adenomas. 40.6% of patients had metabolic syndrome. 81.9% patients were categorized as ‘overweight.’ 29.2% patients had diabetes mellitus 18.1% patients were active smokers. 51.3% of patients had a sedentary or insufficiently active lifestyle (total leisure activity score <14). See table 1. Conclusion: Our study did not confirm the previously documented associations between metabolic and lifestyle risk factors and colonic adenomas. Further data from large screening centres may help establish the risk of adenomatous poly formation in patients with metabolic syndrome.

References

Disclosure: Nothing to disclose

P1643 THE USE OF NSAIDS, PAAs AND OACs IN HEMORRHAGE ASSOCIATED WITH DIVERTICULAR DISEASE

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Introduction: Diverticular Disease (DD) is one of the most frequent benign gastrointestinal condition in older adults, is an asymptomatic condition, however, complications can occur in 5% of cases. The increasing use of non-steroidal anti-inflammatory drugs (NSAIDs), platelet anti-aggregators (PAAAs) and oral anticoagulants (OACs) in this population raises the probability of hemorrhage associated with DD. Aims and Methods: The aim of this study is to evaluate if the use of NSAIDs, PAAAs and/ or ACOs influence the presentation and the course of hemorrhage episodes associated with DD. Retrospective analysis of patients admitted for DD complicated with hemorrhage between January 2015 and December 2017. Demographic, clinical, analytical and number of days of hospitalization were evaluated. Statistical analysis was performed using SPSS v.24.

Results: 68 patients were included; average age was 80.85 ± 9.49 (53-97) years and 57.4% were male. At the entrance, average hemoglobin was 95.4 ± 25.1 (46–150) mg/dL, systolic blood pressure 115.10 ± 18.64 (80–159 mmHg and heart rate 79 ± 10.7 (50–99) bpm. The mean days of hospitalization was 6.56 ± 5 (2–40) days and the mean hemoglobin at discharge was 104.6 ± 16.9 (81–142) mg/ dl. 22.1% of the patients were on NSAIDs, 45.6% PAAAs and 42.7% on ACOs. Differences were found between patients with PAAAs and ACOs and the highest INR (p<0.00) and INR (p<0.000, respectively), as well as with those with OACs with a higher number of days of hospitalization (p<0.036). In the categorization of the variables, it was verified that the patients who performed ACOs had HR at entry >80 and patients on OACs had HR at entry <80. Among patients with DD and under PAAAs, 86% patients had HR at entry >80, while 90% patients had HR at entry <80. 40 days of hospitalization (OR 0.22, 95% CI 0.075–0.67, p<0.007 and OR 3.68, 95% CI 1.34–10.13, p<0.012, respectively). The use of NSAIDs did not present statistical significance in the influence of those variables. Conclusion: The use of OACs influences the presentation and evolution of hemorrhage and is associated with a greater number of days needed for surveillance and treatment. Given the increasing use of these drugs, it is important to rethink the indications as well as the risk-benefit of use.

Disclosure: Nothing to disclose

References
P1644 HOW OLD IS REALLY OLD IN COLORECTAL CANCER

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Introduction: How old is really old is a controversial topic in colorectal cancer. Whether the old patients did have different outcomes comparing with younger CRC.

Aims and Methods: Our study aims to determine an optimal cutoff age of defining older patients in CRC, and present a real-world impact of the factor of old on CRC, which could provide more evidence in future clinical practices.

A total of 76,858 eligible patients from Surveillance, Epidemiology and End Results (SEER) database were included in the study. Cox proportional hazards regression model and covariate test were used to explore the suitable cutoff age. The propensity score matching method was performed to adjust the heterogeneity between the groups. Kaplan-Meir survival curves were plotted. Competing risk regression model was used to explore the impact of age on cancer-specific death (CCSD) and non-CCSD. An external validation was performed based on the data from 1998 to 2003 from SEER database.

Results: The age of 70 years was determined as the optimal cutoff value. Based on the cutoff value, patients was divided into younger group (n = 51,915, < 70 years old) and older group (n = 24,943, ≥70 years old). Compared with younger patients, older patients were related with high rate of male, Caucasians, right CRC, mucinous carcinoma, poorer differentiated grade, and more likely to have less lymph nodes sampled, less possibility to receive chemotherapy and radiotherapy. After adjustment for covariates and propensity score weighting, older patients (age ≥70 years) remained associated with decreased CSS (HR, 1.67 95 CI, 1.60–1.74, p < 0.001). To account for competing risks (non-CCSD), the competing analysis indicated that older group did have more CCSD as well as increased non-CCSD. The external validation consistently showed that age of 70 years was a suitable cutoff value and older patients have poorer prognosis.

Conclusion: The age of 70 was a suitable cutoff value for defining "young". Old Patients with CRC was not only associated with more non-CCSD but also more CCSD. Older patients might receive extra strengthened treatment if possible.

Disclosure: Nothing to disclose.

References

P1645 ENDOSCOPIC FINDINGS IN A COLORECTAL SCREENING PROGRAMME BELOW THE THRESHOLD OF 100 NG/ML (50–99 NG/ML)

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Introduction: The colorectal screening programmes based on the detection of FOBT (FIT – Faecal Immunological Test) in asymptomatic subjects between 50–69 years old, has proved its efficacy in the reduction of incidence and mortality of colorectal cancer (CRC). The established threshold in this context is 100 ng/ml. Given that values over 50 ng/mL are considered positive outside of the screening programme, there might be a percentage of asymptomatic individuals with values between 50–99 ng/mL, that could have undetected lesions.

Aims and Methods: We retrospectively analysed the FIT results (OC-SENSOR, Biogen®) received at our hospital in the first round of screening between the years 2014-2016. We selected those patients with results between 50–99ng/mL that underwent a colorectal screening colonoscopy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10-years interval. The main target lesions of the CRC screening program are the adenomas and early cancers. Therefore, the relation between number of colorectal cancers/endoctic polypectomies and CRC incidence and mortality decrease was evaluated. The analysis was based on the aggregate data from the Health Insurance Companies Databases, Preventive Colonoscopies Database and National Oncology Registry.

Results: Between years 2000 and 2015, there was significant reduction of the CRC incidence (18.4%) and mortality (32.4%) observed. The number of colorectales and endoscopic polypectomies has been raising continuously every year. In 2015, there were 264,399 colorectales performed from the following indications: 227,905 (86.2%) symptoms, follow-up and therapy; 25,463 (9.8%) FIT positivity and 13,031 (4.9%) screening at age ≥55. In the same year, overall 60,120 endoscopic polypectomies were done (22.7% of all colorectales) in follow age group 50–54, followed by FIT+c polypectomy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10-years interval. The main target lesions of the CRC screening program are the adenomas and early cancers. Therefore, the relation between number of colorectales/endoctic polypectomies and CRC incidence and mortality decrease was evaluated. The analysis was based on the aggregate data from the Health Insurance Companies Databases, Preventive Colonoscopies Database and National Oncology Registry.

Disclosure: Nothing to disclose.

References

P1646 COLORECTAL CANCER INCIDENCE AND MORTALITY REDUCTION IN THE CZECH REPUBLIC – EFFECT OF THE NATIONAL SCREENING PROGRAM

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Introduction: The organized non-population-based national Colorectal Cancer (CRC) Screening Program in the Czech Republic has been running since year 2000. In January 2014, the transition to population-based setting has been implemented. Currently, the annual immunochromegal FOBT (FIT) is offered at the age group 50–54, followed by FIT+c polypectomy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10-years interval. The main target lesions of the CRC screening program are the adenomas and early cancers. Therefore, the relation between number of colorectales/endoctic polypectomies and CRC incidence and mortality decrease was evaluated. The analysis was based on the aggregate data from the Health Insurance Companies Databases, Preventive Colonoscopies Database and National Oncology Registry.

Results: Between years 2000 and 2015, there was significant reduction of the CRC incidence (18.4%) and mortality (32.4%) observed. The number of colorectales and endoscopic polypectomies has been raising continuously every year. In 2015, there were 264,399 colorectales performed from the following indications: 227,905 (86.2%) symptoms, follow-up and therapy; 25,463 (9.8%) FIT positivity and 13,031 (4.9%) screening at age ≥55. In the same year, overall 60,120 endoscopic polypectomies were done (22.7% of all colorectales) in following age group 50–54, followed by FIT+c polypectomy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10-years interval. The main target lesions of the CRC screening program are the adenomas and early cancers. Therefore, the relation between number of colorectales/endoctic polypectomies and CRC incidence and mortality decrease was evaluated. The analysis was based on the aggregate data from the Health Insurance Companies Databases, Preventive Colonoscopies Database and National Oncology Registry.

Disclosure: Nothing to disclose.

References

P1647 RIGHT-SIDED LESIONS CHARACTERISTICS AND SURVIVAL IN A POPULATION-BASED COLORECTAL SCREENING PROGRAMME

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Introduction: Colorectal cancer (CRC) is one of the most frequent cancer entities in Europe and most cases of CRC arise through malignant transformation of benign adenomas known as the adenoma-to-carcinoma-sequence. Screening colorectales is less effective in reducing the incidence of proximal compared to distal colorectal cancer, presumably because of missed adenomas and advanced lesions during
endoscopy. Thus, effectiveness and success of colorectal cancer (CRC) screening programs depend decisively on the quality of the endoscopic procedures.

Aims and Methods: We aimed to provide a detailed analysis of the epidemiology and survival of right-sided detection lesions (adenomas and CRC) in a population based screening programme with a high participation and colonoscopy compliance. A total of 2,145 screening colonoscopies (SCRC) and 16 post-colonoscopy interval cancers (PCSCRC) and 19 surveillance cancers (PSCSRC) were diagnosed. The rate of post-colonoscopy cancer (PCCRC) for the right-sided was 0.3% and for left-sided 0.6%. 20% of the SCRCs were located in the right colon. The mean age was 62.6 ± 5.4 years, slightly lower than left-sided, being 46.4% in the age range 64–69 years. 62.8% were men compared to 66.4% in left-sided. We did not find differences in the distribution in the deprivation index, nor in the stage at the diagnosis time. In the right-sided 68.1% were in early stage. The most frequent histology by faeces detected by the immunohistochemical test in the right-sided was 234.9 (IQR = 1427), finding a significant difference with left-sided, 526.0 (IQR = 2105); p < 0.0001. The degree of differentiation was also different: 93.5% well/moderate in right-sided and 95.9% in left-sided; p = 0.043. We did not find differences in endoscopists adenoma detection rates (ADR). The 5-year survival for right-sided was 87.2% with an average of 7.86 years and 90.8% for left-sided with an average of 7.90 years; p < 0.001.

Regarding adenomas, 26.5% had right–side location. We did not find differences in endoscopists ADTs between locations. We found significant differences (p < 0.0001) regarding the histology of the adenomas, being mostly tubular in right-sided and tubulovillious in left-sided. The mean size of the largest polyp was somewhat higher in the left colon (13.9 ± 8.1 mm) with respect to the right colon (13.7 ± 12.6 mm).

The PCSCRC were located in right colon in 31.6% of the cases. 83.3% of right-sided and tubulovillious in left-sided. The mean size of the largest polyp was somewhat higher in the left colon (13.9 ± 8.1 mm) with respect to the right colon (13.7 ± 12.6 mm).

The survival for right-sided was 87.2% with an average of 7.86 years and 90.8% for left-sided with an average of 7.90 years; p < 0.001.

Conclusion: Available evidence is supporting the hypothesis that the natural history and survival of lesions in the right and left colon differ. Screening programs have greatly increased the detection of premalignant lesions. It is important to know the results and characteristics related to the locations of the lesions to implement measures that increase the effectiveness of the screening programs, improving survival, especially in right colon lesions.

Disclosure: Nothing to disclose

References

P1649 MITOTIC AND APOPTOTIC ACTIVITY IN SPORADIC COLORECTAL NEOPLASIA
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Introduction: Colorectal cancer (CRC) is third most commonly diagnosed cancer worldwide. Dysregulation of mitosis and apoptosis contributes to the development of colorectal neoplasia. In the present study we evaluated mitotic and apoptotic activity of epithelial cells at each stage of colorectal neoplasia.

A total of 61 persons were enrolled into the study: 18 patients with non-advanced colorectal adenoma (non-a-A), 13 patients with advanced colorectal adenoma (a-A), 17 patients with left-sided cancer and 17 controls individuals with normal findings on colonoscopy. Biopsy samples were taken from pathology (patients) and healthy mucosa (patients and healthy controls). Samples were formalin-fixed paraffin-embedded and stained with haematoxylin-eosin. Mitotic and apoptotic activity were evaluated in lower and upper part of the crypts and in the superficial compartment. Apoptotic activity was also assessed using detection of activated caspase-3.

Results: In controls, mitotic activity was present in lower part of crypts, accompanied by low apoptotic activity. Mitotic and apoptotic activity decreased (to almost zero) in upper part of crypts. In superficial compartment, increase in apoptotic activity was observed. Transformation of healthy mucosa into non-a-A was associated with significant increase of mitotic activity in lower and upper part of the crypts and with significant increase of apoptotic activity in all three compartments: p < 0.05. Transformation of non-a-A into a-A did not lead to any further significant increase in apoptotic activity, but was related to significant increase in mitotic activity in upper part of crypts and superficial compartment. A significant decrease in apoptotic activity was detected in all three compartments when compared to normal tissue in patients with left-sided colorectal neoplasia: p > 0.05.

No differences in mitotic and apoptotic activity between biopsies from healthy mucosa in patients with colorectal neoplasia were observed: p > 0.05. Mitotic and apoptotic activity was not different in the left sided colonic neoplasia (distally from splenic flexure) compares to samples from right-side colonic polyp: p > 0.05. No differences in mitotic and apoptotic activity were found in biopsies from normal tissue in patients with right-sided neoplasia when compared to normal tissue in patients with left-sided colorectal neoplasia: p > 0.05. No differences in mitotic and apoptotic activity between females and males were observed: p > 0.05.

Detection of activated caspase-3 confirmed the above findings in apoptotic activity.

Disclosure: Nothing to disclose

References

P1649 EXOGENOUS AND ENDOGENOUS ASSOCIATED FACTORS TO EARLY ONSET COLORECTAL CANCER
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Introduction: Early onset colorectal cancers (eCRC), defined as arising before 50 years of age, are a growing health hazard in western and eastern countries alike. The incidence of colon and rectal cancers in young individuals is projected to increase significantly, as much as 90% by 2040, respectively, by 2030. Although several known cancer risk factors have been investigated, there is no single compelling explanation for this epidemiological trend. While some eCRC are associated with germline mutations in cancer predisposition genes, these appear to account for only a fraction of these cancers (~20%) and do not explain increasing incidence.

Aims and Methods: To investigate the role of exogenous risk factors (alcohol intake and smoking habits) and endogenous conditions (delays in diagnosis, gastrointestinal hereditary tumors) as associated factors of eCRCs. Clinical, anamnestic and pathological data were retrieved on eCRC patients from June 2017 to April 2018. These patients were compared with a group of late onset CRC (loCRC) evaluated in the same period.

Results: We enrolled 33 eCRC patients and 48 loCRCs. According to definition, eCRC patients were younger than loCRC, with a mean age of 40.7 ± 7.3 and 66.1 ± 9.8, respectively (p < 0.001). Gender was not different in the two groups with a prevalence of females (54.5% in eCRCs and 52.1% in loCRCs). The diagnostic delay was higher in eCRC group: only 42.4% of eCRCs received the diagnosis in the 6 months from symptoms onset versus 100% of loCRC patients (p < 0.001). The syndromic familiarity (Lynch syndrome) was more frequent in eCRC (12%) than loCRC group (0%), with a statistically significant difference (p = 0.02).

We also found a statistically significant difference in alcohol habit, with a percentage of non-drinker in 66.7% of eCRCs and 41.7% of loCRCs (p = 0.04). Also, there was a trend through significance for no-smokers in eCRCs. Clinical data of eCRCs should be identified earlier in their diagnosis in young patients. We confirmed alcohol as cofactor in the development of eCRC and we underlined that familial history should be collected to identify mutations carriers.

Disclosure: Nothing to disclose

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Disclosure: Nothing to disclose

References
P1650 SLC25A22 MEDIATES EPIGENETIC REPROGRAMMING TO PROMOTE STEMNESS IN KRAS-MUTANT COLORECTAL CANCER C.C. Wong1, Y. Qian2, W. Li3, W. Kang4, J.J.Y. Sung4, J. Yu5
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Introduction: Epigenetic dysregulation plays essential roles in the tumorigenesis of KRAS-mutant colorectal cancer (CRC). However, the mechanism underlying epigenetic deregulation and its functional implications remain unclear. Our preliminary data revealed that SLC25A22 gene knockdown in colorectal cancer cells induced epigenetic reprogramming via methylation of DNA and histones; and that SLC25A22, a mitochondrial glutamate transporter, plays a key role in this process.
Aims and Methods: We aim to 1) investigate the role of SLC25A22 in the epigenetic reprogramming in KRAS-mutant CRC; 2) elucidate the mechanisms whereby epigenetic alterations mediate an oncogenic effect; and 3) devise a therapeutic strategy to target epigenetic reprogramming in KRAS-mutant CRC.
Results: Using isogenic cell lines harbouring wild-type and mutant KRAS (DKS857 vs DLD1L112D, IC50 vs IC112G), we demonstrated that mutant KRAS drives histone and DNA hypermethylation. Stable metabolic analyses revealed that mutant KRAS drives glutaminolysis via TCA cycle, leading to increased succinate/fumarate to α-ketoglutarate (αKg) ratio. An altered metabolite ratio, in turn, suppressed histone/DNA demethylases, thereby inducing hypermethylation. We thus utilized the CRISPR-Cas9 approach to knockout SLC25A22, a mitochondrial glutamate transporter essential for glutaminolysis, in two KRAS-mutant CRC cell lines (DLD1, SW1116). SLC25A22 knockout reversed KRAS-mediated glutaminolysis and reduced succinate/fumarate to αKg ratio, which consequently resulted in enhanced DNA demethylation, as evidenced by the increased levels of H3K4me3. Illumina 80K Methylation BeadChip was employed to profile the methylome of SLC25A22 knockout DLD1 cells. pathway analysis unveiled that WNT and cadherin signal-precipitation revealed that SLC25A22 knockout reduced H3K4 methylation, particularly H3K4me3 at the promoters of ASCL2 and LG35, WNT target genes that are markers of CRC stem cells. Interestingly, SLC25A22 knockout knockdown inactivates promoter demethylation and re-expression of genes within protocadherin cluster (PCHD48), putative tumor suppressors that were shown to negatively WNT/β-catenin signaling. Consistently, SLC25A22 knockout or ectopic expression of PCHD48 isosomers suppressed WNT/β-catenin signaling, as evidenced by decreased nuclear localization of active β-catenin, TOPP1phosphatase and reduced expression of WNT target genes. Moreover, histone methylation profiling identified that SLC25A22 knockout reduced H3K4 methylation, particularly H3K4me3 at the promoters of genes that directed active WNT signaling. Chromatin-immunoprecipitation revealed that SLC25A22 knockout suppressed enrichment of H3K4me3 at the promoters of ASCL2 and LG35, WNT target genes that are markers of CRC stem cells. Accordingly, ASCL2 and LG35 expression were diminished in SLC25A22 knockout CRC cells. Corroborating our mechanistic findings, SLC25A22 knockout suppressed tumorigenicity and stemness of CRC cell lines in vitro and in xenograft models. Conversely, promotes methylation of DNA/histone by either promoting methylation or inhibiting demethylation, we hypothesized that it may be possible to reverse aberrant DNA methylation and tumorigenesis by co-targeting methyltransferases (DNMT inhibitor) and glutaminolysis (GLS inhibitor). Consistently, SLC25A22 and GLS inhibitors (compound 968, BPTES, or CB389) synergistically inhibited growth of KRAS-mutant CRC cells.
Conclusion: SLC25A22-dependent glutaminolysis drives DNA/histone hypermethylation in CRC and promotes tumorigenesis and cancer stemness. A novel epigenetic therapy co-targeting DNMTs and GLS synergistically suppressed the growth of KRAS-mutant CRC cells.
Disclosure: Nothing to disclose

P1651 TRANSCRIPTION FACTORS ATF6 AND XBIPS OF THE UNFOLDED PROTEIN RESPONSE REDUCE COLORECTAL CANCER CELL PROLIFERATION AND STEMNESS THROUGH INHIBITING THE SENESCENCE-ASSOCIATED SECRETORY PHENOTYPE VIA THE NF-κB PATHWAY C.N. Spaan1
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Introduction: The unfolded protein response (UPR) is a cellular stress response activated upon accumulation of misfolded proteins in the lumen of the endoplasmic reticulum (ER). Activation of the UPR results in differentiation of intestinal epithelial stem cells and colon cancer stem cells via UPR kinase PERK, which results in increased chemoresistance and metastasis. Activation of PERK and downstream phosphorylation of eIF2α attenuates protein translation. Transcriptional activity of XBP1 and ATF6 in contrast result in expansion of the ER. Previously, it was shown that knockout of XBP1 increases proliferation and tumor formation in vivo. Therefore, we hypothesized that XBP1 signaling results in reduction of stemness and cellular proliferation in colon cancer cells. Since XBP1 and ATF6 have overlapping transcriptional targets, we additionally examine colorectal cancer cell proliferation upon ATF6 and XBP1 inhibition.
Aims and Methods: We generated LS174T colorectal cancer cell lines that stably express transcription factors of the UPR (XBPs (XBP1s or ATF6 (ATF6-373 truncated protein). In these cell lines, we measured downstream activation of UPR signaling using quantitative RT-PCR or protein immunoblot. We determined proliferation using crystal violet and EdU incorporation. Global translation was measured with 35S methionine incorporation.
Results: Enforced expression of transcriptionally active forms of XBPs or ATF6 resulted in marked increase of downstream UPR target genes GRP78 and CHOP. Cellular proliferation was decreased significantly. We additionally found reduced expression of intestinal epithelial stem cell markers LGR5 and HES5. Interestingly, we found that XBPs or ATF6 increased activation of PERK-eIF2α signaling, with decreased cellular translation as a result. Inhibition of eIF2α phosphorylation via constitutive expression of phosphate GADD34 rescued XBP1 and ATF6 reduced growth retardation.
Conclusion: Activation of UPR signaling in the intestinal epithelium, adenomas and colorectal cancer cells results in differentiation of stem cells. We observed that activation of transcription factors XBPs and ATF6 inhibit proliferation and induce differentiation. XBPs and ATF6 induced differentiation inhibited expression of intestinal epithelial stem cell markers LGR5 and HES5. Mechanistically, XBPs and ATF6 inhibition exposed a novel interaction with PERK-eIF2α signaling. We identify eIF2α phosphorylation as responsible for XBPs and ATF6 induced differentiation. Targeting PERK-eIF2α in colon cancer may thus be utilized for colorectal cancer cell differentiation and to increase chemosensitivity.
Disclosure: Nothing to disclose

P1652 KLOTHO SUPPRESSES SENESCENT MESENCHYMAL CELLS AND THE PROGRAMMED CELL DEATH PHENOTYPE IN HUMAN CIRCULATING Endothelial PROGENITOR CELLS BY INHIBITING THE SENESCENCE-ASSOCIATED SECRETORY PHENOTYPE VIA THE NF-κB PATHWAY Y. Liu1,2, X. Pan3, S. Chen4, J. Pan3, Z. Lin5, T. Su6, S. Lai7, L. Wu8, F. Chen9, Q. Ge8, L. Chen9, S. Ye10, L. Wang1,2
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Introduction: The risk of colorectal cancer (CRC) is increasing with age, and cellular senescence plays an important role in tumorigenesis. We have previously showed that Klotho, an anti-senescence gene, was regulated by DNA hypomethylation and involved in CRC cell proliferation.
Aims and Methods: This study was designed to determine the molecular mechanism of Klotho in cellular senescence and expression of senescence-associated secretory phenotype (SASP), and clarify its clinical significance and biological fusions in CRC. Immunohistochemical staining was applied to identify Klotho expression in 143 CRC tissues. Senescent human mesenchymal cells were established and cultured with CRC cells. In vitro and in vivo studies were performed to determine the growth and metastatic phenotypes of colon cancer cells in response to senescent cells. Secretes of the senescent phenotype (SASP) molecules were screened after administration with recombinant Klotho. CCL-2, a candidate SASP, was validated and its functional role in CRC cell proliferation was studied.
Results: IHC staining showed that Klotho was down-regulated in CRC tissues and closely correlated with elderly age. High expression of Klotho was an independent prognostic factor for favorable survival in CRC patients. In addition, senescent mesenchymal cells significantly stimulated the proliferation of CRC
Our results suggest that DNA hypomethylation including S100P, sites in the intron 1 wasthe strongest among these regions. Conclusion: Senescent mesenchymal cells may alter the tissue microenvironment vialineage selection including CCL-2 promoting colorectal cancer growth and metastasis, which could be blocked by Klotho pretreatment. The inhibition of senescent stroma-cancer signaling pathways by Klotho has the potential to restrain colorectal cancer progression.

Disclosure: Nothing to disclose.
alteration was found. Further prospective data are needed to confirm those results.

Disclosure: Nothing to disclose

References

P1656 SCNN1B FUNCTIONS AS A TUMOR SUPPRESSOR IN COLORECTAL CANCER BY INHIBITING THE MEK-ERK PATHWAY
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Introduction: Promoter hypermethylation plays a vital role in cancer through transcriptional silencing of tumour suppressive genes. Integrated epigenomic and transcriptomic analyses of the Cancer Genomic Atlas (TCGA) colorectal cancer (CRC) cohort showed that SCNN1B is an outlier gene aberrantly silenced in CRC. In this study, we investigated the function, molecular mechanism and clinical significance of SCNN1B in CRC.

Aims and Methods: In this study, we aim to 1) evaluate the clinical significance of SCNN1B in CRC; 2) investigate the biological function of SCNN1B in CRC; and 3) molecular pathways involved in tumor suppression by SCNN1B. Clinical significance was validated by methylation-specific PCR (MSP), bisulfiite sequencing (BGS) and real-time PCR analysis. In vitro functional assays were carried out by cell viability, colony formation, apoptosis, cell cycle analysis, invasion, and migration assays. Pathway analysis was performed by Gene Set Enrichment Analysis (GSEA), and validated by Western blot and luciferase reporter assay.

Results: Using volcano plots analyses of RNAseq and 450K methylation array data, we identified that SCNN1B is an outlier gene in TCGA CRC cohort which is silenced at mRNA level, but hypermethylated at its promoter CpG sites. RT-PCR showed that SCNN1B mRNA was silenced in all ten CRC cell lines tested compared to normal colonic tissues. MSP and BGS analysis confirmed SCNN1B hypermethylation and in ten CRC cell lines. SCNN1B expression was restored by demethylation treatment, suggesting that promoter methylation mediates its transcriptional silence. In a Hong Kong CRC cohort, we validated the silencing of SCNN1B mRNA and protein expression, by real-time PCR and immunohistochemistry (IHC), respectively, concomitant with its promoter methylation. Survival analysis of TCGA dataset demonstrated that mRNA expression of SCNN1B is independently associated with good outcome in CRC (P < 0.001); whereas its promoter methylation predicts poor survival (P < 0.001). SCNN1B might be a functional tumor suppressor silenced by promoter methylation in CRC. Ecotropic expression of SCNN1B in two CRC cell lines inhibited cell proliferation and colony formation. SCNN1B exerted its effect by inducing apoptosis and cell cycle arrest. Consistent with this, Western blot analysis revealed that activation of caspase-3 and PARP, up-regulation of cell cycle inhibitors p21, p27 and p53, together with the down-regulation of cyclin D1. Moreover, SCNN1B suppressed cell migration, as determined by wound healing assays. A panel of cancer cell lines that can be regulated by SCNN1B, GSEA analysis was performed on TCGA CRC cohort. GSEA revealed a significant association of SCNN1B with down-regulation of KRAS oncogenic signature. Consistent with this observation, Western blot showed that SCNN1B overexpression decreased the expression of p-MEK and p-ERK, key downstream factors of oncogenic KRAS. Moreover, ectopic SCNN1B expression inhibited SRE luciferase activity, indicating suppression of RAS-MEK-ERK oncogenic signalling. Conclusion: SCNN1B is a tumor suppressor silenced by promoter methylation in CRC. This silencing may participate in the oncogenicity of RAS-MEK-ERK signalling. SCNN1B mRNA expression and promoter methylation may serve as an independent prognostic biomarker for CRC patients. Disclosure: Nothing to disclose

P1657 DIAGNOSTIC AND PROGNOSTIC ROLE OF CIRCULATING CELL FREE DNA (cfDNA) IN DIFFERENT STAGES OF COLORECTAL CANCER
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Introduction: Cell-free DNA (cfDNA) represents DNA originating from dying cells and from active release from viable cell. cfDNA reflects the dynamic mutation profile of the tumor. The clinical utility of blood level of (cfDNA) in patients with metastatic colorectal cancer (mCRC) hasn’t been much described before.

Aims and Methods: To assess the level of (cf DNA) as a serum biomarker in diagnosis and progression of colorectal cancer (surgically resected and non-resected) at different tumor stages. A cross sectional study was conducted on 90 persons who fulfilling the designed inclusion criteria and classified into four groups, Group I include 30 patients with colorectal cancer (pre-operative), Group II : 30 patients with colorectal cancer (post-operative), Group III : 15 patients with colorectal polyps (low-grade dysplasia), Group IV : 15 healthy volunteers as control group. All participant after detailed history, clinical examination, imaging study and endoscopic assessment were subjected to routine laboratory investigation, carcinoemryonic antigen (CEA) and serum level of cfDNA.

Results: The mean DNA concentration was 2.46 μg/ml for CRC (pre-operative), 0.519 μg/ml for CRC (post-operative), 1.684 μg/ml for colorectal polyps (low-grade dysplasia) and 1.068 μg/ml for healthy controls. DNA concentration was determined significantly higher in CRC (pre-operative) patients compared with healthy controls (P = 0.05). The mean DNA concentration was significantly higher in CRC (pre-operative) patients compared with CRC (post-operative) patients (P = 0.01). But the mean DNA concentration was non-significantly higher in CRC (pre-operative) patients compared with CRC (post-operative) patients (P = 0.3). The sensitivity, specificity, positive and negative predictive values of DNA concentration in distinguishing CRC patients from healthy controls were 36.7% and 100%, 100% and 50.5% respectively.

Conclusion: cfDNA is a useful non-invasive tumor biomarkers and can improve diagnostic and prognostic value for CRC disease at different tumor stages, and the results suggest that the combination of cfDNA with CEA could improve the diagnostic performance for benign tumor and CRC.

Disclosure: Nothing to disclose

References
Disclosure: Nothing to disclose

Conclusion: dently associated with favorable CSS (specific survival (CSS) was significantly associated with favorable cancer-...over-expression of ARID3A was significantly associated with favorable cancer-

References

P1662 DELAYING AND DRYING EFFECTS ON THE RESULTS OF GUILA FAECAL OCCULT BLOOD TESTING
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Introduction: In the UK, guaiac-based faecal occult blood testing (gFOBT) is the primary means of national screening for colorectal cancer (CRC). However, variations in positivity rates not easily explained by background disease levels are seen across the country. In particular, kits sent to the Eastern England Hub are 50% more likely to be tested positive than those sent to other hubs which has significant consequent affects for example on colonoscopy services.
Aims and Methods: We aimed to determine if delays in kit processing could be impacting positivity rates through the effects of sample drying.
In the Eastern Hub of the UK Bowel Cancer Screening Programme ~2500 gFOBT kits are processed daily.
1) For one month during winter 2017 received kits were randomly assigned to usual practice (test on day of receipt) or drying 24hrs spread out in a warm room (average temp 21°C).
2) For a further month received kits were randomly assigned to usual practice (test on day of receipt) or drying with kits left for 24hrs spread out in a warm room (average temp 21°C).
Results: 1) The study consisted of n = 1783 in the no delay group and n = 1741 in the delay group.
Kits positivity of the control group was 18.4%, decreasing to 17.4% in the 2 day delayed group (n = 1192) and 16.7% in the 3 day delayed group (n = 221).
Window positivity was then investigated and showed a significant decrease in the positivity of windows 5 & 6 (the 3rd stool sample) when testing of the kit was delayed; particularly in window 6 where the proportion of positives decreased from 10.0% to 7.4%. Little effect was seen in the first 2 samples (windows 1–4).
2) In the second study n = 1793 in the control group and n = 1810 in the drying group.
Overall kit positivity was shown to decrease from 21.1% to 17.5%.
Window positivity showed a decrease in the positivity of windows 5 & 6 as with the 1st trial, but this time a larger decrease was experienced in those kits left in the warmer laboratory (10.5% to 8.4% and 11.4% to 8.0% in windows 5 & 6 respectively).
Conclusion: Positivity rates in kits delayed and dried were significantly lower than those processed quickly and whilst still moist. This was most notable for the 3rd sample from patients (i.e. the most recently sampled).
It is likely that variation in the timing of receipt and processing of samples will lead to variations in positivity rates found.
Further research is required to determine the positive predictive value of different delaying strategies for the detection of colorectal cancer in order to determine optimal operational protocols.

<table>
<thead>
<tr>
<th>Trial 1</th>
<th>Trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 DAYS</td>
<td>0 DAYS</td>
</tr>
<tr>
<td>DELAY</td>
<td>DELAY</td>
</tr>
<tr>
<td>DRYING</td>
<td>DRYING</td>
</tr>
<tr>
<td>(n = 1783)</td>
<td>(n = 1741)</td>
</tr>
<tr>
<td>Total positive kits</td>
<td>18.4%</td>
</tr>
<tr>
<td>21.1%</td>
<td>17.5%</td>
</tr>
<tr>
<td>Sample 1</td>
<td>6.7%</td>
</tr>
<tr>
<td>6.8%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Sample 2</td>
<td>7.1%</td>
</tr>
<tr>
<td>8.4%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Sample 3</td>
<td>11.6%</td>
</tr>
<tr>
<td>14.2%</td>
<td>10.7%</td>
</tr>
</tbody>
</table>

Disclosure: Nothing to disclose
P1665 LATE DIAGNOSIS OF COLORECTAL CANCER IN MOROCCO: WHAT REASONS BEHIND?

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Introduction: Because of its frequency and seriousness, colorectal cancer is a major challenge for public health. In our country it is the first digestive cancer according to the two major regional registers. Early detection allows better survival and certainly reflects the strength of the health system. Our work aims to analyze the reasons for late diagnosis of colorectal adenocarcinoma to provide solutions for improving early diagnosis.

Aims and Methods: We analyzed the preliminary results of a multicenter prospective cohort including 220 patients with colorectal adenocarcinoma between February 2016 and April 2017 in 5 hospital departments. A period exceeding 30 days between the appearance of first symptoms and the date of diagnosis is considered as delay of diagnosis. Factors related to this late diagnosis were analyzed.

The descriptive and analytic study of the data was carried out with SPSS software version 16.0.

Results: The mean age of our patients was 56.72 years [22 -86] with a sex-ratio F/H of 1.12.

In 25% of cases, patients were under age of 45 [n=55]. The initial clinical symptoms were dominated by transit troubles (42.30%), abdominal pain in 36.54% of cases and lower bleeding in 21.16% of cases. Fifty-six percent of patients were diagnosed at the locally advanced or metastatic stage. The average time between appearance of symptoms and diagnosis was 7 months on average with 79% of the time exceeding 30 days [n=83]. In 31% of cases [n=68], an underestimation of the severity of symptoms was reported by patients as the cause of the consultation delay. In 36% of cases [n=79] the symptoms were attributed to hemorrhoidal pathology and in 14% of cases [n=30] the first visit indicated symptomatic treatment without any endoscopy investigation. Analysis of certain factors that explain the delay in diagnosing age under 45, sex, location of tumor, symptomatic treatment without any endoscopy investigation. Analysis of certain factors that explain the delay in diagnosing age under 45, sex, location of tumor, symptomatic treatment without any endoscopy investigation.

Conclusion: The late diagnosis of colorectal cancer is a real public health problem in our country with an average delay of 7 months. Only the presence of lower bleeding seems to alert the patients. The reinforcement of public awareness campaigns could certainly shorten this diagnostic delay and improve the prognosis.

Disclosure: Nothing to disclose

Reference


P1666 THE EFFECT OF METFORMIN ON TUMOR RESPONSE OF NEOADJUVANT CHEMORADIATION THERAPY IN A SINGLE INSTITUTION IN TAIWAN

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Introduction: Colorectal cancer is the most common malignancy in Taiwan, and colorectal cancer was about 36.9% of these patients. Neoadjuvant concurrent chemoradiation therapy (CCRT) before radical surgery is the choice for advanced rectal cancer. Some lucky cases got complete clinical response after CCRT. Therefore, “watch and wait” without radical surgery could be the choice for the selected patient. We hereby presented the long-term result of “watch and wait” without radical surgery for complete clinical response of rectal cancer after CCRT in Tri-Service General Hospital in Taiwan.

Aims and Methods: This was a retrospective study in a single institution in Taiwan. The patients of advanced rectal cancer with complete clinical response after CCRT were included from Jan, 2007 to Oct, 2017.

Results: There were 40 patients diagnosed with rectal cancer following the “watch and wait” without radical surgery policy. Three residual tumors were found among 13 cases (13/40, 32.5%), who got transanal wide excision for obvious mucosal lesions, 3 months to 1 year later after CCRT. No local recurrence was noted after local excision. Among the 27 cases without local excision, 2 patients (2/40, 5%) had local recurrence and 1 (1/40, 2.5%) got distal metastases within one year after CCRT. Salvage radical surgery was successful for these patients and no associated morbidity or mortality.

Conclusion: According to our study, the long-term result revealed no mortality or morbidity in the selected patients of rectal cancer with complete clinical response after CCRT.

Therefore, “watch and wait” without radical surgery could be the choice for the selected case of rectal cancer with complete clinical response after CCRT.

Disclosure: Nothing to disclose

P1667 LONG-TERM RESULT OF “WATCH AND WAIT” WITHOUT RADICAL SURGERY FOR COMPLETE CLINICAL RESPONSE OF RECTAL CANCER AFTER NEOADJUVANT CONCURRENT CHEMORADIATION THERAPY IN A SINGLE INSTITUTION IN TAIWAN

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Introduction: Colorectal cancer is the most common malignancy in Taiwan, and colorectal cancer was about 36.9% of these patients. Neoadjuvant concurrent chemoradiation therapy (CCRT) before radical surgery is the choice for advanced rectal cancer. Some lucky cases got complete clinical response after CCRT. Therefore, “watch and wait” without radical surgery could be the choice for the selected patient. We hereby presented the long-term result of “watch and wait” without radical surgery for complete clinical response of rectal cancer after CCRT in Tri-Service General Hospital in Taiwan.

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Conclusion: According to our study, the long-term result revealed no mortality or morbidity in the selected patients of rectal cancer with complete clinical response after CCRT.

Therefore, “watch and wait” without radical surgery could be the choice for the selected case of rectal cancer with complete clinical response after CCRT.

Disclosure: Nothing to disclose

P1668 ACID-RESPONDENT DRUG-COMPLEXED POLYPEPTIDE NANOPARTICLE EFFECTIVELY AND SAFELY TREATS COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is one of the most common malignant tumors worldwide, and in which chemotherapy plays an irreplaceable role. However, the efficacy is seriously unsatisfactory for the poor distribution specificity, short circular half-life and dosage-dependent side effects of traditional drugs. For this situation, a facilely prepared pH-responsive nanoparticle was prepared based on polypeptide to deliver antimumor drugs more efficiently and safely.

Aims and Methods: Epirubicin (EPI) is a model drug was loaded into nanoparticle (NP/EPI) via the electrostatic interaction between poly (ethylene glycol)-block-poly (L-glutamic acid) (mPEG-b-PGA) and EPI, and the subsequent
hydrophilic interaction among PGA/EPI complexes. The characterizations of NP/EPI were ensured by transmission electron microscopy (TEM) and Dynamic laser scattering (DLS). In vitro release experiment and nanoparticle stability assessment were employed to detect the pH-responsibility of NP/EPI. Subcutaneous C26-xenografted CRC murine model was established to evaluate the antitumor efficacy and security of NP/EPI with 4 times drug administration at EPI equivalent dose of 8.0 mg/kg. The tumor volumes and body weights of mice were measured every other day. Furthermore, the microscopic examinations were carried out by H&E staining and in situ apoptosis assay of isolated tumors.

Results: The loading nanoparticle appeared spherical with a medium hydrodynamic diameter of 93.71 ± 8.37 nm. The NP/EPI had faster release efficiency and higher cumulative release rate in intratumoral microenvironment of pH 6.8 than that in physiological condition (i.e., pH 7.4), and in intracellular acidic microenvironment of pH 5.3 the difference was more significant. Similarly, the particles exhibited nearly constant diameters in solution of pH 7.4, which increased gradually with the decline of pH value, and further confirmed the pH-responsibility of NP/EPI. In vivo, the two drug formulations both inhibited the growth of C26 tumors while showed a significantly enhanced efficacy than that of EPI. Microscopic examinations displayed that nanoparticle could improve tumor tissue necrosis and cell apoptosis caused by EPI effectively. In the aspect of safety, the body weight of mice in NP/EPI group was 22.08 ± 1.76 g, which was significantly higher than that in EPI group (i.e., 18.02 ± 1.84 g). Moreover, only 30% mice survived with EPI administration while that with NP/EPI reached 70%.

Conclusion: With perfect pH-responsibility, drug-loaded nanoparticle based on mPEG-b-PEG could significantly enhance efficacy and reduce side effects of traditional drugs, and holds great potential for the CRC chemotherapy in clinic.

Disclosure: Nothing to disclose

Table 1

<table>
<thead>
<tr>
<th>Metric</th>
<th>Group 1 (n:73)</th>
<th>Group 2 (n:21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastatic lymph node</td>
<td>3.29 ± 5.1</td>
<td>3.8 ± 3.29</td>
<td>0.65</td>
</tr>
<tr>
<td>End stage (median)</td>
<td>3.00</td>
<td>3.00</td>
<td>0.006</td>
</tr>
<tr>
<td>N stage (median)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.98</td>
</tr>
<tr>
<td>Hospital stay (mean ± SD)</td>
<td>10.40 ± 10.25</td>
<td>11.10 ± 10.49</td>
<td>0.88</td>
</tr>
<tr>
<td>Endostomy</td>
<td>49% (n:36)</td>
<td>16% (n:3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Laparoscopic approach</td>
<td>4% (n:3)</td>
<td>33% (n:7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Complications</td>
<td>15% (n:11)</td>
<td>23.8 ± 5.5</td>
<td>0.35</td>
</tr>
<tr>
<td>Overall survival (mean ± SD)</td>
<td>34.83 ± 3.2 months</td>
<td>49.61 ± 4.4 months</td>
<td>0.041</td>
</tr>
<tr>
<td>Disease free survival</td>
<td>33.23 ± 2.8 months</td>
<td>49.71 ± 4.4 months</td>
<td>0.10</td>
</tr>
</tbody>
</table>

P1669 DOES BRIDGE-TO-SURGERY STENT PLACEMENT PROVIDE BETTER ONCOCLOGICAL OUTCOMES FOR OBSTRUCTIVE COLORECTAL TUMORS?

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Introduction: Endoscopic self-expanding metal stents (SEMS) placement as a bridge to surgery is an option for obstructive colorectal tumors. SEMS could be used for definitive palliative treatment for unreactable or inoperable patients. Also SEMS are used as a bridge to elective curative resections. Although it is thought that emergency colorectal resections may cause worse oncological outcomes, the debate is still ongoing regarding to SEMS superiority and oncological safety. In this study, it is aimed to determine the benefits of SEMS placement in obstructive colorectal tumors.

Aims and Methods: Between 2012-2018, 136 patients admitted to University Hospital Emergency Clinic with acute obstructive colorectal tumors. Ninety-four of them were included in the study. Palliative SEMS placements for multi organs and/or peritoneal metastatic patients, patients whom underwent emergency surgery regarding to SEMS complications, palliative decompressive ostomy patients, patients with benign obstructive causes, patients with complications of previous surgery, were excluded. Patients underwent elective surgery procedures immediately, were defined as Group 1 and patients who underwent elective surgery after SEMS placement were defined as Group 2.

The demographic data, signs in emergency service, operation techniques, ostomy entity, pathological results and oncological follow-up were reviewed retrospectively. Statistical analysis of groups with Chi-square test, Fisher Exact t test, student’s t test, log rank and Kaplan-meier tests were done on SPSS Version 23.

Results: The demographic data, pathological results, clinical findings and surgical outcomes were summarized in Table 1. The tumor localization of the Group 1 and 2 were, 53% and 10% right sided tumors, 8% and 29% descending colon, 33% and 45% sigmoid colon tumors, 6% and 38% for rectal tumors, respectively. There was no difference between groups as to distant organ metastasis (p=0.77). End ostomy (without anastomosis) was created for 36 patients (49%) in Group 1. Only 36% of these ostomies were reversed. Overall survival rates were significantly higher in Group 2 but there was no difference between groups according to disease free survival rates (p=0.041 and 0.1 respectively).

Conclusion: SEMS placement as a bridge to surgery provided better results in reference to permanent ostomy and overall survival.

Disclosure: Nothing to disclose

P1670 ENDOSCOPIC FULL-THICKNESS RESECTION OF NEUROENDOCRINE TUMORS IN THE RECTUM – A SUBGROUP ANALYSIS OF THE GERMAN FTRD-REGISTRY

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Introduction: Subepithelial tumors (SET) in the colorectum are rare and usually detected incidentally during colonoscopy. The incidence of SET in the colorectum is reported to be about 0.3% and up to 27% are described to be malignant or to have malignant potential. Neuroendocrine tumors (NET) and gastrointestinal stromal tumors (GIST) are the most common SET with malignant potential. Endoscopic ultrasound (EUS) allows further characterization of SET, but is associated with limited diagnostic accuracy. In consequence, histological examination should be performed but obtaining a diagnostically conclusive sample might be difficult as SET are originating from deeper layers than the mucosa. Management of colorectal SET depends on dignity, tumor size and presence of symptoms. Further surveillance, endoscopic resection (ER) or surgical resection (SR) are potential options. ER of SET using the standard techniques such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is difficult and associated with an increased risk of bleeding or perforation. Clip-assisted endoscopic full-thickness resection (EFTR) has shown to be feasible, effective and safe for smaller colorectal SET (1).

Aims and Methods: The FTRD-System (Full-Thickness-Resection Device) is available for clip-assisted EFTR in the lower gastrointestinal tract since 2014 in Europe. In September 2015 an online FTRD-registry has been created as part of a post-market clinical follow up (PMCF). FTRD-procedures of 31 German centers were entered into the database. This retrospective analysis further evaluates EFTR of rectal NET. The aim of this analysis is to show that EFTR with the FTRD-System is feasible, effective and safe for rectal NET and allows definite histological diagnosis and therapy (complete resection, R0).

Results: 501 procedures were entered from September 2015 to May 2017. 20 German centers contributed to the registry of SET (7%). 10 cases were excluded (4 lost to follow up, 2 lipomas, GIST, MALT, Inflammatory polyp, histological diagnosis incorrect). SET (Neuroendocrine tumor) and 25 NET (24 rectum, 1 sigmoid) were included for this analysis. The median age of the patients (11 male, 14 female) was 57 years (range 28–81 years). The median size of the lesion was 8.3 ± 7.5 mm (from 3 ≤ mm to 25 ± 10 mm), mainly located in the middle rectum. EUS was performed in 9/25 patients (36%) and could not provide a definite diagnosis. Biopsies were taken before EFTR in 19/25 patients (76%) and all biopsies showed well differentiated (G1) NET. However, in all cases resection status was unclear or incomplete (Rx in 7 patients, R1 in 5 patients, missing statement in 7 patients). 5 NET (20%) were recurrent NET and had been treated previously (multiple forceps biopsies or snare resection). Mean procedure time of EFTR was 23 minutes (range 7–69 min). EFTR with the FTRD-System was macroscopic and histological complete (R0) in all cases. However in 7 cases (28%) a NET could no longer be proven. A full-thickness-resection specimen could be obtained in all cases. In 3 cases (12%) minor peri-interventional bleeding occurred and was managed endoscopically. Follow-up was available for 20/25 patients (80%) with a median of 17 weeks after EFTR (range 1–48 weeks). The OTSC was dislocated in 14/20 (70%) and in situ in 6/20 (30%) cases (no removal). No signs of a residual or recurrent tumor were observed.

Conclusion: EFTR with the FTRD for rectal NET is feasible, safe and effective and allows a definite diagnosis and therapy at once.

Disclosure: Nothing to disclose

Reference

**P1671 RED BLOOD CELL DISTRIBUTION WIDTH INDEPENDENTLY PREDICTS SURVIVAL IN R0 RESECTED COLORECTAL CANCER**

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**Conclusion:** The expression level of LINK-A in colon adenocarcinoma was higher between the high and low LINK-A expression groups. Then relationships between LINK-A expression and clinicopathological characteristics at baseline: Group 1, 1–2 non-advanced adenomas; Group 2, 3 non-advanced, diminutive (1 to 5 mm) adenomas; Group 3, ≥3 non-advanced, diminutive (1 to 5 mm) adenomas; Group 4, ≥3 non-advanced, small (6 to 9 mm) adenomas; and Group 5, ≥3 non-advanced, advanced adenomas. This high value was detected in the unique symptomatic case. CT was better than MRI for imaging IAD in 13 vs 9 patients.

**Disclosure:** Nothing to disclose

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**P1672 SURVEILLANCE PROTOCOL FOR ABDOMINAL DESEOMD TUMOURS IN FAMILIAL ADENOMATOUS POLYPOSIS (FAP): EXPERIENCE OF A REGIONAL REFERRAL CENTRE**

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Intercolorectal Tumours (DTs) are a malign proliferations of stromal cells, rare in the general population and common in patients with Familial Adenomatous Polyposis (FAP) who have undergone prophyllactic colectomy. In 10% of the cases DTs show a locally aggressive and rapid growth and are a main cause of death after prophyllactic colectomy in FAP patients. Nevertheless International Guidelines have not defined a surveillance protocol yet.

**Aims and Methods:**

- Aims of the present study were: to define a surveillance protocol and to evaluate the best diagnostic tool between MRI and CT; to identify DTs with aggressive behavior.
- From January 2010 to March 2018, patients who referred to the “Regional Referral Centre for FAP of Lazio Region” with a proven diagnosis of FAP were enrolled in the study. All patients underwent contrast-enhanced (CE) abdominal CT and abdominal MRI with a 1-year interval in all patients with prophyllactic colectomy. Patients with DTs and without intestinal obstruction and ureteral compression received follow up examination after 6–12 month or alternatively after 2–3 month. Patients without DTs underwent follow up examination after 3 years. DTs growth assessment was performed by using RECIST criteria 1.1. The “average monthly growth rate” was also evaluated.

**Results:**

- One hundred patients (55F/45F) were enrolled in the study. DTs were detected in 13/100 (13%) cases (5F/8M): 2 abdominal wall DTs (AWD), 10 intrabdominal DTs (IAD), one patient presented lesions in both localizations. The average age at diagnosis was 32.5 years (range 19–53), the average time of onset after colectomy was 43.9 months (range 13–228). In 5/13 cases (38.5%) the IAD showed an aggressive behavior (asymptomatic intestinal obstruction and ureteral compression seen at imaging in 3 cases and symptomatic intestinal per- foration in two cases). The “average monthly growth rate” was 0.58 cm (range 0.47–0.75 cm) for an average follow up of 11 months (range 4–20 months).

**Disclosure:** Nothing to disclose

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**P1673 HIGH EXPRESSION OF LONG NON-CODING RNA LINK-A ASSOCIATES WITH POOR SURVIVAL IN PATIENTS WITH COLORECTAL CANCER**

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**Introduction:** Long non-coding RNAs (IncRNAs) have been proved to be involved in the development of many diseases, including cancers. Long intergenic non-coding RNA for kinase activation (LINK-A), a newly discovered IncRNA, has been reported to enhance the occurrence and progression of breast cancer. LINK-A promotes breast cancer tumorigenesis via activating AKT or normoxic HIF-1α signaling pathway. AKT and HIF-1α pathway activation has been demonstrated to promote tumor formation, progression, and metastasis of colorectal cancer (CRC). However, whether LINK-A is related to the tumorigenesis of CRC is remained unknown.

**Aims and Methods:** To evaluate the expression of LINK-A in colon adenocarcinoma and establish the correlation between LINK-A and CRC prognosis. The expression of LINK-A was evaluated by qRT-PCR on DNA tissue microarray, which contained 15 pairs of human colon adenocarcinoma and paracancerous tissues and another 65 colon adenocarcinoma tissues. The total 80 patients were divided into low and high expression groups according to the LINK-A level. Then relationships between LINK-A expression and clinicopathological characteristics of colon adenocarcinoma were analysed between that two groups. Kaplan-Meier survival analysis was used to assess the LINK-A function on the survival of colon adenocarcinoma. Multivariable Cox regression analysis was also used to explore the risk factors for prognosis of colon adenocarcinoma between the high and low LINK-A expression groups.

**Results:** The expression level of LINK-A in colon adenocarcinoma was higher than those in paracancerous tissues (P = 0.047). Furthermore, overexpression of LINK-A was proved to be associated with advanced TNM stage (P = 0.013), positive lymph nodes (P = 0.024), low 5-year survival rate (P = 0.024) and even 10-year survival rate (P = 0.007). Besides LINK-A, advanced age (P = 0.036), high TNM stage (P = 0.023), deep infiltration degree (P = 0.032) and positive lymph nodes (P = 0.013) were also identified to be positively associated with poor over 5-year survival by Kaplan-Meier survival analysis. Then, multivariable Cox regression analysis revealed that LINK-A was an independent risk factor for prognosis of colon adenocarcinoma (P = 0.047).

**Conclusion:** High expression of LINK-A associates with poor survival in patients with colorectal cancer. And LINK-A may serve as a candidate prognostic biomarker for colon cancer.

**Disclosure:** Nothing to disclose

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**P1674 RISK OF METACHRONOUS ADVANCED NEOPLASIA IN PATIENTS WITH MULTIPLE DIMINUTIVE ADENOMAS**


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**Introduction:** Individuals with advanced adenomas or three or more adenomas have a higher risk for metachronous advanced neoplasia (AN) and are recommended to undergo surveillance colonoscopy at shorter intervals. Recently, improvements of colonoscopy technology have resulted in higher detection rates for colorectal neoplasms. In more recent screening studies, adenoma detection rate of 40% or more have been reported. Therefore, it is questionable whether patients with multiple (three or more) non-advanced diminutive adenomas should be considered as high-risk.

**Aims and Methods:** We analyzed 5,482 patients diagnosed with 1 or more adenomas during their first colonoscopy screening and who underwent a follow-up colonoscopy. Patients were categorized into four groups based on adenoma characteristics at baseline: Group 1, 1–2 non-advanced adenomas; Group 2, ≥3 non-advanced, diminutive (1 to 5 mm) adenomas; Group 3, ≥3 non-advanced, small (6 to 9 mm) adenomas; and Group 4, advanced adenomas.

**Results:** During a median follow-up of 38 months, the incidence of metachronous AN at surveillance colonoscopy was 5.6%. The incidence of AN was 3.9% in
group 1, 5.9% in group 2, 10.6% in group 3, and 22.1% in group 4. The adjusted hazard ratios (HRs) [95% confidence intervals (CIs)] for metachronous AN were 1.71 (0.99–2.94), 2.76 (1.72–4.44), and 2.53 (3.57–7.68), respectively. Compared with group 4, 4, the adjusted HRs (95% CIs) for group 1, group 2, and group 3 were 0.19 (0.13–0.28), 0.32 (0.18–0.59), and 0.52 (0.31–0.89), respectively.

Conclusion: Risks for advanced neoplasia among individuals with high-risk features vary based on baseline adenoma characteristics. We found that patients with a deleterious MMR mutation have a higher risk of metachronous AN compared with patients with low-risk adenomas. The surveillance interval for patients with multiple diminutive adenomas may be lengthened from the recommended interval for patients at high risk.

Disclosure: Nothing to disclose.

References:

P1675 ONCOLOGICAL RECURRENT RATE OUTCOMES AFTER SBTS: AN ES BRIDGE TO SURGERY COMPARED TO EMERGENCY SURGERY FOR LEFT-SIDED MALIGNANT COLONIC OBSTRUCTION: RETROSPECTIVE RIBONERIC STUDY

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Introduction: Symptomatic left-sided malignant obstruction is a medical and surgical emergency that requires an urgent intervention, which has been classically emergency surgery (ES), which still represents a high morbidity (30–60%), and mortality (10–30%);3

Stents bridge to surgery (SBTS) restore intestinal transit and allows to transform emergency surgery into elective surgery. SBTS is widely accepted in palliation, but disagreement exists about its role in patients whose disease is potentially curable due to the possible risk of tumour spread. At present, there are no consistent studies able to demonstrate that one strategy is superior to the other in terms of oncological benefit.

Aims and Methods: Our aim is to evaluate the oncological outcome in terms of recurrence and recurrence-free survival of stented patients who went on to elective surgery compared to those who had ES. We retrospectively selected patients who were clinically and radiologically left-sided malignant obstruction between January 2006 to May 2012 in two Specialty Hospitals in the south of Spain.

Exclusion criteria were age under 18, tumour located in right or transverse colon, or in medium/inferior rectum; metastatic disease (stage IV of the American Joint Committee on Cancer (AJCC) independently of the location or resectability of the metastases and perforation at the moment of the diagnosis.

Firstly, we analyzed pediometric data, recurrence rate (RR) and recurrence-free survival (RFS) between both hospitals, without finding statistically significant differences and achieving an homogeneous sample for the analysis. Then we analyzed RT and RSFs comparing SBTS vs ES groups. Multivariate analysis was made to find relative factors to oncological recurrence.

Results: We found a higher RR near statistical significance in the ES group, 5.9% in group 2, 10.6% in group 3, and 22.1% in group 4. The adjusted HRs (95% CIs) for group 1, group 2, and group 3 were 0.19 (0.13–0.28), 0.32 (0.18–0.59), and 0.52 (0.31–0.89), respectively.

Conclusion: There is a higher risk of recurrence near statistical significance in the ES group, which still represents a high morbidity (30–60%), compared to the SBTS group (79.3% and 75.6%), but the Kaplan-Meier analysis on cancer tissue have to be shown cost effective. Nonetheless, the approach of a universal vs a selective screening on tumor tissue is still debated. A pre-selection with family history criteria could improve the cost effectiveness of molecular screening.

Aims and Methods: The approach of our study was to evaluate the prevalence of LS in early-onset EC patients without family history compared with those with family history. Early-onset EC patients (≤50 years) were prospectively recruited in the study.

Results: Twenty-two early-onset EC cases with a median age at diagnosis of 43 years were analysed. Patients were categorized in three groups according with family history of LAC.

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Disclosure: Nothing to disclose.

References:
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Conclusion: Early-onset EC with or without family history of LAC are at high risk to develop colorectal cancer. In our series we identified 40.9% LS cases. However, despite what reported for early onset CRC family history could not be used as a pre-screening tool to evaluate whether or not patients should undergo tissue molecular screening.

Disclosure: Nothing to disclose.

P1677 STENT OR DECOMPRESSION COLOSTOMY AS BRIDGE-TO-SURGERY VERSUS ACUTE RESECTION IN OBSTRUCTING LEFT-SIDED COLON CANCER: A NATIONWIDE ANALYSIS OF 2587 PATIENTS

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Introduction: Resection of obstructing left-sided colon cancer in the acute setting is associated with an increased risk of postoperative morbidity and mortality, especially in the elderly, frail patient (1–4). Bridge-to-surgery management with stent placement or decompressing colostomy may improve postoperative outcomes (5–6).

Aims and Methods: In this nationwide retrospective cohort study, our aim was to describe national practice and compare mortality and morbidity rates between acute resection and stent or stoma as bridge-to-surgery. All patients with curable obstructing left-sided colon cancer treated between 2009–2016 were included from the Dutch Surgical Colorectal Audit. Additional data including 90-day mortality and morbidity as primary outcomes were retrospectively collected.

Results: In total, 2587 patients were included of whom 2013 underwent acute resection and 574 bridge-to-surgery by stent (n = 229) and stoma (n = 345). Acute resection showed a 90-day mortality rate of 7.6% versus 1.4% with stoma (p < 0.001) and 5.2% with stent (p = 0.2). Complication rate was 38.4% in the acute resection group compared to 31.9% in the stent group (p = 0.02). In patients ≥ 70 years, acute resection showed a mortality rate of 11.7% versus 3.2% with stoma (p = 0.001) and 8.3% with stent (p = 0.2). In patients with an ASA score of ≥ 3, mortality was 15.5% with acute resection versus 6.4% with stoma (p = 0.03) and 12.3% with stent (p = 0.5). The acute resection group showed a significantly lower primary anastomosis rate of 39.5% compared to the stoma group (84.9%, p < 0.001) and the stent group (79.4%, p < 0.001).

Conclusion: In this nationwide population, colostomy or bridge-to-surgery significantly reduced postoperative morbidity and mortality. Both decompressing colostomy and stent placement were associated with an increased primary anastomosis rate.

Disclosure: J.V. Veld: research grant Koningin Wilhelmina Fonds (KWF) Kankerbestrijding (funding for cancer research)

References

P1678 COLD SNARE PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION (CSP-EMR) OF LARGE SESSILE COLONIC POLYPS ≥20 MM IS FEASIBLE, SAFE AND EFFECTIVE

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Introduction: Endoscopic Mucosal Resection (EMR) is the standard care for adoption. Large (>20mm) non-pedunculated sessile polyps. Serious adverse events are mostly due to electrocautery. This could potentially be avoided by cold snare EMR. Traditionally it was thought impossible to resect large polyps with cold snare. We hypothesized that aggressive wide field cold snare piecemeal EMR (CSP-EMR) could be as effective as conventional EMR, but with fewer adverse events.

Aims and Methods: The study aimed to evaluate safety and efficacy of CSP-EMR of sessile colonic polyps sized ≥20mm. All cases of CSP-EMR performed by a single endoscopist at two academic hospitals for sessile polyps ≥20mm, from Jan 2016 – Dec 2017, were identified retrospectively. During this period, all lesions that were not suspicious for submucosal invasion, and were not very large Paris 0-Is lesions where cold snare resection would be technically very difficult, were performed by CSP-EMR. Efficacy was defined as the absence of residual or recurrent polyp tissue during the first surveillance colonoscopy. At surveillance, EMR scars were rigorously inspected using Olympus 190 series colonoscopes with high definition white light, then NBI, and then multiple cold biopsies of the resection and margins of the polyp resection. Adverse events including intra-procedurally or post-procedurally bleeding, perforation, post-procedural pain requiring hospital admission, post-polypectomy syndrome, histological outcomes and surveillance colonoscopy findings were assessed by reviewing electronic medical records.

Results: 148 polyps sized ≥20mm were successfully excised by CSP-EMR in 133 patients (median age 67 yrs, IQR 56–74 yrs; men 31.1%). Mean polyp size was 25.3 mm (median 20mm, IQR 20–30mm; range 20–60mm) and 137 (92.5%) polyps were Paris class 0IA. 85% of polyps were lifted with submucosal injection of Gelofusine with Methylene-Blue and Adrenaline (1:100,000 before resection. Histology was 90 (60.8%) sessile serrated adenomas, 42 (28.4%) tubular adenomas, and 13 (8.8%) tubulovillous adenomas. Complete resection was absent in 89 (60.1%) polyps, low-grade in 57 (38.5%) and high-grade in 2 (1.3%). 110 of 133 patients had surveillance colonoscopy for 124 polyps over a median follow-up of 5 months (range 2–16 months). EMR scar biopsies were taken of 113 of 124 polyps (90.4%). Residual or recurrent polyp was noted in 41 cases (3.2%). Clinically significant intra-procedural bleeding occurred in 2 patients (1.5%) and was successfully treated with clips. 4 patients (3%) experienced clinically significant post-procedural bleeding that settled spontaneously. 1 patient (0.7%) required overnight hospital admission for post-EMR abdominal pain that settled spontaneously. None experienced post-polypectomy syndrome, deep mural injury or perforation.

Conclusion: CSP-EMR of sessile colonic polyps ≥20mm is technically feasible and potentially more effective than conventional EMR, but with a superior adverse event profile. We hypothesise that the enhanced safety of cold snare resection allowed for an aggressive and wide field resection that reduces recurrence rates. However, due to the likelihood of selection bias in terms of the patient cohorts, randomized controlled trials with large multicentre prospective observational studies are required to more rigorously demonstrate the non-inferiority and improved safety profile of CSP-EMR compared to conventional EMR, and to further determine which polyp morphologies are best suited to CSP-EMR.

Disclosure: Nothing to disclose.
COMPREHENSIVE TREATMENT DECISION SUPPORT OF Disclosure: genesis is stronger than that of single use of aspirin or metformin. With single treatment of aspirin or metformin. Combination treatment significantly suppressed cell proliferation in both in normal tissue, adenoma and cancer compared with single treatment of aspirin or metformin. Considering their clinical application such as safety, they could be possible strategy for increasing radiotherapy efficiency without additional toxicity.

Disclosure: Nothing to disclose

References

P1680 THE CHEMOPREVENTIVE EFFECT OF COMBINATION TREATMENT OF ASPIRIN AND METFORMIN FOR COLORECTAL CARCINOGENESIS

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Introduction: The prevalence and mortality of colorectal cancer (CRC) are increasing worldwide. New strategies for prevention, such as chemoprevention, are needed to lower the burden of this disease. The most precise chemoprevention agent for CRC is NSAIDs, especially aspirin. However, the chemoprevention effect of aspirin is not so strong and has some adverse effect, such as gastrointestinal bleeding. We previously analyzed the chemopreventive effect of low dose metformin in rodent model and conducted clinical trial for adenoma preven­tion, and reviewed the response for colorectal cancer patients. Considering their clinical application such as safety, they could be possible strategy for increasing radiotherapy efficiency without additional toxicity.

Disclosure: Nothing to disclose

References
The statistical difference was shown in IL-10 and claudin2 mRNA between old (≥65 years old) human, old IBS patients and young IBS patients. The change of colonic mucosal biopsies were acquired from old (≥65 years old) human, old IBS patients and young IBS patients. The change of sphingolipid which was known to be related with epithelial permeability and role of aging on colonic permeability and the relation between the change of sphingolipid and age was known to be related with epithelial permeability and gut tight junction.

Aims and Methods: The overall goal of the current study was to investigate the role of aging on colonic permeability and the relation between the change of sphingolipid which was known to be related with epithelial permeability and gut tight junction.

Colonic mucosal biopsies were acquired from old (≥65 years old) human, old IBS patients and young IBS patients. The change of sphingolipid which was known to be related with epithelial permeability and role of aging on colonic permeability and the relation between the change of sphingolipid and aging was uncertain.

Aims and Methods: The overall goal of the current study was to investigate the role of aging on colonic permeability and the relation between the change of sphingolipid which was known to be related with epithelial permeability and gut tight junction.

Further studies are needed to clarify the relation between sphingolipid and gut aging and IBS patients might be related with the disruption of intestinal barrier.
CXR\textsuperscript{1}\textsubscript{1}-GFP\textsuperscript{1} mice were used to identify and count microglia cells in the L6-S1 dorsal spinal cord. IL-1β injection alone or in combination with LPS increased the number of microglia by 2.8-fold and 3.7-fold, respectively. Using qRT-PCR, expression of Nk1 receptor was quantified in the spinal cord by western-blot.

**Results:** We observed a chronic cross-sensitization model in conscious mice. In this model, intrathecal administration of acetic acid induced a transient increase in colonic permeability, and a long lasting colonic hypersensitivity to distension, that involved neural interactions and Nk1 receptors.

**Conclusion:** We developed a chronic cross-sensitization model in conscious mice. In this model, intrathecal administration of acetic acid induced a transient increase in colonic permeability, and a long lasting colonic hypersensitivity to distension, that involved neural interactions and Nk1 receptors.

**Disclosure:** Nothing to disclose
P1690 HYPERPLASIA OF ENTERIC GLIAL PROCESS TOWARD THE COLONIC MUCOSA AND NETRIN-1 EXPRESSION IN THE COLONIC SUBMUCOSA IN A RAT MODEL OF VISCERAL HYPERSENSITIVITY

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Introduction: Elongation of enteric neuron toward the gastrointestinal mucosal surface leads to visceral hypersensitivity, which is one of the pathogenesis of irritable bowel syndrome (IBS). Among a variety of physiological roles of enteric glial cell (EGC), we reported that activated EGC in the myenteric plexus of the colon contributes to motor hypercontraction according to the stress intensity (Neurogastroenterol Motil., 2015). However, it is unknown how submucosal plexus, particular in submucosal EGC involv in neuronal elongation. Although netrin-1 is a well-characterized chemoattractant involved in neuronal guidance in the developing enteric nervous system, it also remains unknown which layer of the colon netrin-1 has crucial roles in under stress circumstances.

Aims and Methods: We used the Wistar Kyoto rats (WKY), a model of visceral hypersensitivity, and Wistar rats (control). Distal colonic segments were obtained from each rat, and the respective layer (mucosa, submucosa, and muscle) were separately stripped from the whole colonic tissues and prepared. According to the layers, we compared mRNA expression of glial fibrillary acid protein (GFAP), netrin-1, nerve growth factors (NGF), glial cell-line-derived neurotrophic factor (GDNF), and GAP-43, neuronal growth factor by real-time RT-PCR. To analyze EGC morphology and its interaction with intrinsic primary afferent neuron (IPAN), whole mount submucosal plexus preparations were used for immunohistochemistry for GFAP, IPAN (calbindin), netrin-1, and a receptor of netrin-1 (DCC, deleted in colorectal cancer).

Results: mRNA expressions of netrin-1 (3.2-fold), NGF (2.2-fold), GDNF (1.6-fold), and GAP43 (3.0-fold) were significantly increased in submucosal layer in the WKY rats (3.0-fold) vs. control rats. As well as the submucosal layer, mRNA expressions of GAP43 (2.6-fold) were tended to be increased in the mucosal layer of the irritated rats. Neuronal connexions were clearly enhanced in the submucosal plexus of the irritated group compared to the control group.

Conclusion: Submucosal layer of the colon has important roles under stress circumstances. In the submucosal layer, both hyperplasia of EGC processes toward the sensory neural body increased and neuronal elongation, and mRNA expression of netrin-1, NGF, and GDNF may be involved in peripheral mechanisms of visceral hypersensitivity in IBS.

Disclosure: Nothing to disclose

References

P1691 ANO-RECTAL SENSORIAL AND MOTOR CHARACTERISTICS IN TYPE 2 DIABETICS WITH OR WITHOUT COMPLAINTS OF GASTRO-OESOPHAEGAL REFLUX: A COMPARATIVE STUDY

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Introduction: Some investigations show up that there is an important overlap of the diverse functional disorders in the digestive system in type 2 diabetics. In diabetics, gastro-oesophageal reflux and anorectal symptoms are frequent.

Aims and Methods: The aim of this study was to compare rectal sensorial and motor characteristics between type 2 diabetic individuals with and without complaints of gastro-oesophageal reflux.

Results: In diabetics with complaints, resting rectal pressure was slightly higher than others without complaints, 13.6 ± 1.2 vs 9.6 ± 1.6 mmHg, but the difference was not significant, p = 0.07. In both groups, diabetics with complaints vs without complaints, other rectal manometric characteristics were the follow: minimum rectal sensitivity, 56.7 ± 6.7 vs 80.0 ± 7.6 mmHg, p = 0.0<;; first urge, 80.8 ± 4.1 vs 132.3 ± 13.5 mmHg, p = 0.002; Intense urge, 108.3 ± 6.0 vs 152.8 ± 14.7 mmHg, p < 0.005; maximum tolerable rectal capacity, 169.2 ± 15.6 vs 225.5 ± 20.8 mmHg, p < 0.03. The relaxing percent during the recto-anal reflex and the sphincters pressures during the squeeze and squeeze endurance were statistically similar. The anal sphincter fatigue during the squeeze endurance was 1.16 ± 0.05 vs. 0.53 ± 0.29 mmHg/sec. When comparing the characteristics according to the degree of reflux, slight to moderate vs. severe to very severe complaints, the resting external sphincter pressure was 31.0 ± 3.4 vs 60.8 ± 5.0 mmHg, and minimum rectal sensitivity was 41.6 ± 6.0 vs. 63.7 ± 6.6 mmHg, p < 0.03.

Conclusion: 1-In type 2 diabetics with complaints of gastro-oesophageal reflux the volume for minimum rectal sensitivity, first urge, and intense urge and for maximum tolerable rectal capacity were lower than in diabetics without the symptoms. 2-The anal sphincter fatigue was higher in diabetics with complaints. 3-The volumes for minimum rectal sensitivity and for maximum tolerable rectal capacity were higher in diabetics with more severe symptoms.

Disclosure: Nothing to disclose

References
Conclusion: Enhancement of glia-glial connections in the submucosalplexus in accordance with the avoidanceof the mucosa andsubmucosa affects neuronal outgrowth toward the colonic mucosa, which may lead to viscerales hypersensitivity aftersmaller irritation with chronic stress.

Disclosure: Nothing to disclose

P1693 MUCOSAL FEATURES AND MOLECULAR MECHANISMS UNDERLYING CHRONIC CONSTIPATION IN PATIENTS WITH PARKINSON’S DISEASE.

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Introduction: Chronic constipation (CC) in Parkinson’s disease (PD) is a severe, usually laxative-resistant condition often worsening the patient’s quality of life. To date, the molecular mechanisms underlying PD/CC pathogenesis are only poorly understood.

Aims and Methods: The present study aimed to investigate neuropathological and neurochemical features in colonic mucosal biopsies of PD/CC patients compared to non-parkinsonian CC patients and asymptomatic controls by examining markers of intestinal epithelial barrier (IEB) and of enteric submucosal neurons andglia. PD/CC patients (n = 6; 2F; 51–79 yrs), CC patients (n = 6; 4F, 31–60 yrs) and control subjects (screening colonoscopy) (n = 6; 3F, 33–64 yrs) were enrolled.

Colonic biopsies (n = 6) were collected from each subject. Total proteins were extracted from n = 4 biopsies and analyzed by Western blot to quantify: glial fibrillary acid protein (GFAP, as index of glial activation) and vasoactive intestinal polypeptide (VIP) and its receptors VPAC1 and VPAC2 as markers of subsets of vaso-secretomotor neurons. In addition, n = 2 biopsies were analyzed by immunohistochemistry to evaluate tight junction (TJ) proteins, i.e. Zonula occludens-1 (ZO-1) and occludin, as indicators of IEB structural integrity. The relative density of TJ immunofluorescence was scored as follows: 4, normal; 3, slightly modified; 2, altered; 1, markedly reduced; 0, no expression.

Results: Western blot data showed no significant differences in VIP protein expression levels in PD/CC vs. CC vs. controls (One-way ANOVA, P = 0.3). Similarly, VPAC1 and VPAC2 expression did not appear significantly different among groups (P = 0.8 and P = 0.1, respectively). However, VIP and VPAC2 expression levels showed a trend to decrease in both PD/CC and CC groups vs. controls. Also GFAP expression did not show significant differences among the three groups (P = 0.5). ZO-1 immunoreactive pattern displayed a normal network in the mucosa of control subjects and PD/CC patients (score = 4), whereas in CC patients ZO-1 immunoreactivity was markedly decreased (score = 2). In contrast, occludin immunoreactivity in PD/CC patients was almost exclusively expressed at the base of the cells and it appears weaker (score = 2–3) than in CC patients and controls (score = 4).

Conclusion: The present study showed that occludin, but not ZO-1, is reduced in PD/CC and CC patients, whereas there were no significant changes in VIP, VPAC1, VPAC2 and GFAP protein expression in PD/CC and CC patients vs. controls. Our data support the concept of selective protein abnormalities in IEB which may contribute to distinct mechanisms in PD/CC.

Disclosure: Nothing to disclose

P1694 A PROSPECTIVE EVALUATION OF GASTROINTESTINAL SYMPTOMS AND DYSMOTILITY IN SUBJECTS WITH AND WITHOUT HYPERMOBILIT Y SPECTRUM DISORDERS.

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Introduction: Hypermobility Spectrum Disorders (HSD) are a continuum of connective tissue disorders characterized by joint hypermobility (JH). Recent studies demonstrated that HSD and PD are often associated with gastrointestinal symptoms. A higher prevalence of HSD has been demonstrated in patients with functional compared to organic GI disorders, pointing towards neuromuscular dysfunction of the GI tract as a possible underlying mechanism.

Aim and Methods: We prospectively evaluated whether subjects with (undiagnosed) HSD present with different symptom patterns and GI motility compared to non-HSD subjects, in an unselected tertiary GI patient population in whom organic pathology had previously been excluded. Sixty-two subjects (53 female; mean age: 40), referred for comprehensive GI motility assessment using gastric emptying test, esophageal, antroduodenal, and/or colonic manometry study, were consecutively included. Brighton criteria were used to diagnose HSD, and JH was assessed using the Beighton score. A Beighton score ≥ 6 was used as the cut-off for clinically significant JH. GI and psychological symptom scores, and outcomes of the Gastrointestinal Symptom Rating Scale, Hospital Anxiety and Depression Scale, and Rand Health Survey Short Form-36.

Results: Eighteen subjects (29.0%) met criteria for HSD. No significant difference between HSD and non-HSD subjects were found for age, BMI, GI symptom severity, depression/anxiety, and mental as well as physical quality of life. Esophageal, gastric, antroduodenal, and/or colonic dysmotility was not significantly more prevalent in the HSD group vs. the non-HSD group (72.2% vs. 47.9%, respectively; p = 0.091). However, subjects with clinically significant JH (i.e. Beighton score ≥ 6) more often showed abnormal GI motility compared to subjects with Beighton < 6 (83.3% vs. 46.8%, p = 0.028). The odds of having any form of GI dysmotility were 5.7 times higher (95%CI: 1.121; 28.788) in cases with Beighton ≥ 6 than Beighton < 6.

Conclusion: In patients with functional GI disorders referred for extensive GI motility analysis, HSD patients did not present with gastric, esophageal, antroduodenal, and/or colonic dysmotility significantly more often than non-HSD patients. However, the clinical phenotype of JH was a significant predictor for GI dysmotility. Therefore, the present study supports a possible role for neuromuscular dysfunction as a pathophysiological mechanism underlying GI symptoms in HSD.

Disclosure: Nothing to disclose

P1695 HISTOPATHOLOGIC SIGNS OF NEURON DEGENERATION IN INDIVIDUALS WITH GASTROINTESTINAL SYMPTOMS MAY BE FOUND IN CONVENTIONAL STAINING IN BOTH SUBMUCOSAL AND MYENTERIC NERVE PLEXA.

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Introduction: Gastrointestinal symptoms are common in the population, many times with unknown reasons. Previous research has described that enteric neuropathy may be the etiology in some cases. Parkinsonism is one disease which often presents itself with gastrointestinal symptoms, especially constipation, where enteric neuropathy may be suspected. Studies of the enteric nervous system and microscopic details of enteric neuropathy have often been performed and described in the myenteric plexa, using full-thickness intestinal biopsy and immunostaining. Since full-thicknes biopsy demands surgery or other advanced methods (Ohlsson et al 2017), and immunostaining is rather time-consuming, diagnosing of enteric neuropathy is often not performed. This leaves the patient without any diagnosis and explanation to the symptoms, and thereby without specific treatment.

Aims and Methods: The aim of the present study was to examine if pathologic changes are present also in the submucosal plexa, and whether these changes could be identified with conventional hematoxylin & eosin (HE) staining. In 20 deceased cases of Parkinson’s disease Parkinsonism with gastrointestinal symptoms the intestinal tract was investigated for potential neuroganglionic disease.

Results: In 15 of these cases of Parkinson’s disease, there were atrophic/pycnotic nerve plexus cells, i.e. signs of ganglionic degeneration in the submucosal and/or myenteric plexa, mostly in both. In some of the cases, the degenerative signs were mild, however corroborated by findings of positive alpha-syuclein immunostaining. In the remaining 5 cases, there was no marked morphologic signs of degeneration in the HE staining, but immunostaining revealed minimal alpha-synuclein deposits in 3 of these cases. None of the controls showed any signs of ganglionic degeneration.

Conclusion: It seems possible to identify a morphologic intestinal disease substrate in individuals with Parkinson’s disease, showing signs of ganglion cell pycnosis and degeneration, visible in both submucosal and myenteric plexa. This finding may serve to indicate a potential of diagnosing a dysfunction in the autonomic nervous system by conventional histopathological methods, which could be the target of a therapeutic approach. Pathologic changes also in the more easily available submucosal plexa which can be reached endoscopically, and not only in the deeper myenteric plexa, facilitate the diagnosing. These histopathologic findings have to be examined along with assessment of long-term gastrointestinal symptoms and autonomic dysfunction, not only in Parkinson’s disease, but also in patients with idiopathic symptoms and dysfunction.

Disclosure: Nothing to disclose

Reference
P1696 MANAGING GASTROINTESTINAL MANIFESTATIONS IN PATIENTS WITH POSTURAL TACHYCARDIA SYNDROME – A UK DISTRICT GENERAL HOSPITAL EXPERIENCE

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Introduction: Postural tachycardia syndrome (POTS) is a heterogeneous clinical syndrome characterised by a rapid increase in heart rate (> 30 bpm) that occurs within 10 minutes upon standing in the absence of orthostatic hypotension and other medical conditions. Gastrointestinal (GI) symptoms are common in patients with POTS and impact on their quality of life. Our objective is to evaluate common GI symptoms, diagnostic work up, final diagnosis and management strategy in POTS.

Aims and Methods: We reviewed the complete medical records of all patients (aged 16 years and older) referred to a District General Hospital Gastroenterology Clinic over a four year period (2014-2017) with GI symptoms and known or suspected POTS. Patients without confirmed POTS were excluded.

Results: A total of 85 patients were included, with a mean age of 28.4 years, 92.9% were female. Constipation, bloating and abdominal pain were the most common GI symptoms in POTS. Gastrointestinal endoscopy, high-resolution manometry, gastric emptying studies and colonic transit studies were most commonly performed investigations. Among 85 patients, 59 (69%) had confirmed or suspected GI dysmotility. Twenty-four patients (28%) had delayed colonic transit studies.

Conclusion: Non-functional GI symptoms prevalence is high among POTS patients therefore careful evaluation is required to provide an adequate diagnosis. The majority of patients with POTS and GI symptoms have a functional disturbance and reduced GI motility, however a small proportion have organic disease. Delayed colonic transit evaluation. Dietary modifications and laxatives are the main treatments. Novel laxatives such as prucalopride and linacotide are effective in managing dysmotility symptoms in patient with POTS.

Disclosure: Nothing to disclose

P1697 COLONIC-TRANSIT TIME AS PREDICTOR OF OUTCOME OF COLONIC MANOMETRY IN PATIENTS WITH CHRONIC CONSTIPATION

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Introduction: Chronic constipation is categorized into normal- (NTC) and slow-transit constipation. Therefore, patients not responding to therapy are often referred to tertiary centers in order to evaluate colonic transit time (CTT) and colonic manometry (CM). Colonic manometry (CM) is of additive value in the diagnostic workup of colonic motility, however, CM is an invasive, demanding procedure and is not readily available in all centers. Colonic transit time (CTT) as measured by solid-state pressure sensors is a less invasive procedure but it is claimed with some studies that colonic motor disturbances occur in both normal- and slow-transit and therefore, the relationship between colonic motor disturbances on CM and colonic transit time remains unclear.

Aims and Methods: The aim of this study was to assess the predictive value of CTT for colonic motor abnormalities on 24-hours colonic manometry in patients with chronic constipation in order to evaluate whether CTT studies might be helpful in identifying for which patients CM is indicated. Prospectively collected data from patients undergoing both a CTT study as well as 24-hours ambulatory CM in our tertiary referral center were reviewed. Healthy volunteers were studied to obtain control values. CTT was measured using radio-opaque markers (X ray at day 4 after ingestion of 20 markers at day 0). A cather with 6 solid-state pressure sensors was positioned endoscopically and clipped to the mucosa in the right colon in order to perform 24-hours ambulatory CM. CM was defined as abnormal when less than three high-amplitude propagating contractions (HAPCs), propagating waves with amplitude ≥80mmHg over at least three sensors, were identified. Results are shown as mean ± SD and proportions and were compared using independent-samples T-test and chi square statistics.

Results: Data of 88 patients (77 women; 42.9 ± 13.8 years) and 12 healthy controls (10 women; 47 ± 14.4 years) were explored. Slow colonic transit (SCT) was based on CTT. Mean number of HAPCs per 24 hours was significantly lower in patients showing SCT compared to patients with normal colonic transit and controls (1.9 ± 2.2 vs. 4.8 ± 1.6 and 5.3 ± 3.0, p < 0.001 and p < 0.001 respectively). In total, 70 patients (SCT) showed SCT, 24 healthy and 54 colonic CM. All 18 patients with normal colonic transit at CTT had normal CM. Therefore, the positive predictive value (PPV) of CTT for colonic hypomotility was 70% and the negative predictive value (NPV) was 100%. Consistently, studies that in the past have reviewed patients with chronic constipation normal colonic transit, as measured by radio-opaque marker study, excludes abnormal colonic manometry with a NPV of 100% (i.e. based on number of HAPCs), whereas slow transit is a strong indicator for finding motor disturbances on colonic manometry. Therefore, colonic transit studies appears to be helpful in selecting patients with chronic constipation for colonic manometry to further characterize colonic motility.

Disclosure: Nothing to disclose

P1698 GUT DYSBIOSIS IS A PROMINENT FEATURE OF CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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Introduction: Chronic intestinal pseudo-obstruction (CIPO) represents a severe form of chronic gut dysmotility. CIPO patients manifest with recurrent intestinal symptoms causing impaired bowel function and mortality. The intestinal microbiota is an important stimulator and regulator of gut motility. However, it is unknown whether gut microbiota is altered in CIPO and whether it is associated with the clinical presentation.

Aims and Methods: (1) To characterize the gut microbiota of patients with CIPO. 2) To identify demographic or clinical features associated with microbiota profiles. This is a prospective pilot study of CIPO patients and healthy controls at two tertiary centres in Hamilton, Canada and Bologna, Italy. Demographic and clinical data were collected by standardized questionnaires. Fecal microbiota analysis was performed using Illumina 16S rRNA gene sequencing.

Results: Fecal samples from 15 patients with sporadic CIPO (7 female, median age 38.6 years (range 3–53), 4 normal and 7 sigmoid colonic motility (range 39.5–9.2 years) were collected. Mean Body Mass Index was similar between groups (19.6 ± 3.3 vs. 21.7 ± 2.9 kg/m²). A subset of CIPO patients (6/15) were on Total Parenteral Nutrition (TPN). Median age at onset of CIPO was 19 years (range 3–53). Most patients (11/15) had a history of intestinal resection. Overall, the microbiota profiles of CIPO patients were significantly different compared to healthy controls (Adonis test). CIPO patients exhibited marked dysbiosis, with a reduced relative abundance of Firmicutes, and a significant increase in Proteobacteria (Q = 0.004), mainly Escherichia species (Q = 0.003), compared to healthy controls. Bacterial richness (Chao index) and diversity (Shannon index) were significantly reduced in CIPO patients. There were no associations of microbiota profiles with clinical characteristics, as dysbiosis was present regardless of ediology, history of intestinal resection or TPN.

Conclusion: This is the first prospective series aimed at characterizing the intestinal microbiota of sporadic CIPO patients. We demonstrate that gut dysbiosis is a prominent feature of CIPO and is present regardless of clinical characteristics. It is important primarily in a qualitative discussion of the potential benefits and expense of Firmicutes. This provides a rationale for the evaluation of microbiota-based therapies for patients with CIPO.

Disclosure: Nothing to disclose

P1699 SYSTEMATIC REVIEW AND META-ANALYSIS: PREVALENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN IRRITABLE BOWEL SYNDROME

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Introduction: Small intestinal bacterial overgrowth (SIBO), with excessive and/or abnormal type of bacteria in the small bowel may play a role for the manifestation of irritable bowel syndrome (IBS). We aimed to compare the prevalence of small intestinal bacterial overgrowth (SIBO) in patients with IBS and controls.

Aims and Methods: Using the search terms ‘small intestinal bacterial overgrowth (SIBO)’ and ‘Irritable Bowel Syndrome (IBS)’ or ‘small intestinal bacterial overgrowth (SIBO)’ and ‘Functional gastrointestinal disorders (FGIDs)’, 21 case-control studies that met inclusion criteria were identified when searching relevant databases. Prevalence rates for SIBO, relevant demographic and geographic data, and information on the diagnostic modalities were extracted and prevalence rates (SIBO%) and 95% confidence intervals (95%CI) of SIBO in IBS and controls calculated. In addition, the influence of the diagnostic modality (breath tests, aspirate or biopsy and culture or both) was determined.

Results: The final dataset contained 21 independent studies that recruited 2,422 adult patients with IBS and 2,879 controls. Sixteen studies employed breath tests (five utilized glucose breath tests (GBT), seven utilized lactulose breath tests (LBT), two utilized xylose breath tests and one each utilized sucrose and fructose breath tests) and five studies utilized culture methods. Across all testing methods, the prevalence of SIBO in patients with IBS compared with controls was increased with an OR = 3.29 (95% CI 1.91–5.67), p < 0.001. In patients with IBS prevalence of SIBO was 37.04% (95% CI 35.11–38.96) as compared to 19.26% (95% CI 21.01–24.07) in controls. When the method of detection was
Introduction: Diabetic enteropathy is one of the complications of diabetes. Symptoms such as chronic constipation, diarrhea or incontinence are important factors among young adults. Various studies have demonstrated that use of probiotics can reduce the overall symptom of IBS, thus our aim was to evaluate the efficacy of probiotics products in the reduction of IBS symptoms after colonoscopy.

Aims and Methods: Our patients were divided among three groups, including immediate probiotic users (21F, 12M, 32.97±10.79 years old), start use of probiotics one month after colonoscopy (19F, 13M, 30.94±8.52 years old), and placebo group (22F, 12M, 35.15±11.20 years old). All the patients were evaluated by presenting IBS symptoms (stoopidity and frequency, gas, abdominal pain, and flatulence) at baseline, 3rd month of follow up and 6th month of follow up.

Results: The mean reduction in abdominal pain was 3.05±1.21, 3.86±0.94 and 3.63 in the control group, immediate probiotic users and one month after colonoscopy, respectively (P value<0.001). On the other hand, the symptoms of the disease, such as stool consistency, the frequency of defecation and flatulence (except gas) in the first quarter, in the two treatment groups were significantly improved more than in the control group (P value<0.05). In contrast, in the second quarter, stool consistency, abdominal gas and bloating were improved only in the immediate probiotics users compared to the control group (P value<0.05), but the frequency of defecation was not significantly different in the control group receiving the probiotics month after colonoscopy compared to the placebo users (P value>0.05).

Conclusion: According to our results, use of probiotics had the beneficial effect on IBS symptoms. Furthermore, it can be said, however, reductions in symptoms and pain in the two treatment groups were not significantly different, but after six months of treatment, the effect of probiotics in patients who immediately use it after colonoscopy was more visible and more stable.

Disclosure: Nothing to disclose

P1700 THE INFLUENCE OF THE DURATION OF THE DIABETES MELLITUS ON THE ANORECTAL FUNCTION

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Introduction: Anorectal dysfunction is one of the complications of diabetes. Long duration of the diabetes predisposes to different complications including those in the anorectal region.

Aims and Methods: The aim of the study was to evaluate the anorectal function with the use of the high-resolution anorectal manometry depending on the duration of the disease. Diabetic patients group with the disease history ≥10 years (group 1), the group with the disease history <10 years (group 2) and the control group included 35, 15 and 20 subjects, respectively. All patients completed the questionnaire (demographic parameters and clinical data). The anorectal manometry was performed using the high-resolution anorectal manometry depending on the duration of the disease.

Results: The mean pressure (MRP), the maximum anal squeeze pressure (MSP), cough reflex, the push/strain maneuver, rectal sensation test and rectal inspiratory reflex (RAIR). Apart from the above mentioned parameters the following factors were also evaluated: length of the high pressure zone (HPZ), duration of sustain squeeze, anorectal pressure gradient, residual anal pressure (CR), rectal pressure during the push maneuver and the rectal compliance. Moreover, other parameters were calculated: MRP/MSP, MRP/CR (CR-residual anal pressure). Data are presented as mean±SD.

Conclusion: All diabetic patients with the symptoms of enteropathy had weakened function of external and internal anal sphincters. All diabetic patients had lower volumes of RAIR first time detection (-5.52±29.56, 1.69±0.56) than the control subjects (52.50±14.10 mmHg p<0.01; p=0.04 respectively). MRP was statistically significantly more often absent in the group of diabetic patients with incontinence, p<0.03. Diabetic patients with incontinence and diabetic patients with chronic diarrhea had lower volumes of RAIR first time detection (-5.52±29.56, 1.69±0.56) than the control subjects (52.50±14.10 mmHg p<0.01; p=0.04 respectively).

Disclosure: Nothing to disclose

P1702 THE EFFECT OF PROBIOTIC ADMINISTRATION IMMEDIATELY AND ONE MONTH AFTER COLONOSCOPY IN DIARRHEA-PREDOMINANT IBS PATIENTS

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Introduction: Irritable bowel syndrome (IBS) is one of the most common disorders among young adults. Various studies have demonstrated that use of probiotics can reduce the overall symptom of IBS, thus our aim was to evaluate the efficacy of probiotics products in the reduction of IBS symptoms after colonoscopy.

Aims and Methods: Our patients were divided among three groups, including immediate probiotic users (21F, 12M, 32.97±10.79 years old), start use of probiotics one month after colonoscopy (19F, 13M, 30.94±8.52 years old), and placebo group (22F, 12M, 35.15±11.20 years old). All the patients were evaluated by presenting IBS symptoms (stoopidity and frequency, gas, abdominal pain, and flatulence) at baseline, 3rd month of follow up and 6th month of follow up.

Results: The mean reduction in abdominal pain was 3.05±1.21, 3.86±0.94 and 3.63 in the control group, immediate probiotic users and one month after colonoscopy, respectively (P value<0.001). On the other hand, the symptoms of the disease, such as stool consistency, the frequency of defecation and flatulence (except gas) in the first quarter, in the two treatment groups were significantly improved more than in the control group (P value<0.05). In contrast, in the second quarter, stool consistency, abdominal gas and bloating were improved only in the immediate probiotics users compared to the control group (P value<0.05), but the frequency of defecation was not significantly different in the control group receiving the probiotics month after colonoscopy compared to the placebo users (P value>0.05).

Conclusion: According to our results, use of probiotics had the beneficial effect on IBS symptoms. Furthermore, it can be said, however, reductions in symptoms and pain in the two treatment groups were not significantly different, but after six months of treatment, the effect of probiotics in patients who immediately use it after colonoscopy was more visible and more stable.

Disclosure: Nothing to disclose

P1701 EVALUATION OF ANORECTAL FUNCTION IN DIABETES MELLITUS PATIENTS WITH DIABETIC ENTEROPATHY

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Introduction: Diabetic enteropathy is one of the complications of diabetes. Symptoms such as chronic constipation, diarrhea or incontinence are important but often underestimated issues in interdisciplinary medical care.
P1703 A SMARTPHONE APPLICATION FOR SYMPTOM ASSESSMENT AND DATA COLLECTION IN MEDICAL TRIALS: EXAMPLE FROM AN IBS DRUG INTERVENTION TRIAL

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Introduction: Patient-reported outcome measures (PROMs) are crucial to assess the efficacy of therapeutic interventions, especially for disorders such as Irritable Bowel Syndrome (IBS), without a well-defined organic substrate and lack of validated biomarkers. The reliability of paper diaries is often affected by recall bias and fake compliance. To overcome this issue, electronic data diaries have been developed and implemented in recent years. However, little has been reported on the compliance rates of these diaries so far, and when available, the rates vary widely between studies.

Aims and Methods: Our aims were 1) to determine the compliance rate to a smartphone application in a randomised placebo-controlled trial (RCT) and 2) to identify sociodemographic and clinical patient characteristics associated with compliance rate.

The PERSUADE study (peppermint oil versus placebo) uses a smartphone application for patients to register their daily symptoms. IBS patients (ROME IV) were instructed to fill out this digital diary during a 8-week treatment period. In addition, patients were asked to complete electronic questionnaires (via email, not smartphone), regarding demographics and lifestyle, symptom severity (IBS-SSS), Quality of Life (IBS-QoL), and anxiety and depression (GAD-7, PHQ-9). Compliance rate was defined as the percentage of days completed in the diary. RESULTS: 154 patients (mean age 33.8 years) had been included so far. The mean compliance rate was high (86.6%, 10.5 SD). No association was found between age, gender, educational level, and compliance. Interestingly, the number of adverse events was positively associated with compliance (B 0.01, p = 0.04), whereas anxiety was inversely associated with compliance (B -0.05, p = 0.01). Moreover, overall compliance declined over time (F(5, 88.6) = 6.07, p < 0.00).

Conclusion: This study demonstrates that compliance to this smartphone application is, on average, more than 80%. However, the compliance rate decreased over time, which might suggest that this method is less suitable to measure treatment efficacy over longer periods of time.

Disclosure: The PERSUADE trial in part funded by WilPharma.

P1704 ADHERENCE TO DIET LOW IN FERMENTABLE CARBOHYDRATES AND TRADITIONAL DIET FOR IRRITABLE BOWEL SYNDROME: WHAT ARE THE CHALLENGES AND OPPORTUNITIES?

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Introduction: Dietary interventions in irritable bowel syndrome (IBS) include a diet low in fermentable oligo-, di-, mono-saccharides and polyols (FODMAPs) and a traditional IBS diet, which focuses on eating habits more than dietary composition.

Aims and Methods: We aimed to evaluate how well IBS patients adhere to common dietary guidelines, which specific food groups prove troublesome to reduce, and which dietary shifts predicted a symptom response. This is a post-hoc analysis of a previously published RCT (Böhrl et al Gastroenterology 2015), in which IBS patients (n = 66) were randomised to a 4-week low FODMAP diet or a traditional IBS diet. Participants completed 4-day diet diaries before and near the end of the intervention, and reported symptoms using the IBS symptom severity scale (cut-off for responder status was an improvement by 50 points). We evaluated compliance and general changes to the diet by principal component analysis, and described which specific food groups were reduced, replaced, or retained during the intervention. Discriminant analysis was used to investigate dietary changes predictive of responder status.

Results: Compliance with the low FODMAP guidelines was good and consistent: all patients had a comparable shift in the diet’s principal components. High FODMAP fruits, nuts, and grains were largely replaced by low FODMAP equivalents (97%, 100%, and 54% of baseline consumption, p < 0.001, Table 1). Intake of confectionery and snacks was reduced by 69% (p < 0.001). High FODMAP vegetables were reduced by 88%, but poorly replaced, leading to a 17% loss of total vegetable intake. Total energy intake fell by 25% in the low FODMAP arm (p < 0.001). The traditional IBS diet did not lead to a major shift in the diet’s principal components. Despite the traditional IBS guidelines, there remained high consumption of coffee (73% of baseline consumption), alcohol (98% of baseline), vegetables, onions, and legumes (67%, Table 1). Pizza and carbonated beverages were fully excluded. Total energy intake fell by 11% in the traditional IBS diet arm (p = 0.15). In both diets, responder status was predicted by reduced consumption of alcohol and coffee and increased consumption of water and tea (p = 0.03).

Conclusion: In both the low FODMAP diet and traditional IBS diet, certain food groups were difficult to replace. Close dietary guidance may enhance the efficacy of these diets.

P1705 EFFECTS OF ALCALINE-REDUCED DRINKING WATER ON IRRITABLE BOWEL SYNDROME WITH DIARRHEA: A RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED PILOT STUDY

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Introduction: The purpose of this study was to investigate whether the ingestion of alkaline-reduced water (ARW) is helpful in improving the symptoms of diarrheagenic predominant irritable bowel syndrome (IBS)

Aims and Methods: Twenty-seven patients (male, 25.9%; mean 41.7 years-old) with diarrheagenic predominant IBS were randomly allocated to two groups. For eight weeks, the ARW group (n = 13) ingested at least 2 liters/day of ARW, while the control group (n = 14) ingested placebo water. IBS symptom scores (quality-of-life, abdominal pain/discomfort), stool form and frequency were assessed before and after treatment via questionnaires.

Results: Eight patients (61.5%) in the ARW group and six patients (42.9%) in the control group indicated that their symptoms had improved in more than four out of the eight weeks of treatment (p = 0.449). The IBS quality-of-life score significantly improved from 57.2 to 30.5 in the ARW group; this improvement was significantly greater than the slight improvement from 48.7 to 42.2 observed in the control group (p = 0.029). The abdominal pain score improved from 1.8 to 0.9 in the ARW group, and from 1.8 to 1.1 in the control group, with no significant group difference (p = 0.232).

Conclusion: Drinking ARW for eight weeks improves the quality-of-life in patients with diarrheagenic-predominant IBS.

Disclosure: Nothing to disclose

References

P1706 FOUCUSED EDUCATION ON IBS IS A HELPFUL INTERVENTION TO REDUCE ANXIETY AND IMPROVE SYMPTOMS

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Disclosure: Nothing to disclose

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Introduction: Patient self-management is central to IBS therapy and recom-
mended in most guidelines. Self-help allows better understanding of the condition and promotes patient implementation of evidenced-based diet, lifestyle and beha-
vioural changes that can improve symptoms. However, co-existent anxiety may limit the response to self-help programmes. We report the impact of anxiety and IBS symp-
toms following a dedicated education program.

Aims and Methods: We present preliminary data from a randomised controlled trial of two forms of educational therapy in IBS, live group sessions versus internet-based education. The educational programme involved six consecu-
tive sessions over 10 weeks. Sixty-nine patients (53 f, mean age 34, range 19–69) were invited to participate. All had baseline and post-treatment HAD score and IBS-SSS to assess anxiety/depression and bowel symptoms severity, respectively. Forty-four patients completed online education and 27 the live group sessions.

Results: Forty-one patients completed the educational programme. There were 14 patients with IBS-C, 14 IBS-D and 13 IBS-M. HAD scores at baseline demonstrated 36 patients had anxiety, 12 (29%) borderline and 24 (59%) overly high scores, for depression, seven (17%) with borderline scores and 10 (24%) patients case-level scores. Fifteen (37%) patients had both anxiety and depression. Mean baseline IBS-SSS was 369 (range 160–480). There was no correlation between anxiety and symptom severity scores at baseline (r = 0.17, p = 0.36).

Table 1: IBS subtypes.

<table>
<thead>
<tr>
<th>Age (mean)</th>
<th>Sex (f)</th>
<th>IBS-D</th>
<th>IBS-M</th>
<th>IBS-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>77%</td>
<td>48%</td>
<td>29%</td>
<td>23%</td>
</tr>
</tbody>
</table>

There was an excellent correlation between reduction in anxiety scores and reduc-
tion in IBS-SSS scores (r = 0.23).

Conclusion: Anxiety is highly prevalent in patients with IBS. Education is an
effective means for reducing anxiety and improving symptom severity.

Disclosure: Nothing to disclose.

P1707 INTESTINAL MICROBIOME IN IRRITABLE BOWEL SYNDROME BEFORE AND AFTER GUT-DIRECTED HYPNOTHERAPY

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Introduction: Irritable bowel syndrome (IBS) is a disorder with brain-gut-micro-
biome alterations. Gut-directed hypnotherapy (GHT) has been shown to improve quality of life and symptoms in IBS. This therapy targets psychological coping, central nervous processing and brain-gut interaction. Studies have also demonstrated effects of hypnosis on the intestinal microenvironment, gastric functions as intestinal transit, and the mucosal immune system. So far, no study has examined the effect of GHT on the intestinal microbiome. This study aimed at examining psychological distress, IBS symptoms, and micro-
biotal alterations before and after GHT.

Aims and Methods: 38 IBS patients (Rome-III criteria, mean age 44 years, 27
decimal, 12 alternating-type and 4 constipation-
dominant) were assessed with validated questionnaires in psychological (per-
ceived stress, PSQ; psychological distress, HAADS-D; quality of life, visual ana-
log scale grades) and IBS symptom-related variables (IBS severity, IBS-SSS; single
symptoms, visual analogue scales) and fecal samples were collected before and after 10 weekly sessions of GHT. Fecal samples underwent microbial 16S rRNA analyses (regions V1-2, Illumina MiSeq) via QIIME pipeline.

Results: Significant reductions in psychological distress (7.0 [5.0–10.5] Median
[Q1-Q3] vs. 5.0 [3.0–7.3], p = 0.001) and symptom severity (322 [264–373] vs. 264
[180–335], p = 0.001) and increased quality of life [105 [91–134] vs. 131 [105–193], p = 0.001] were observed after GHT. No differences were observable in microbial alpha diversity before and after GHT (chaol 2591 vs. 2381, p = 0.92).

Conclusion: Reductions in IBS symptoms and psychological burden were ob-
erved after gut-directed hypnotherapy. No systematic alterations were found in intestinal microbiota. Hypnosis seems to act predominantly by central modulation.

Disclosure: Nothing to disclose.

P1708 COLONIC DIVERTICULA: RISK FACTOR FOR COLORECTAL ADENOMAS?

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Introduction: There are conflicting data concerning the association between diver-
ticular disease and colorectal cancer (CRC).

Aims and Methods: The aim of this study was to determine whether colonic
diverticula are associated with colorectal adenomas.

In a case-control, retrospective study, we analysed the colonscopy reports of
complete colonoscopies with the diagnosis of colonic diverticula of all patients
referred for screening colonoscopy between January 2011 and January 2016. As a
case-control, a same number of complete colonoscopies performed for colo-
rectal cancer screening and without the diagnosis of colonic diverticula were
randomly selected in the same period of time. Patients who met any of the fol-
lowing criteria were excluded from study participation: positive fecal occult
blood test, history of previous colorectal surgery, CRC, known colonic polyps or
polypsis syndromes. Advanced adenomas were defined as adenomas ≥10 mm
and/or villous architecture and/or high-grade dysplasia.

Results: A total of 414 patients were included in this study, 207 in each group.
In the group with colonic diverticula, the mean age was 67.2±8.9 years, 52.2%
female (n = 108). In the control group the mean age was 63.3±10.6 years, 48.8%
female (n = 101). One or more adenomas were detected in 30.4% (n = 63) of the patients in the colonic diverticula group and 26.1% (n = 54) in the
control group (p = 0.326). One or more advanced adenomas were detected in
10.6% (n = 22) of the patients in the colonic diverticula group and in 6.8% (n
= 14) in the control group (p = 0.293). One or more adenomas were found ex-
clusively in a proximal location in 10.6% (n = 22) of patients in the colonic diverticula
and in 7.7% (n = 16) in the control group (p = 0.689). One or more adenomas were found exclusively in a distal location in 15.9% (n = 33) of the
patients in the colonic diverticula group and 11.6% (n = 24) in the control
(p = 0.572).

Conclusion: No significant association was found in this series between colonic
diverticula and colorectal adenomas or advanced adenomas. There was no asso-
ciation between colonic diverticula and proximal or distal adenomas.

Disclosure: Nothing to disclose.

P1709 ASSOCIATION BETWEEN COLONIC DIVERTICULA AND THE DETECTION OF ADENOMAS AND SERRATED POLYP

SUBTYPES DURING SCREENING COLONSCOPY IN INDIVIDUALS WITH AN AVERAGE RISK FOR COLORECTAL CANCER

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Introduction: Colonic diverticular disease is one of the most frequently diagnosed
diseases of the lower gastrointestinal tract and includes a broad spectrum of
disease manifestations ranging from asymptomatic diverticula to diverticulitis
with associated complications like abscess formation and perforation. Studies
investigating the association between colonic diverticula and colorectal polyps
and cancer (CRC) have reported conflicting results.

Aims and Methods: We aimed to evaluate the association for all relevant dif

histological polyp subtypes, i.e. hyperplastic polyps (HPs), sessile and tradition-
ally serrated adenomas (SSAs and TSAs, respectively), clinically relevant serrated
polyps (cSPs), non-advanced and advanced adenomas, in an exclusive colono-
scopy screening cohort. We conducted a retrospective analysis of individuals ≥50
years with average risk for CRC who underwent a screening colonoscopy between
01/01/2012 and 14/12/2016 at a tertiary academic hospital and 6 com-

munity-based private practices. Exclusion criteria were conditions with increased
risk for CRC (e.g. chronic inflammatory bowel disease, history of CRC, heredi-
tary cancer syndromes), previous colonoscopy at the same institution, and
incomplete procedures.

Results: 4916 colonoscopies were included (mean age 63.4±7.6 years, 48.6%
men). Individuals with diverticula were significantly older (65.6±8.0 years vs.
62.0±7.0 years, p = 0.001), whereas there was no gender difference (40.2% vs.
37.2%, p = 0.003). Detection rates of HPs and non advanced adenomas were
significantly higher in patients with diverticula (19.4% vs. 15.8%, p = 0.001,
12.5% vs. 7.4%, p = 0.003, respectively). No differences were found with respect to
detection rates of SSA, TSA and cSP. Corresponding odds ratios (OR) were 1.340
(95% CI 1.133-1.584, p = 0.001) for the detection of HPs overall and 1.459
(95% CI 1.280-1.763, p = 0.001) in the distal colon as well as 1.355
(95% CI 1.144-1.604, p = 0.001) for non advanced adenomas in the distal colon.
The mean numbers of different histological polyp subtypes per person with at
least one of the histological polyp subtype detected were not different in the
presence or absence of diverticula.

Conclusion: Hyperplastic polyps and non-advanced adenomas, but not advanced
polypoid lesions were detected more frequently in the presence of colonic diver-
ticula during screening colonoscopies of individuals with an average risk for
The aim of the study was to reveal associations between the primary relaxant neurotransmitters of the intestinal musculature and a receptor activity-modifying protein 1 (RAMP1) resulting in a further playing a significant role in the non-adrenergic non-cholinergic regulation of Calcitonin gene-related peptide (CGRP) is a potent smooth muscle relaxant in the ENS which then interact to intricate peristaltic movements, initiating local wall of the GI tract. More than 30 neurotransmitters have been identified nervous system (ENS) [2]. The ENS is an integrative network located along incomplete evaluations (due to poor intestinal cleansing, exam suspension for all reasons, and ecum intubation failure) were excluded from the analysis.

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Introduction: Colonic diverticular disease (DD) ranges among the most common benign disorders of the gastrointestinal tract (GI). Despite its ever-growing burden on the national health systems, high prevalence and complicated clinical management, over the years DD has drawn relatively little research effort and has remained to be named the “neglected disease”[1]. The etiology of DD is known to involve structural remodeling of the enteric nervous system (ENS) [2]. The ENS is an integrative network located along the wall of the GI tract. More than 30 neurotransmitters have been identified in the ENS which then interact to intrinsic peristaltic movements, initiating local reflexes to regulate motility and secretion [3]. Calcitonin gene-related peptide (CGRP) is a potent smooth muscle relaxant playing a significant role in the non-adrenergic non-cholinergic regulation of the GI tract. CGRP acts through a heteroreceptor composed of a G-protein coupled receptor called calcitonin receptor-like receptor (CRLR) and a receptor activity-modifying protein 1 (RAMP1) [4] resulting in a further activation ofvasoactive intestinal peptide (VIP) and nitric oxide (NO) – two of the primary relaxant neurotransmitters of the intestinal musculature [5].

Aims and Methods: The aim of the study was to reveal associations between CGRP and vergic and nitriergic neurons within myenteric (MP), inner (ISP) or outer (OSP) submucosal plexuses of the ENS, suggesting an altered relaxa- tion mechanism for DD. Control (n=10, age: 50-75 years) and asymptomatic DD (ADD) (n=10, age: 57–76 years) sigmoid samples were obtained from patients undergoing surgery for non-obstructing colorectal carcinoma if colonic diverticula were present and patient had no previous anamnestic DD associated symptoms. Symptomatic DD (SDD) samples (n=10, age: 39–80 years) were obtained from patients who underwent sigmoid resecion or left hemicolectomy after recurrent attacks of diverticulitis. Double immunohistochemical staining for NO synthase 1 (NOS1) or VIP and CGRP or its receptors – calcitonin receptor-like receptor (CRLR) and receptor activity modifying protein 1 (RAMP1) – was performed on full-thickness sections of sigmoid colon and analysed with quantitative fluores- cence microscopy.

Results: According to our data, along the wall of the sigmoid colon NOS1 and VIP positive neurons were found to be distributed unevenly – NOS1 positive neurons were mainly located within the myenteric plexus, while VIP positive neurons predominantly situated submucosal plexuses. Both NOS1 as well as VIP positive neurons were found expressing a significant amount of CRLR and RAMP1, demonstrating a close association with CGRP positive fibers and sus- ceptibility to CGRP activation.

Quantitative fluorescence intensity revealed decreased CGRP levels within the enteric ganglia of the sigmoid colon of DD patients. In the MP, as well as in the ISP, the amount of CGRP decreased by 51.7% (p<0.0001) and 52.4% (p<0.0001), respectively. In the OSP, the decrease was less expressed and reached 27.3% (p=0.04).

CRLR levels were increased within the enteric ganglia of SDD patients. Compared to CGRP, this reflected an opposite trend between the experimental groups. The greatest increase of 41.3% (p<0.0001) was found in the OSP, whilst the OSP, the decrease was less expressed and received 22.7% (p=0.022), respectively.

Conclusion: In conclusion, CGRP has all the necessary components for direct activation of nitriergic and vergic neurons within both enteric plexuses and this disturbance in neuronal activation may cause the disturbed myorelaxation in DD.

Disclosure: Nothing to disclose

References
Primary outcome of the study is the reduction of abdominal pain and inflammatory markers (C-ICP) in the group treated with L. Reuteri 4569 supplementation compared to placebo.

Secondary outcome is the comparison of the days of hospitalization between the two groups.

Aim and Methods: A double-blind, placebo RCT was conducted in 88 (34M:54F mean age 61.9 ± 13.9 years) consecutive patients who came to the Emergency Department of Foundation Policlinico A. Gemelli Hospital with a diagnosis of AUD. All patients performed routine blood test, dosage of C – reactive protein values and they were randomly assigned to the two groups.

- Group A (44 patients, 26F), treated with ciprofloxacin 400mg twice a day and metronidazole 500mg three times a day for one week, with a supplementation of L. Reuteri 4569 twice a day for 10 days.

- Group B (44 patients, 26F), treated with ciprofloxacin 400mg twice a day and metronidazole 500mg three times a day for one week plus placebo twice a day for 10 days.

All patients filled a daily Visual Analog Scale (VAS) for abdominal pain, with a range value from 0 (asymptomatic) to 10, and C-ICP value was determined at admission and at discharge.

Results: All patients completed the study. No side effect were observed. According to the VAS values: between day 1 and 3, group A decreased 4.5 points of VAS scale, group B decreased 2.36 points of VAS scale (p < 0.0001); between day 1 and 5 group A decreased 6.6 points of VAS scale, group B decreased 4.4 points of VAS scale (p < 0.0001); between day 1 and 7 group A decreased 7.6 points of VAS scale, group B decreased 5.6 points of VAS scale (p < 0.0001); between day 1 and 10 group A decreased 8.1 points of VAS scale, group B decreased 6.7 points of VAS scale (p < 0.0001).

Regarding C-ICP value, the difference between the admittance value and the discharge value was 45.3 mg/l for group A and 27.49 mg/l for group B (p < 0.0001).

Finally, group A has a mean of 4 days of hospitalization, meanwhile group B has a mean of 4.7 days of hospitalization (p < 0.0001).

Conclusion: This study has clearly showed that the supplementation with L. Reuteri 4569 in the standard AUD therapy, significantly reduce abdominal pain and inflammatory markers compared to placebo group, conducting also to a shorter hospitalization period, thus influencing also with an economical factor.

Disclosure: Nothing to disclose.

P1714 EVALUATING GASTROINTESTINAL MORPHOLOGY AND ENTERIC NERVOUS SYSTEM VIABILITY IN THE DYSTROPHY MUSCULORUM MOUSE MODEL OF HEREDITARY SENSORY AND AUTONOMIC NEUROPATHY TYPE VI

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Introduction: Hereditary sensory and autonomic neuropathy type VI (HSAN-VI) is a newly identified neuronal disorder caused by mutations in the human dystonin gene (DST). Patients may present with joint contractures, problems with eating and breathing, motor deficits, as well as gastrointestinal symptoms such as chronic diarrhoea, and abdominal pain. Similarly, a mouse mutant known as dystonia musculorum (Dyr) also arises due to mutations in the dystonin gene. In our studies, we have also come to recognize certain gastrointestinal pathologies present within this mouse model. At a level of gross morphology, we have observed discolouration of the gastrointestinal tract, as well as an accumulation of gas, which often causes distension of the ileum, cecum, and colon.

Aims and Methods: As HSAN-VI and Dyr mice are primarily sensory neuron disorders, we hypothesize that the underlying cause for these gastrointestinal defects is due to impairments in the enteric nervous system. Here we aim to assess gut motility by hematocytometry, evaluating the myenteric and submucosal plexuses by wholemount immunofluorescence staining, and assess function by GastroSense 750 tracking via in vivo imaging system.

Results: In late stage Dyr mice (postnatal day 15) we observed small but significant reductions in ileum villi width and crypt length, as well as decreased smooth muscle wall thickness at all levels of the gastrointestinal tract. Despite the reduced muscle size, motility as assessed by tracing of the fluorescent GastroSense 750 marker appears to be normal in Dyr mice. Investigation of the enteric nervous system also revealed no differences in markers for cell death, determined by cleaved caspase 3, Fluorodec C, and TUNEL staining, though total number of neurones per ganglia still remains to be characterized.

Conclusion: Thus far we have observed no major changes to the enteric nervous system of Dyr mice. Although we have determined that dystonin ISH was expressed in the enteric nervous system, their role my not be as critical to neuronal survival as in dorsal root sensory neurones. It may also be that autonomic dysfunction (possibly by the vagus nerve) could be responsible for observed gastrointestinal defects. Investigation into higher neuronal circuits centres inputting onto the gut will be performed in future work.

Disclosure: Nothing to disclose.

P1715 GASTROINTESTINAL BLEEDING AFTER LEFT VENTRICULAR ASSIST DEVICE IMPLANTATION IS ASSOCIATED WITH A SHIFT TOWARD A PRO-ANGIOGENIC PHENOTYPE IN THE ANGIOPOIETIN AXIS

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Introduction: Gastrointestinal bleeding (GIB) occurs in approximately 20% of continuous-flow left ventricular assist device (CF-LVAD) recipients after device implantation, predominantly from angioectasias in the upper GI tract or small intestine. While a higher risk of GIB has been observed in CF-LVAD recipients with lower device pulsatility, a mechanism linking changes in hemodynamics to GIB in CF-LVAD recipients that developed GIB after device implantation vs. those who did not.

Aims and Methods: The aims of our study were to:
1. Compare levels of angiopoietin-1 (Ang-1) and angiopoietin-2 (Ang-2) levels, a growth factor that promotes vascular destabilization, suggesting that alterations in the molecular regulation of angiogenesis may play a role in GIB in this population.

Aims and Methods: The aims of our study were to:
1. Compare levels of angiopoietin-1 (Ang-1), a growth factor with vascular protective effects, vascular endothelial growth factor A (VEGF-A), an inducer of angiogenesis, and Ang-2 in (a) CF-LVAD recipients vs. control patients and (b) in CF-LVAD recipients that developed GIB after device implantation vs. those who did not.
2. Assess whether CF-LVAD pulsatility and pulse pressure are correlated with CF-LVAD GIB.

Results: In CF-LVAD recipients as compared to controls, Ang-2 levels were higher (9674 pg/mL vs. 4456 pg/mL, respectively; p = 0.001) and Ang-1 levels were lower (5639 pg/mL vs. 8239 pg/mL, respectively; p = 0.023). There was no
difference in VEGF-A levels between the two groups. In CF-LVAD recipients who developed GIB after device implantation as compared to those who did not, Ang-1 levels were (4021 pg/mL vs. 7258 pg/mL; P = 0.028). Neither levels of Ang-2 nor VEGF-A differed between the two groups. While there was no correlation between CF-LVAD pulsatility index and levels of Ang-2, Ang-1, or VEGF-A, Ang-2 pressure was negatively correlated with levels of Ang-2 (r = -0.578, P = 0.003) and positively correlated with levels of Ang-1 (r = 0.496, P = 0.014). There was no correlation between pulse pressure and VEGF-A.

Conclusion: CF-LVAD recipients in our study demonstrated a shift toward a proangiogenic phenotype in the angiopeptin axis, a main regulatory pathway of angiogenesis, with increased serum levels of Ang-2 and lower serum levels of Ang-1 as compared to controls. Additionally, lower serum levels of Ang-1 was observed in CF-LVAD follow-up CF-LVAD implantation, suggesting a role for alterations in the regulation of angiogenesis in GIB in this population. Lastly, lower pulse pressure was associated with higher Ang-2 levels and lower Ang-1 levels, suggesting a link between the lower pulse pressures that follow CF-LVAD implantation and changes in the regulation of angiogenesis.

Disclosure: Nothing to disclose.

P1717: WHOLE TRANSCRIPTOMIC ANALYSIS IN TURKISH PATIENTS WITH ACHALASIA

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Introduction: Achalasia is an esophageal motor disorder characterized by incomplete relaxation of the lower esophageal sphincter (LES) and by the absence of esophageal peristalsis. Patients typically present with regurgitation, dysphagia, retrosternal pain, and marked weight loss. Exact pathogenesis of the disease still remain to be clarified while it has been known for more than 300 years. However, the most widely accepted hypothesis of the development of achalasia is that a viral infection or some other environmental factors trigger autoimmune response resulting in chronic inflammation that leads to myenteric neuronal loss and neuronal fibrosis in susceptible subjects who may be genetically predisposed. Therefore genetic factors may play an important role in its pathogenesis.

Aims and Methods: The aim of our research was to reveal candidate genes involved in pathogenesis of achalasia. We performed 12 achalasia and 5 intact esophageal resection tissue samples from patients operated on because of achalasia and esophagus cancer respectively. We characterized whole-transcriptome profiles (47,231 gene transcripts) by using Illumina Human HT-12 v4.0 Expression BeadChips. Expression data were analyzed with Genome Studio data analysis software.

Results: We detected that 733 differentially expressed genes, of these, 519 were up-regulated and 214 were down-regulated in achalasia. Pathway analysis by KEGG online tool revealed that up-regulated genes were involved in the pathways of focal adhesion and smooth muscle contraction. Moreover miR-targeted genes expressed in muscle cell, epithelium and lymphocytes were also mostly upregulated. Conclusion: To best of our knowledge, our research is first transcriptomic study in Turkish patients with achalasia. We here firstly identify the candidate genes in pathogenesis of achalasia. However, further analysis is needed to reveal the genetic interactions with each other and other pathways.

Disclosure: This study was supported by grants from Marmara University, Scientific Research Research Projects Committee (Project No:SAG-B-030114-0005)

P1718: ROLE OF HIGHLY Deregulated Micrornas in GastrinTestinal Stromal Tumors

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Introduction: Micrornas are small non-coding RNAs involved in post-transcriptional regulation of gene expression. Deregulated microRNA profiles and their contribution to carcinogenesis have been observed in different types of cancer, making them a promising tools for cancer diagnosis and targeted therapy. However, their involvement in pathogenesis of the most common mesenchymal tumors of gastrointestinal tract – gastrointestinal stromal tumors (GISTs) – is not well defined yet.

Aims and Methods: The aim of this study was to evaluate the role of highly deregulated microRNAs in pathogenesis of gastric GISTs. Investigated microRNAs (hsa-miR-375, hsa-miR-200b-3p, hsa-miR-490-3p) were selected from sequencing and TaqMan Low Density Array validation data from our previous study on microRNA profiling in GIST. Potential targets of selected microRNAs were predicted using TargetScan (Release 7.1) database. Further functional analysis in GIST representing GIST-T1 cell line was performed after transfections of microRNA mimics and mimic negative control using a lipofection approach. Changes in target gene expression were detected using TaqMan primers and probes, protein expression analysis was performed using Western Blot technique. Alterations in cell viability and migration rate were evaluated by MTT and Wound Healing Assays. Statistical analysis was performed using the computing environment R.

Results: Increased amounts of hsa-miR-375 significantly reduced expression of its potential target gene Kit (FC = 0.57, p < 0.05), however KIT protein expression remained unchanged in GIST-T1 cell line. Overexpression of hsa-miR-200b-3p significantly reduced EGF and ETV1 gene expression (FC = 0.7 and FC = 0.57, respectively, p < 0.05) and significantly reduced levels of EGF protein (FC = 0.55, p < 0.05). Analysis of physiological changes of GIST-T1 cells revealed that only hsa-miR-375 significantly reduced both viability and migration rate of GIST-T1 cells, while hsa-miR-200b-3p significantly reduced cell migration rate and showed slight, but not significant impact on cell viability. Hsa-miR-490-3p did not affect expression of its predicted target genes and was not further investigated.

Conclusion: Analysis of highly deregulated microRNAs in GIST-T1 cell line showed that microRNA hsa-miR-375 potentially targets known GIST associated oncogene KIT and therefore affects cell viability and motility. Another microRNA hsa-miR-200b-3p might be involved in GIST pathogenesis by targeting essential genes EGF and ETV1. Therefore, microRNAs hsa-miR-375 and hsa-miR-200b-3p should be further investigated as a potential components of GIST pathogenesis and a promising tools for targeted therapy in GIST.

Disclosure: Nothing to disclose.

P1719: Granulomatous Gastritis: Clinical and Pathological Features

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Introduction: Granulomatous gastritis is an infrequent lesion characterized by the presence of granulomas in the gastric mucosa. Etiopathogenic diagnosis is obtained only by combining morphological examination with clinical and laboratory investigations. The purpose of our study is to evaluate the clinical features and to determine the etiologies of granulomatous gastritis.

Aims and Methods: This is a retrospective study of all cases of granulomatous gastritis noted in the histopathological examination of gastric biopsies, collected between 2012 and 2016 in the department of gastroenterology in the university hospital of Monastir. The clinical, endoscopic, histological characteristics as well
P1720 CHARACTERIZATION OF IMMUNE CELLS INFILTRATING THE CORPUS MUCOSA OF THE STOMACH IN AUTOIMMUNE ATROPHIC GASTROENTERITIS

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Introduction: Autoimmune atrophic gastritis (AAG) is an organ-specific autoimmune disease affecting the corpus-fundus mucosa of the stomach. Little is known regarding the pathogenic mechanisms underlying AAG. Chronic T cell-induced activation of B cells seems to be responsible for the local production of anti-parietal cell autoantibodies, peripheral hallmark of AAG.

Aims and Methods: Aim of our study was to characterize immune cells infiltrating the gastric corpus mucosa of patients with AAG in comparison to control subjects. We isolated lamina propria mononuclear cells (LPMCs) from gastric corpus of six patients with AAG (mean age 58.3 ± 13.5 years, F:M ratio 2.3:1) enrolled as controls. Freshly isolated LPMCs were stained with the following antibodies: CD45, CD3, CD4, CD8, CD19, CD56, CD66b and CD68, then analyzed by flow cytometry in order to identify CD4+ and CD8+ T cells, B cells, natural killer cells, neutrophils and macrophages.

Results: As shown in Table 1, the percentage of gastric B cells was significantly (p < 0.05) higher in patients with AAG (mean 26.7 ± 6.4%) than in those with functionally normal mucosa (mean 9.9 ± 1.7%). Conversely, the frequency of all other immune cell types did not significantly differ between AAG and those with functional dyspepsia (Table 1).

Disclosure: Nothing to disclose.

Disclosure: Nothing to disclose.

Table 1: Frequencies of the main immune cell type subsets in the lamina propria of gastric corpus

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Autoimmune atrophic gastritis (n = 6)</th>
<th>Functional dyspepsia (n = 10)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD45+ LPMCs, mean ± SEM</td>
<td>39.8 ± 7.0%</td>
<td>29.6 ± 2.6%</td>
<td>NS</td>
</tr>
<tr>
<td>CD3+ T cells, mean ± SEM</td>
<td>41.5 ± 10.3%</td>
<td>61.9 ± 8.9%</td>
<td>NS</td>
</tr>
<tr>
<td>CD3+ CD4+ T cells, mean ± SEM</td>
<td>15.2 ± 3.1%</td>
<td>14.8 ± 2.3%</td>
<td>NS</td>
</tr>
<tr>
<td>CD3+ CD8+ T cells, mean ± SEM</td>
<td>43.6 ± 13.2%</td>
<td>48.2 ± 7.6%</td>
<td>NS</td>
</tr>
<tr>
<td>CD19+ B cells, mean ± SEM</td>
<td>26.7 ± 6.4%</td>
<td>9.9 ± 1.7%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CD56+ natural killer cells</td>
<td>2.3 ± 0.9%</td>
<td>4.5 ± 1.5%</td>
<td>NS</td>
</tr>
<tr>
<td>mean ± SEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD66b+ neutrophils, mean ± SEM</td>
<td>7.6 ± 3.1%</td>
<td>11.9 ± 2.8%</td>
<td>NS</td>
</tr>
<tr>
<td>CD68+ macrophages, mean ± SEM</td>
<td>4.3 ± 0.5%</td>
<td>10.2 ± 2.5%</td>
<td>NS</td>
</tr>
</tbody>
</table>

P1721 EVALUATION OF A NEW ASSAY FOR THE QUANTITATIVE DETERMINATION OF CALPROTECTIN IN HUMAN FECES (CALIAGOLD)

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Introduction: The objective of this study is to evaluate the analytical and clinical performances of a new assay for the quantitative determination of calprotectin in human fecal samples. SENTI-FIT 270 analyzer meet the requirements for its use as quantitative determination of calprotectin in human feces. Fecal samples are dissolved in the extraction buffer using the CALiAGold Tube device. The extracts are incubated with reaction buffer and mixed with polystyrene nanoparticles coated with calprotectin-specific antibodies (immunoparticles). Calprotectin in the sample mediates immunoparticles agglutination. Sample turbidity, measured by light absorbance, increases with calprotectin-immunoparticle complex formation and is proportional to the calprotectin concentration. The detected light absorbance allows quantification of calprotectin concentration via interpolation on an established calibration curve.

Results: The Limit of Blank (LOB) (1 saline sample x 20 replicates x 3 runs) was 12.2 ug/g. The Limit of Detection (LOD) (1 sample at 4-fold LOB concentration) was 21.2 pg/g. The LOD (8 dilution levels starting from sample at concentration 100 pg/g x 10 replicates x 1 run) was 21.3 pg/g at LOQ lower than 20. The Intra Assay (3 runs x 3 samples x 20 replicates) gave 6.6% CV at 50.7 pg/g (Level 1), 4.5% CV at 161.4 pg/g (Level 2), and 4.9% CV at 1435.2 pg/g (Level 3). Total imprecision study (44 testing days x 2 runs x 2 observations x 4 level samples – during total time of 66 days) gave 6.7% CV at 59.1 pg/g (Level 1), 3.3% CV at 161.3 pg/g (Level 2), 2.0% CV at 509.9 pg/g (Level 3), and 2.3% CV at 1435.2 pg/g (Level 4). The test was linear up to 2 mg/g, considering the bias versus theoretical concentration lower than ±10% for each dilution point of linearity curve. Reagent on board stability was up to 66 days, retaining bias versus Time 0 (mean value) -4.6% at 60.0 pg/g (Level 1), 0.0% at 161.4 pg/g (Level 2), -0.6% at 509.9 pg/g (Level 3), and -0.2% at 1433.2 pg/g (Level 4). This test (y) was compared with Buhlmann ICAL turb in AbcICL 6000 (x) that uses the same methodology and gave the following results: y = 8.17 + 1.0x; correlation coefficient (r) = 0.979; number of samples = 114. The test is not affected by the presence of conjugated bilirubin, hemoglobin and urea up to 0.5 mg/L, hemolysis up to 12.5%, and lipids up to 1.2 g/L. There is no Hook effect/antigen excess up to 1323.9 pg/g. High concentration samples up to (10000 pg/g) were flagged by the instrument (no false negative results).

Conclusion: Analytical and clinical performances of CALiAGold assay on SENTI-FIT 270 analyzer meet the requirements for its use as quantitative determination of calprotectin in human feces. Specificity and precision make this assay very suitable for routine measurement of this analyte. Disclosure: Nothing to disclose.

Disclosure: Nothing to disclose.

P1722 SUSPICIOUS PATHOGENIC BACTERIA WITH HIGH AFFINITY BINDING WITH IGA IN THE STOMACH

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Introduction: H. pylori may not be the only one that could colonize in the gastric mucosa, and the other potential pathogens may trigger gastric disease except for H. pylori. Hosts select adaptive immunity to immunoglobulin A (IgA).12 IgA binds those bacteria invading into the mucosal epithelium and threatening the host, therefore identifying the IgA-coated bacteria can give an insight into the potential pathogens in the stomach.

Aims and Methods: To investigate the IgA-coated gastric bacteria, gastric juice specimens without bile, blood and other contamination were collected from 12 individuals during endoscopy examination. Six cases were diagnostic with chronic atrophic gastritis and the others were non-atrophic gastritis. We used Flow Cytometer to separate the IgA positive and IgA negative bacteria in gastric juice. Firstly, bacterial flora from the gastric juice were extracted by centrifugation. Then gastric microbiota were stained with FITC-conjugated Goat Anti-Human IgA alpha chain (Abcam) and Goat IgG FITC – isotype control by flow cytometry (BD FACS Aria III). V4 region of 16S rDNA gene sequencing was performed by MiSeq sequencer (Illumina). Species relative abundance in the IgA positive (P group), negative (N group) and the total bacterial flora (T group) was assessed by bioinformatics analysis. IgA-coating index (ICI) was use to assess the affinity of bacteria with IgA.

Results: The proportion of IgA positive bacteria in the gastric juice of atrophic gastritis was higher than that from non-atrophic gastritis juice (33.55% vs. 23.15%), though there was no statistical difference. ICI of Rota hanae and Rothia dentocariosa were as high as 19.2 and 18.2 respectively, while the ICI of H. pylori was about 6.8. And other species with a higher ICI than H. pylori were Streptococcus anginosus (8.6), Streptococcus infantis (7.9), and Prevotella...
P1723 AUTOMMO GASTRITIS: FREE RADICALS PRODUCTION BUT NOT OXIDATIVE STRESS-RELATED GENOMIC DAMAGE

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Introduction: Reactive oxygen Species (ROS) are physiologically produced within the organism but, when their concentration increases, exceeding the physiologic capacity of repair, they induce "oxidative stress", a condition that can be seen in many chronic inflammatory processes and in autoimmune diseases as well. The most relevant damage, hitting genomic DNA, involves the formation of 8-hydroxydeoxyguanosine (8-OHdG), a biomarker identified in gastric carcinogenic processes and gastric cancer.

Aims and Methods: This study, which, in our findings, is the first one to consider the relation between oxidative stress and gastric autoimmune disease, was aimed at investigating the presence, the entity and the characteristics of oxidative stress in autoimmune atrophic gastritis (AAG) compared with multifocal H. pylori related gastritis (MAG) and superficial non atrophic gastritis (SG).

The study included 90 patients sub-grouped in 40 with AIG, 24 with MAG and 26 SG. droms test of the detection of ROS was performed in the serum of 37 AIG and 13 MAG patients and the test levels were subclassified in borderline, mild, moderate, high and very high. The levels of 8-OHdG were investigated by HPLC in gastric biopsies of 40 AIG patients, 24 MAG and 26 SG. The OLGA staging system was used for staging gastric disease. Levels of Pgl, Fgl and gastrin were evaluated in AIG patients. Statistics was performed using Kolmogorov-Smirnov test, i test, chi square and Fisher's exact test. We also performed linear regression, ROC curves, Odds Ratios, sensitivity and specificity tests.

Results: ROMS levels in AIG and MAG were similar, with medium/high levels in 62% and 55.5% of the cases, respectively. 8-OHdG levels were lower in AIG and SG with respect to MAG (mean ± SEM: 17 ± 3, 30 ± 3 and 32 ± 6 adducts/105DG, respectively), with a statistically significant difference overall (p = 0.016), strongly supported by the difference between AIG and MAG (p < 0.01). A trend towards a significant difference (p = 0.06) was found comparing OLGA 1-2 AIG vs OLGA 2-3. Lastly, a cut-off for 8-OHdG between AIG/ SAG and MAG was calculated (AUC 68%; sensitivity 83%, specificity 90%, positive predictive value 82%, negative predictive value 52%), with 93% of AIG and 50% of MAG presenting levels lower than the cut-off. The OR of patients with 8OHdG above the cut-off of having AIG was 0.08 (p = 0.0002).

Conclusion: Both AIG and MAG present high levels of oxidative stress. However, when the genomic oxidative damage is expressed as 8-OHdG, a carcinogenesis biomarker, AIG presents much lower levels of oxidative genomic damage than MAG that, conceptually, could correlate with the lower risk of neoplastic evolution of AIG.

Disclosure: Nothing to disclose

Reference

P1724 THE IMPORTANCE OF ESOSINOGLIA IN PREDICTION OF TREATMENT RESPONSE IN PATIENTS WITH CHOLANGITIS

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Introduction: We aim in this study to compare the effectiveness of esoinophilia in predicting response to cholangitis treatment with C-reactive protein and procalcitonin which are the other inflammatory reagents.

Aims and Methods: Patients who applied to our unit between September 2016 and September 2017 who have cholangitis diagnosis (cholangitis group) and who do not have cholangitis but have undergone ERCP by reason of choledoch stone (control group) were prospectively examined in our study. After having compared both groups in terms of esoinophil counts at time of application, additionally the relationship between esoinophil level and other inflammatory reagents (CRP and Procalcitonin) of the patients in cholangitis group during the period they are hospitalized at time of application was examined.

Cholangitis diagnosis and severity classification have been performed with Toly, Lichtiger (1) and examined in 3 groups according to disease severity. The patients with esoinohil count <100 were considered as esoinophilic.

Results: 62 patients in cholangit group [age average 66.9 ± 1.8 years old; 21 male (%41.2), and 57 patients in the control group [age average 57.3 ± 2.3 years old; 31 female (%57.8)] were examined (For age p < 0.05. For type p < 0.05). The average esoinophil count in the cholangitis group at time of application was 55.7 ± 10.5 103/μL, while this count was significantly higher in the control group (201.8 ± 42.9 103/μL) (p < 0.001). 20% of the patients were Grade-1 (40%), 27 were Grade-2 (17%) and 10 were Grade-3 (17%) according to cholangitis severity. The higher the disease severity, esoinophil levels decrease and any statistical significance was not determined. (respectively 86.4 ± 22.4 103/μL, 0.1 ± 10 103/μL, 2.1 ± 7.6 103/μL; p = 0.19). ERCP process was applied on all patients (median 0 within (0–5) days) and the patients were followed-up for 3.5 ± 0.1 days in average after the ERCP. All patients were discharged with full recovery, esoinophil values tended to increase while CRP and Procalcitonin values tended to decrease to a statistically significant extent beginning from the second day.

ROC curve analysis suggested that the optimal esoinophil level cut-off point for cholangitis was 100.5 103/μL, with sensitivity, specificity, positive and negative predictive value of 87, 65, 72, and 81%, respectively (area under operating characteristic curve 0.877). According to this evaluation, esoinophilia is existing in 87% of the patients with cholangitis and this ratio was determined as 36.8% in the control group when the esoinophilia threshold is taken as 100.5 103/μL (p < 0.001).

CRP upper limit was taken as 5 mg/L and this was taken as 0.15 ng/mL for Procalcitonin in the hospital laboratory where the study was performed. According to this, there was a distinct recovery in the number of patients whose esoinophilia recovered in 1st, 2nd, 3rd day beginning from hospitalization and at time of discharge (last day) (percentage of patients with esoinophilia is respectively 87, 68, 45, 39%) while the ratio of patients whose CRP and Procalcitonin values became negative and recovered was determined lower (1.6% for 1st day, 3.2% for 2nd day, 3.2% for 3rd day, 4.8% at time of discharge for CRP and PCT).

Conclusion: Esoinophilia is an inflammatory reagent that may be used in patients with cholangitis. Its inexpensiveness and applicability everywhere are the most significant advantages.

Disclosure: Nothing to disclose

References

P1725 EFFICACY OF HEMOSPRAY AND ENDOCLOT IN THE TREATMENT OF GASTROINTESTINAL BLEEDING: RESULTS FROM A TERTIARY REFERRAL CENTER

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Introduction: Gastrointestinal (GI) bleeding frequently leads to hospital admission and is associated with relevant morbidity and mortality, particularly in the elderly. Consequently, to the increasing administration of direct oral anticoagulants in the last years and the emerging role of antiplatelet agents treatment of gastrointestinal bleeding may be challenging. Hemostatic powders (HP) represent novel “touch-free” and easy to use items for the management of gastrointestinal bleeding.

Aims and Methods: Our aim was to analyze the short-term (ST-within 72 hours-) and long-term (LT-within 30 days-) success for achieving hemostasis with HP and to directly compare the two agents Hemospray (HS) and Endoclot (EC) in their hemostatic efficacy. Data were prospectively collected on patients who received HS and EC between September 2013 and September 2017 for endoscopic hemostasis in our center. Patients were followed-up for at least one
month after index endoscopy and data analysis was performed after follow-up was complete.

Results: HP was applied in 154 consecutive patients (mean age 67 years) with GI bleeding in our center. Patients were followed up for at least 1 month (mean FU: 3.2 months). The majority of HP applications were in the upper GI tract (89.0%) with the following bleeding sources: peptic ulcer (55%), esophageal varices (7%), tumor bleeding (11.7%), reflux esophagitis (8.7%), diffuse oozing bleeding and erosions (15.3%). Overall ST success with HP was achieved in 125 pts (81.2%) and LT success in 81 patients (67%). Re-bleeding occurred in 26.6% of all patients treated with HP. In 72 patients (47%), HP was applied as a salvage hemostatic therapy, therefore ST and LT success was 93.1% and 64.3%, respectively, with re-bleeding in 31.9% of patients. As a primary hemostatic therapy, ST and LT success were 81.7% and 69.2%, respectively, with re-bleeding occurring in 21.9%. Subgroup analysis showed a ST and LT efficacy for cancer bleeding of 83.3% and 86.7%, for peptic ulcer disease of 81.6% and 56.2% and in patients under therapeutic anticoagulation of 80% and 60.5%. There was no statistical difference in the ST or LT efficacy between EC and HS for the various indications; however, HS was more frequently applied for upper GI bleeding (p = 0.04).

Conclusion: Both HS and EC allow for effective hemostasis with high ST success when applied as primary or salvage therapy. No differences in ST, LT success and re-bleeding between HS and EC were detected.

Disclosure: Nothing to disclose.

P1726 HEMOSPRAY USE IN ACUTE GASTROINTESTINAL BLEEDING- A 4-YEAR SINGLE-CENTRE EXPERIENCE
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Introduction: Upper GI bleeding (UGIB) has a mortality of about 10% in United Kingdom (UK) despite advances in treatment. The current guidelines recommend dual modality of treatment which could include injection of adrenaline, argon photocautery or using endoscopic clips to achieve haemostasis. A recent addition to therapeutic options is Hemospray. Since June 2013, there has been an increase in the use of Hemospray as a mode of treatment for managing an acute gastrointestinal bleed. All relevant clinical data was compiled using electronic records.

Results: 45 consecutive patients (M = 31), with median age 72 years (range 35–91) were included. The mean haemoglobin prior to endoscopy was 92 g/L. 40% were on antiplatelets or anti-coagulants and 32% on platelet or anticoagulant therapy. Of all patients who needed Hemospray, 1 ERCPC and 1 had colomoscopy. The details of diagnosis are in Table 1.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Ulcer</td>
<td>14 (32%)</td>
</tr>
<tr>
<td>Oesophageal/gastric ulcer</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>Malignancy related</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Intestinal bleeding</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Other including unclear cause of bleed</td>
<td>13 (29%)</td>
</tr>
</tbody>
</table>

Disclosure: Nothing to disclose.

P1727 70-DAY MORTALITY OF ADMISSIONS TO INTENSIVE CARE UNIT WITH UPPER GASTROINTESTINAL BLEEDING
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Introduction: Acute upper gastrointestinal bleeding (UGIB) is a common hospital presentation. The incidence of UGIB in New Zealand is reported as 59.2 per 100,000 adults per year (1). The estimated mortality rate ranges between 6% and 10% (2), but can be even higher in patients admitted to the intensive care unit (ICU). There is very little data on what predicts outcomes of patients with UGIB requiring intensive treatment.

Aims and Methods: The aim of this study is to determine the 30-day mortality of UGIB post-ICU admission and potential risk factors that predict an outcome.

Results: A total of 30 patients with UGIB were admitted to ICU. Median age was 61 years (interquartile range 52–72). Bleeding from peptic ulcer was the most common endoscopic diagnosis (70%), followed by oesophageal varices (17%). Overall, 30-day mortality was 83.3% (25/30) of which 78% (24/30) had high Rockall score which was the primary cause of death. Logistic regression revealed high Rockall score and high lactate were significant independent predictive factors for 30-day mortality. On Receiver Operating Characteristic (ROC) analysis, these two variables, when combined, had the greatest accuracy (area under ROC curve 0.94, sensitivity 90%, specificity 90%) for predicting 30-day mortality.

Conclusion: Patients presenting with UGIB requiring intensive treatment have a high mortality rate of 11% at 30 days and, in the majority, this was due directly to gastrointestinal bleeding. High Rockall score and elevated lactate at admission to ICU were the strongest independent predictors of 30-day mortality in patients presenting with UGIB and should be used as prognostic markers to predict an outcome.

Disclosure: Nothing to disclose.

References

P1728 REBLEEDING AND MORTALITY ARE HIGHER IN PATIENTS WITH GASTROINTESTINAL BLEEDING TREATED WITH ANTI-PLATELETS THAN ANTI-ANTICOAGULANTS
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Introduction: Antithrombotic (AT) drugs increase the risk of overt gastrointestinal bleeding but their effects on clinical outcomes are not well established.

Aims and Methods: The aim of this study was to determine the effect of anti-platelet (AP) and anticoagulant (AC) drugs on rebleeding and mortality in patients with gross GIB.

This was a prospective study on all patients admitted to the American University of Beirut Medical Center with melena, hematochezia, hematemesis, or coffee ground emesis between Jan. 2013 and Feb. 2018. The patients' characteristics of Beirut Medical Center with melena, hematochezia, hematemesis, or coffee ground emesis between Jan. 2013 and Feb. 2018. The patients' characteristics and clinical outcomes were compared among the following groups: (a) patients on any one or more antiplatelet (AP) only (aspirin, clopidogrel, ticagrelor, prasugrel, and dipyridamole), (b) patients on any anticoagulant (AC) only (warfarin, heparin, low molecular weight heparins, direct acting oral anticoagulants), (c) patients on combination therapy (AP and AC), and (d) patients on no AT therapy.

Clinical features associated with rebleeding and mortality were assessed using the Chi-square and Student’s t-tests, respectively. Stepwise Cox proportional hazards regression analysis was used to adjust for potentially confounding variables when assessing the association between mortality, rebleeding, and the following: type of AT therapy, age, Charlson Comorbidity Index (CCI), blood transfusion, severe GIB (systolic blood pressure <100 mmHg, >2 units of blood transfused or <2 units drop in Hb), stigmata of recent hemorrhage (SRH), and endoscopic therapy.

Results: Complete follow-up information for a mean of 22 months was available for 447 patients. The clinical characteristics of patients are shown in table 1. Patients on any AT were significantly older and had higher CCI than controls.
**P1729 ENDOSCOPIC RADIOFREQUENCY ABLATION IS AN EFFECTIVE THERAPY IN PATIENTS WITH SYMPTOMATIC ANAEMIA SECONDARY TO GASTRIC ANTRAL VASCULAR ECSTASIA**

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**Introduction:** Gastric antral vascular ectasia (GAVE) is a rare cause of gastrointestinal bleeding (GIB). Patients often require regular blood transfusions and long-term oral or intravenous iron supplementation to manage symptomatic anaemia impacting on quality of life. Endoscopic therapy (ET) for GAVE includes argon plasma coagulation (APC), laser therapy and endoscopic band ligation. In some patients, these measures are not successful with significant effects on their health and quality of life. Radio-frequency ablation (RFA) may provide a solution in these patients.

**Aims and Methods:** A single-centre prospective study to evaluate the efficacy and safety of RFA in patients with GAVE refractory to first line ET. The primary outcome was an increase in haemoglobin (Hb) 3 months after treatment. Secondary outcomes were a reduction in frequency of blood transfusions and/or iron (PO or IV) in the 3 months before and after RFA treatment. Endoscopic surface area (SA) regression of GAVE was analysed by 3 experts estimating % change in SA following treatment by examining images before and after treatment.

**Methods:** Patients who remained anaemic and/or transfusion or iron dependent after other ET were eligible. Other causes of GIB were excluded. Treatment with RFA was with focal RFA at 12J/cm2 with 3 applications to visible areas of GAVE under cone-beam. Patients had up to 2 RFA treatments 6 weeks apart. Data were collected before and after treatment.

**Results:** 20 patients had RFA for refractory GAVE. The median age was 69 years (IQR 62–82) (70% (85%) were female. 13 were previously treated with APC, 4 with laser and 3 with band ligation. In the 3 months prior to treatment, 11/20 were on oral iron, 6/20 were on IV iron. 14/20 required regular blood transfusions prior to treatment, with 11 of these on both iron supplementation and blood transfusions. The median number of RFA treatments was 2 (IQR 1–2). No patients had recorded complications of RFA. The mean pre-treatment Hb was 95.1 g/L (95% CI 87.4–102.6 g/L). The mean Hb at 3 months after final RFA treatment was 112 g/L (95% CI 103.9–120.1 g/L). The mean change in Hb was +12.6 g/L (95% CI 11.7–24.3 g/L) (p < 0.0001) (paired t-test).

Post treatment, only 3/14 (21%) of the patients who required blood transfusions prior to the procedure had ongoing transfusions. Only 3/17 (29%) patients who were previously on iron had ongoing iron needs. The mean surface area reduction when scored by 3 expert endoscopists was 64.2% (95% CI 56.3–72.1).

**Conclusion:** RFA for patients with symptomatic anaemia secondary to GAVE remains a novel treatment therapy for a difficult cause of GIB. This feasibility study shows that this approach can significantly reduce blood transfusion dependence and iron supplementation in some patients with improved Hb after treatments. The required number of treatments is small and it appears safe.

**Disclosure:** Nothing to disclose.
recommendations in 37/83 (45%) patients. Age, gender, treating specialty, major bleeding, use of blood products, Charlson comorbidity index, admission to inten- sive care unit, need for reendoscopy, rebleeding or endoscopic stigmata were not associated with management of APA. Management of ACT was assessed as not following the guideline recommendations in 68/127 (53.5%) patients. After including the use of heparin in therapeutic dosage, number decreased to 61/127 (48%). In univariate analysis, age (66 years, IQR 57–74.75, vs. 73 years, IQR 66– 78, p = 0.005) and treating specialty (internal medicine 61.8% vs. 88.1%, p = 0.003) were significantly associated with inappropriate management of ACT. All other patients received combination therapy.

Conclusion: Management of APA or AC in patients with NVUHG was not according to current ESGE guidelines in a significant number of patients. Efforts need to be made to improve management of these patients as they are at an increased risk for cardiovascular events.

Disclosure: Nothing to disclose

Reference


P1731 COFFEE GROUND VOMIT: DOES IT JUSTIFY AN URGENT ENDOSCOPY?

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Introduction: Coffee ground vomit is vomit that subjectively like coffee grounds. It is thought to occur due to the presence of coagulated blood in the vomitus. Coffee ground vomit is a common indication for patient admission and thereafter endoscopy. In an increasingly stretched inpatient endoscopy service it is important not to overburden it with endoscopies that could be performed safely as an outpatient.

Aims and Methods: Therefore, our aim is to evaluate the need for inpatient gastroscopy in patients who are deemed to have coffee ground vomit. We hypothesize that patients with coffee ground vomiting do not have significant upper gastrointestinal bleeding requiring endoscopic intervention.

A single-center, retrospective analysis was performed on patients endoscopied for the primary indication of coffee ground vomit. Data was collected and scru- tinizied from the Electronic Patient Records (EPR) and Unisoft endoscopy-reporting tool at Barnet and Chase Farm Hospitals, Royal Free London for 12 months of 2017. Gastroscopy reports were studied to see whether endoscopic therapy was required (defined as use of adrenaline injection, banding, clips, haemostasis or gold probe). EPR was subsequently used to assess whether these patients had a significant drop in their haemoglobin (Hb) defined as a Hb drop ≥20 g/dl. Two independent researchers carried this out.

Results: There were 2618 gastroscopies during the study period. Of these, 37 were indicated due to coffee ground vomiting with 29 being performed as an inpatient. Of these 29 patients, 27 (93%) had a significant drop in their Hb level prior to gastroscopy. One (3.4%) patient required endoscopy admission thereafter and further endoscopy. In a single-centred stretched endoscopy service it is important not to overburden it with endoscopies that could be performed safely as an outpatient.

Conclusion: From this study we conclude that the majority of patients endos- coped for coffee ground vomit do not require intervention during endoscopy. This study confirms our hypothesis and adds weight to the notion that patients with coffee ground vomiting do not necessarily require inpatient gastroscopy despite a significant Hb drop. If findings from this study were to be repeated in other centers we may be able to discharge stable patients with coffee ground vomiting to early OPD endoscopy thus reducing length of stay and pressure on already stretched inpatient emergency workload.

Disclosure: Nothing to disclose

P1732 ORAL ANTICOAGULANTS AND UPPER GASTROINTESTINAL BLEEDING: POTENTIAL RISK FACTORS AND OUTCOMES – A SINGLE-CENTRE EXPERIENCE

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Introduction: Acute non-variceal upper gastrointestinal bleeding (UGIB) is a common medical emergency requiring prompt management. Available data sug- gest that use of oral anticoagulants (OAC) is associated with more frequent AUGIB, mostly peptic ulcer-related, and more severe outcomes.

Aims and Methods: To identify patients with AUGIB who use OAC and deter- mine aetiology and outcomes and potential endoscopists' factors for adverse outcomes. Retrospective, prospective analysis of all patients over 18 years of age consecutively admitted for AUGIB in a tertiary centre in Latvia – Riga East Clinical University Hospital from November 2013 to December 2014. Patients were asked to complete a questionnaire regarding their history of OAC use and INR control. Data were collected on bleeding-related interventions, length of hospital stay and outcomes. Bleeding severity on endoscopy was evaluated according to Forrest classification. Data was analysed using SPSS 20.0.

Results: Two hundred thirty-six patients with AUGIB were identified (138 (58%) men and 98 (42%) women, mean age 62 ±7.36 years). Twenty-seven (11.4%) patients used OAC (mean age 73 ±11.3 years), mostly warfarin (n = 22, 82%). Only 5 (18%) of OAC users were on new OAC – dabigatran (n = 3, 11%) and rivaroxaban (n = 2, 7%). Thirty-six percent of OAC users received this therapy for > 2 years, most commonly because of permanent atrial fibrillation. Among OAC users 8 (30%) were on double antiplatectic (OAC-antiplateplet) therapy. The most common diagnoses in patients using OAC were haemorrhagic gastro- intestinal haemorrhage (42.9%), oesophageal ulcer (21.7%) and peptic ulcer disease (PUD, with Forrest IA, IA or IIb bleeding with equal frequency (n = 4, 14%) in each). Despite previously experienced spontaneous haemorrhages (n = 5, 18%) and episodes of severe bleeding, such as gastrointestinal bleeding, epistaxis and post-traumatic bleeding, 8 patients were on OAC, and AUGIB were not regularly controlling INR levels. One hundred eight patients (45.7%) were hospitalized in intensive care unit (ICU), most often with Forrest IIb PUD bleeding – 36 (33.3%). Of those hospitalized in ICU one was using OAC. There was no statistically significant difference in severity of PUD bleeding between OAC users and non-users (t = −0.189, p = 0.004, Pearson Correlation). There was also no statistically significant difference between OAC users and non-users in non-urgent length of ICU stay (p = 0.05, Chi-Square Test) and total length of hospital stay. Transfusion of red blood cells was required in 133 (56.3%) cases, fresh frozen plasma in 106 (44%) cases and cryoprecipitate in 39 (16.5%) cases. Surgery was performed in 37% of patients. Ninety-seven (41%) of all patients died. Ten (4%) patients died, 2 of them (8.3%) were OAC users.

Conclusion: OAC use was not associated with more severe ulcer bleeding, longer hospitalization in ICU or longer total hospital stay. OAC use-related bleeding could be minimised with thorough patient education about risks and regular INR control.

Disclosure: Nothing to disclose

P1733 GASTROINTESTINAL BLEEDING, A SERIOUS COMPLICATION OF PATIENTS WITH ACUTE CORONARY SYNDROME

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Introduction: Gastrointestinal bleeding (GIB) is frequent in patients receiving anti thrombotic treatment. This situation is more delicate in patients with an acute coronary syndrome (ACS). There is no specific recommendation whether anti- platelet medications should be interrupted or not. The aim of this study is to evaluate the clinical outcome and therapeutic features of patients who developed gastrointestinal bleeding while on anti-thrombotic treatment.

Aims and Methods: We retrospectively reviewed the medical files of patients with ACS who were complicated with GIB from January 2012 to December 2017. Clinical, biological and endoscopic findings were collected. Only patients included in the first hundred sixty-five cases were included in our study. There were 68% males and 32% females. The median of age was 52 years. The average time between the ACS onset and GIB was 5 days. All patients had dual antiplatelet therapy (DAPT). Haemorrhage was externalized by hematemesis in 72% of the cases, melaena in 28% and rectal bleeding in 12%. Upper endoscopy showed: erosive gastritis (24%), bulbular ulcer (28%), antral ulcer (16%), esophagitis (20%), erosive duodenitis (2.6%), esophageal ulcer (8%), esophageal varices (2.6%), gastric varices (4%) and portal hypertensive gastropathy (2.6%). Colorectal revealed: diverticulosis coli (20%), appendicitis coli (45%) and colic polyps (35%). DAPT was maintained in all patients because of the high thrombotic risk. Patients had intravenous proton pump inhibitors and endoscopic management (endonasal injection, argon plasma coagulation, vari- ceal banding). Bleeding stopped, the majority (89.1%) of patients (n = 70, 10.7%) patients died after endoscopic haemostasis failure or because of an early recurrence.

Conclusion: GIB is a severe complication that can occur in patients with ACS. Management is based on medical treatment and endoscopic haemostasis.

Disclosure: Nothing to disclose

P1734 ENDOSCOPIC APPLICATION OF HIGHLY MUCO- ADHESIVE POWDER (NEXPOWDER) FOR TREATMENT OF DIFFUSE OR REFRACTORY ACTIVE UPPER GASTROINTESTINAL BLEEDING (UGIB): PRELIMINARY RESULTS

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Clinical presentation and outcome of the patients were evaluated. Descriptive statistical analysis

**Aims and Methods:**

Between October 2014 and January 2018, 5 patients with AEFs were detected by endoscopy. The clinical presentation, comorbidities, endoscopic appearance, management and outcome of the patients were evaluated. The etiology of the AEFs was classified as primary (60%) and secondary (40%). In the treatment of peptic ulcer bleeding, various endoscopic treat-

**Results:**

In 94 patients having gastrointestinal bleeding, primary hemostasis was 88.6% successful, while the rest of the patients required one or more sessions, including 1 therapy combined with coils and surgical shunt after the 4 session failure. In the latter case, the endoscopic finding included active bleeding in 21 cases (19.8%), sticking clot in 11 (10.3%), red dots in 12 (11.3%), platelet plug in 34 (32%), and adherent clot to the base of the ulcer in 2 (1.9%). Therefore, muco-adhesive Nexpowder seems to be a good option in patients with diffuse or refractory UGIB.

**Disclosure:**

Nothing to disclose

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**Reference:**

P1736 EXPERIENCE WITH N-BUTYL-2-CYANOACRYLATE GASTRIC VARIX INJECTION IN AN UNIVERSITY HOSPITAL OF LA PLATA, ARGENTA

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**Introduction:**

Gastric varices are found in 20% of patients with portal hypertension. Their bleeding rates ranges between 55 to 78%, associated to high mortality (45%). According to literature, management with N-butyl-2-cyanoacrylate (NBCA) is a better option between 87% and 100%, while the rebleeding rates ranged between 24% and 50%. Severe complications related to the procedure (sepsis, thromboembolism, fistulas, adherence of the needle to the varix) are rare. Even though prospective studies are lacking, the linear echoendoscopy placement of coils associated to N-Butyl-2-Cyanoacrylate is a promising therapeutic option for the varix obliteration and the achievement of hemostasis. Besides, it enables to use less cyanoacrylate doses and thus decreases the risk of any complications.

**Aims and Methods:**

Retrospective, observational study of 106 patients having gastric varices who were treated in our unit with butyl-cyanoacrylate. A 0.5 ml of N-butyl-2-cyanoacrylate + 0.5 ml of lipiodol solution was used. 21 gauge needle was used. EUS-guided or upper GI endoscopy procedures were performed under sedation with propofol.

**Results:**

106 patients were included, 41 women and 65 men, with a 54 year old average age (16–92 years). Portal hypertension (HTP) causes: cirrhosis HTP (67%), chronic viral cirrhosis HTP (2.8%), and segmentary HTP (2.8%). 49% were Child A, 36.7% Child B, 9.4% Child C, 5 patients were not classified. Esophageal varices were classified as esophagogastric (GOV) or isolated gastric (IGV) in accordance with the classification of Sarin: 17.9% GOV-I, 44.3% GOV-II, 7.6% GOV-1 Y GOV-II, 22.6% IGV-I, 2.8% IGV-I and GOV-II. In 94 patients having gastrointestinal bleeding, primary hemostasis was 88.6% successful, while the rest of the patients required one or more sessions, including 1 therapy combined with coils and surgical shunt after the 4 session failure. In the latter case, the endoscopic finding included active bleeding in 21 cases (19.8%), sticking clot in 11 (10.3%), red dots in 12 (11.3%), platelet plug in 34 (32%), ulcer on varix in 12 (11.3%), tumoral varices in 14 (13.2%). Rebleeding rate during the 6-week follow-up period was 11.3%, they were retreated with N-Butyl-2-cyanoacrylate confirming its usefulness. In our series, the greatest complication of treatment was thrombosis of the splenic vein.

**Conclusion:**

The use of N-butyl-2-cyanoacrylate is a safe and efficient option for gastric varix management. To our knowledge, in accordance with the international literature, the achievements were as follows: primary hemostasis (88.6%); final hemostasis (99%); and rebleeding low risk and complications (1%). In order to obtain good results, it is essential to follow the technical recommendations during the injection procedure.

**Disclosure:**

Nothing to disclose

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**Reference:**

P1737 A RANDOMIZED TRIAL OF MONOPOLAR SOFT-MODE CACOOGULATION VERSUS HEMOCLIP FOR PEPTIC ULTER BLEEDING

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**Introduction:**

In the treatment of peptic ulcer bleeding, various endoscopic treat-

**Results:**

The mean age was 59.6 ± 11.9 years of which 4 (80%) were men. Clinical presentation: Toracalgia-2 (40%), hematemesis-2 (40%), meleina-1 (20%), anemia-2 (40%) and hematemesis-2 (40%). In patients presenting with gastrointestinal hemorrhage, 30% (60%) had no hemodynamic repercussion. The lowest median value of hemoglobin in the first 24 hours was 8 g/dL. Endoscopy: Primary – 3 (60%); secondary – 2 (40%). Actively bleeding moderate gastrointestinal comorbidities and 1 (20%) had esophageal neoplasia. Aniplatelet agents were documented in 3 (60%) and antiproteinase agents in combination with anticoagulants were noted in 2 (20%) patients. Endoscopically, the median distance of the ulcer in the esophagus from the dental and gastric cardia was (7.2±3.2) cm. Active gastrointestinal bleeding was noted in 1 (20%) at the adherent clot to the base of the ulcer in 2 (40%) and an ulcer with evident endoscopic stent mesh visible in the ulcer base in 2 (40%) patients. The AEF were confirmed by computed tomography of the chest in all patients. Mortality was defined as endoscopic stent placement in 4 (20%) esophageal and endovascular stent in 1 (20%) and esophageal stent in 1 (20%) in the patient with esophageal neoplasia. There was a recurrence of bleeding in 3 (60%) patients. Mortality was documented in 4 (80%) patients after a median of 33 (1-112) days. Proton pump infusion therapy was started at the time of diagnosis to all patients and continued until 72 hours after the procedure. Patients were randomized to MHFC and HCl groups. The patients were given 200 mg of MHFC and HCl, were approximately 96% and 78.5%, respectively and we planned a total of 56 patients per group, considering an alpha error of 0.05 and to achieve statistical power of 80%. In patients who do not have adequate hemostasis with the first method, the other method applied. Rebleeding was defined as hemorrhage from the first 7 days after endoscopic hemostasis. Patients with stomach operation history, malignant ulcers, and patients who could not be followed for 7 days after discharge were excluded. Both groups were compared in terms of initial hemostasis.
success, rebleed rate, endoscopic procedure time to achieve hemostasis, and hospitalization time.

**Results:** During the study period, a total of 245 patients were referred to our clinic with hematemesis or melena. Emergency endoscopy was performed within 24 hours after the presentation of 238 patients. According to the study protocol, 193 patients were included in the study. After randomization, the patients were randomized into the MHFSC (n = 56) and HC (n = 56) groups. The mean age was 61.36 ± 19.3 years and 80 (71.4%) were male. There was no statistically significant difference between the two groups in terms of demographic and laboratory parameters, drug use and underlying chronic diseases.

The initial hemostasis was achieved in MHFSC alone in 55 patients (98.2%) and HC group in 45 patients (80.4%) in HC group, higher in MHFSC group (p = 0.004). All 11 patients who were not able to receive the first hemostasis in the HC group were successfully treated with hemostatic forceps. One patient who could not undergo hemostasis with hemostatic forceps was stabilized by medical treatment and hemorrhage was not observed at 24 hour control endoscopy. Rebleeding was detected in ten patients (2 MHFSC, 8 HC). In the MHFSC group, the duration of endoscopic procedure (302 ± 87.8 vs 568 ± 140.4 s, p < 0.0001) and the length of hospital stay were shorter (3,50 ± 1.03 vs 4,37 ± 1.86 days, p = 0.016). None of the patients needed transarterial embolization or emergency surgical treatment.

**Conclusion:** MHFSC method is more effective and safe treatment method than HC and can be applied more rapidly in the endoscopic treatment of peptic ulcer bleeding.

**Disclosure:** Nothing to disclose.

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**P1738 SAFETY AND EFFICACY OF NALDEMIDINE IN THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN CHRONIC NON-CANCER PATIENTS WITH OR WITHOUT INADEQUATE RESPONSE TO LAXATIVES**

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**Introduction:** Opioid-induced constipation (OIC), a common side effect of opioid utilization in treating chronic non-cancer pain, is caused by the action of opioids on peripheral μ-opioid receptors in the enteric nervous system. Naldemedine (NAL), a peripherally acting μ-opioid receptor antagonist (POMORA), has demonstrated consistent efficacy and safety in the treatment of OIC from two phase 3, randomised, placebo-controlled, double-blind clinical trials [NCT01965158 (COMPOSE-1) and NCT01993940 (COMPOSE-2)]. In both studies there were significant improvements in the frequency of Spontaneous Bowel Movements (SBMs) and in the OIC symptoms of incomplete evacuation and abdominal pain in inadequate responders (LIR) as well as non-LIR subjects. A post-hoc analysis from pooling two phase 3, randomised, placebo-controlled, double-blind clinical trials of inadequate responders (LIR) has not been reported.

**Aims and Methods:** To understand the therapeutic effect of naldemedine in LIR relative to PBO as well as non-LIR subjects. A post-hoc analysis from pooling two phase 3, randomised, placebo-controlled, double-blind clinical trials (COMPOSE-1; COMPOSE-2) was performed in the LIR and Non-LIR subgroup. LIR was defined as subjects who were on laxative therapy prior to entering the study and those who stopped its use within 30 days prior to screening, and who signed the informed consent which required the subject to have self-reported OIC (ie, incomplete bowel movement, hard stools, straining, or false alarms). Non-LIR was defined as those subjects who did not receive laxatives or only received rescue laxatives at or after screening. SBM responders, defined as having ≥3 SBMs/week with ≥2 SBMs/week increase over baseline for ≥9 of 12 weeks and ≥3 of the last 4 weeks, were compared between groups. Treatment emergent adverse events (TEAEs) were defined as those that were reported after randomization and were assessed as well.

**Results:** A significantly higher proportion of SBM responders was observed in both the LIR and non-LIR groups for both studies (Table 1). TEAEs were comparable between the NAL and PBO in both LIR and non-LIR groups. The most common TEAEs were gastrointestinal-related.

**Conclusion:** These data demonstrate that NAL is efficacious and well tolerated in the treatment of OIC in those subjects who were LIR or non-LIR. These results suggest that the effect of NAL is independent of previous laxative utilization and is a useful treatment option in the management of OIC in patients with chronic non-cancer pain.

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**P1739 RNA SEQUENCING OF DUODENAL MUCOSA SAMPLES BEFORE AND AFTER FECAL MICROBIOTA TRANSPLANTATION DEMONSTRATES TRANSCRIPTOMIC CHANGES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME-DIARRHEA**

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**Introduction:** The interactions occurring in the gut microenvironment following gut microbiota manipulation are believed to play an important role in the pathophysiology of irritable bowel syndrome (IBS) and yet to be studied. A previous study demonstrated the role of mucosal factors in the pathobiology of IBS by conducting RNA sequencing of colon samples showing transcriptomic changes that affect immune function, cell adhesion and barrier function in IBS-diarrhea (IBS-D) patients [1]. The use of fecal microbiota transplantation (FMT) in IBS-D patients improves their symptoms and manipulates their gut microbiota [2].

**Aims and Methods:** In this study we conducted RNA-sequencing to evaluate disease biology in Formalin-Fixed Paraffin-Embedded (FFPE) tissue samples of duodenal mucosa of the same cohort of IBS-D patients before and after FMT. Twelve IBS-D patients received freshly donated feces from their family members’ donors and were instilled via a gastroscope into the descending part of the duodenum. Biopsy samples were collected before and three weeks after FMT. They were fully characterized with full transcriptome next-generation RNA sequencing (NGS) of duodenal samples, both before and after FMT. Half of the patients had idiopathic constipation (n = 6) and the remaining half had post-infectious (PI) etiology. NGS libraries were prepared with the illumina TruSeq® RNA Access protocol and sequenced on an illumina HiSeq 4000 apparatus [3]. Assembly of reads and alignment was guided by Tophat and Bowtie. Comparative analysis was done using voom/Limma package in R software version 3.4. Quality expression filter for all mRNA species was set at 3 counts per million for at least 50% of the samples evaluated. Differentially expressed genes (DEGs) were considered significant with a p-value cut-off at 0.05 and fold change greater than 1.5.

**Results:** Both subgroups of IBS-D patients showed different characteristics of gene expression following FMT with 85 and 108 DEGs in the idiopathic and post-infectious group, respectively. Table 1 shows the differentially expressed genes following FMT with 85 and 108 DEGs in the idiopathic and post-infectious group, respectively. Table 1 shows the differentially expressed genes following FMT with 85 and 108 DEGs in the idiopathic and post-infectious group, respectively.

**Conclusion:** RNA sequencing appears to be complementary in identifying changes in mucosal mRNA expression of genes of interest. This is the first study to show that RNA sequencing of duodenal mucosa samples demonstrates transcriptomic changes that affect immune function, cell adhesion, ion channels,
cytokines, stem cells and neurotransmitters in patients with irritable bowel syn-
drome-diarrhea following fecal microbiota transplantation.

References

Results: The median concentration of anti-vinculin antibody was 0.12µg/mL (IQR 0.04–0.45), the median number of ICC in inner circular muscle with posi-
tive c-Kit stain was 93 per 2.5mm2 (IQR 54–155), the median number of ICC in myenteric plexus with positive c-Kit was 60 per 2.5mm2 (IQR 32–89), while the number of ICC in inner circular muscle with positive DOG-1 stain was 161 per 2.5mm2 (IQR 25–337), and the number of ICC in myenteric plexus with positive DOG-1 stain was 31 per 2.5mm2 (IQR 7–81). Level of circulating anti-vinculin antibody correlated significantly with density of ICC in myenteric plexus (p = 0.008; Spearman correlation). Increased level of circulating anti-vinculin antibodies were significantly associated with reduced number of ICC in myen-
teric plexus, but not inner circular muscle.

Conclusion: Increased level of circulating anti-vinculin antibody was significantly correlated with decreased density of ICC in myenteric plexus of human stomach, which suggest regulation of ICC expression by anti-vinculin antibody in patients with gastrointestinal dysmotility. Further studies are needed to determine such relationship in functional dyspepsia.

Disclosure: Nothing to disclose

P1740 ASSOCIATION BETWEEN INTERSTITIAL CELLS OF CAJAL AND ANTI-VINCULIN ANTIBODY IN HUMAN STOMACH
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Introduction: Interstitial cells of Cajal (ICC) are known as the pacemaker cells of gastrointestinal tract that regulate gastrointestinal motility. It was reported that small intestinal bacterial overgrowth induce intestinal dysmotility by decreasing ICC through antibody to vinculin, a cytoskeletal protein in gut, and it can be used as a biomarker for irritable bowel syndrome. However, there are no data on relationship between ICC and anti-vinculin antibody in human stomach. Thus, this study aimed to investigate correlation between levels of circulating anti-vinculin antibody and ICC density in inner muscular layer and myenteric plexus of human stomach.

Aims and Methods: Paraffin-embedded gastric specimens from 46 patients (mean age 65.1 years; 21 male, 24 female; 21.7 years; type 2 diabetes mellitus 21.7%), with gastric cancer who received gastric surgery at Kangwon National University Hospital from 2013 to 2017 were used for immunohistochemistry. Each specimen was stained with c-Kit and DOG-1 specific antibodies, then number of positive cells in inner circular muscle, and myenteric plexus were counted. Corresponding patient’s blood samples were used to determine the amount of anti-vinculin anti-
body by enzyme-linked immunosorbent assay (ELISA).

Table 1: Differentially expressed genes common in idiopathic and post-infectious IBS-D patients before and after fecal microbiota transplantation

<table>
<thead>
<tr>
<th>Gene (HGN)</th>
<th>Function</th>
<th>Idiopathic IBS</th>
<th>Post-infectious IBS</th>
<th>log FC</th>
<th>FC A-B</th>
<th>P value</th>
<th>log FC</th>
<th>FC A-B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-C motif chemokine ligand 21 (CCL21)</td>
<td>Cytokine gene involved in immune regulation and chemotaxis</td>
<td>1.30</td>
<td>2.46</td>
<td>0.008</td>
<td>1.79</td>
<td>3.45</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemicentin 2 (HMCN2)</td>
<td>Smooth muscle contraction, cell adhesion and cell migration. Calcium ion binding</td>
<td>0.76</td>
<td>1.70</td>
<td>0.002</td>
<td>0.80</td>
<td>1.75</td>
<td>0.025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostaglandin D2 synthase (PGD2)</td>
<td>Prostaglandin D2 (PGD2) functions as a neuro-modulator and regulates smooth muscle contraction/relaxation</td>
<td>0.73</td>
<td>1.66</td>
<td>0.012</td>
<td>0.67</td>
<td>1.59</td>
<td>0.032</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calponin 1 (CNN1)</td>
<td>Regulation and modulation of smooth muscle contraction</td>
<td>0.68</td>
<td>1.61</td>
<td>0.015</td>
<td>0.98</td>
<td>1.98</td>
<td>0.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytochrome P450 family 2 subfamily family 2 member 8 (CYP2C8)</td>
<td>A cytochrome P450 encoding gene</td>
<td>0.83</td>
<td>1.77</td>
<td>0.009</td>
<td>0.68</td>
<td>1.60</td>
<td>0.024</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musashi RNA binding protein 1 (MASH1)</td>
<td>Musashi RNA binding protein 1 (stem cell progenitor)</td>
<td>0.08</td>
<td>1.06</td>
<td>0.760</td>
<td>0.20</td>
<td>1.15</td>
<td>0.374</td>
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<td></td>
</tr>
<tr>
<td>Neuronal differentiation 1 (NEUROD1)</td>
<td>Neuronal differentiation gene</td>
<td>0.46</td>
<td>1.37</td>
<td>0.108</td>
<td>0.12</td>
<td>1.09</td>
<td>0.696</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chromogranin A (CHGA)</td>
<td>Chromogranin A encoding gene</td>
<td>0.17</td>
<td>1.13</td>
<td>0.289</td>
<td>0.43</td>
<td>1.34</td>
<td>0.069</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solute carrier family 6 member 4 (SLC6A4)</td>
<td>Solute carrier family 6 member 4 (SLC6A4)</td>
<td>0.05</td>
<td>1.04</td>
<td>0.787</td>
<td>0.67</td>
<td>1.59</td>
<td>0.056</td>
<td></td>
<td></td>
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<tr>
<td>Somatostatin (SST)</td>
<td>Somatostatin encoding gene</td>
<td>0.22</td>
<td>1.16</td>
<td>0.220</td>
<td>0.10</td>
<td>1.07</td>
<td>0.511</td>
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</tbody>
</table>

HGNC: Hugo Gene Nomenclature Committee, log FC: logarithmic fold change, FC A-B: Fold change after vs. before.

P1741 OVERALL SAFETY AND TOLERABILITY OF RELAMORELIN IN ADULTS WITH DIABETIC GASTROPAESIS: ANALYSIS OF PHASE 2A AND PHASE 2B TRIAL DATA
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Introduction: Relamorelin (RLM) is a pentapeptide ghrelin receptor agonist with prokinetic effects, shown in Phase 2 trials to accelerate gastric emptying signifi-
cantly and improve symptoms in patients with diabetic gastroparesis (DG). Ghrelin agonists may increase appetite and glycaemia.

Aims and Methods: The aim was to assess overall safety and tolerability of RLM in adults with DG using Phase 2 trial data. Randomised, double-blind, placebo-
controlled Phase 2a and 2b trials (NCT01571297, NCT02357420; results published previously) were conducted in DG patients aged 18–75 years over 4 weeks (RLM 10 mg once or twice daily [BID] or placebo BID) and 12 weeks (RLM 10, 30 or 100 µg or placebo BID) with 2- and 2-week, single-blind placebo run-in periods, respectively. Safety assessments included weight, adverse events (AEs) and laboratory tests, including blood glucose and HbA1c. Analysis of covariance on the change from baseline (CFB) values was used post hoc to assess the effect of treatment on HbA1c and glucose; a test for linear trend was also performed. All other data were summarised descriptively.

Results: Among 204 Phase 2a and 393 Phase 2b patients, mean age was 56 years, 64% were female. 90% had Type 2 diabetes and mean (range) body mass index was 32 (18–60) kg/m². Proportions of patients with ≥1 treatment-emergent AE (TEAE) were generally similar across treatment groups (Table). TEAEs occurring in ≥5% of RLM-treated patients included headache and dizziness in Phase
Abstract No: P1741

Table 1

<table>
<thead>
<tr>
<th>TEAE summary</th>
<th>Phase 2a placebo</th>
<th>Phase 2a relamorelin</th>
<th>Phase 2b placebo</th>
<th>Phase 2b relamorelin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥ 1 TEAE, n (%)</td>
<td>(n = 69)</td>
<td>(n = 67)</td>
<td>(n = 68)</td>
<td>(n = 104)</td>
</tr>
<tr>
<td>10 µg QD PM</td>
<td>30 (45.5)</td>
<td>32 (47.8)</td>
<td>25 (36.8)</td>
<td>49 (47.1)</td>
</tr>
<tr>
<td>10 µg BID</td>
<td>46 (69)</td>
<td>46 (69)</td>
<td>63 (57.8)</td>
<td>45 (54.9)</td>
</tr>
<tr>
<td>Serious TEAEs, n (%)</td>
<td>2 (2.9)</td>
<td>1 (1.5)</td>
<td>4 (5.9)</td>
<td>8 (7.7)</td>
</tr>
<tr>
<td>Patients with ≥ 5% in any treatment group, n (%)</td>
<td>2 (2.9)</td>
<td>5 (7.5)</td>
<td>1 (1.5)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>TEAEs leading to study drug discontinuation, n (%)</td>
<td>30 (43.5)</td>
<td>32 (47.8)</td>
<td>25 (36.8)</td>
<td>49 (47.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (2.9)</td>
<td>1 (1.5)</td>
<td>4 (5.9)</td>
<td>8 (7.7)</td>
</tr>
<tr>
<td>Constipation</td>
<td>4 (5.8)</td>
<td>1 (1.5)</td>
<td>1 (1.5)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2 (2.9)</td>
<td>3 (4.5)</td>
<td>1 (1.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (2.9)</td>
<td>4 (5.9)</td>
<td>1 (1.5)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>4 (5.8)</td>
<td>1 (1.5)</td>
<td>1 (1.5)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Constipation</td>
<td>4 (5.8)</td>
<td>1 (1.5)</td>
<td>1 (1.5)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2 (2.9)</td>
<td>2 (3.0)</td>
<td>5 (7.4)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (2.9)</td>
<td>2 (3.0)</td>
<td>0 (0.0)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>1 (1.4)</td>
<td>1 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Increased blood glucose</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>1 (1.5)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>2 (3.0)</td>
<td>2 (3.0)</td>
<td>5 (7.4)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>4 (5.8)</td>
<td>2 (3.0)</td>
<td>2 (2.9)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Constipation</td>
<td>4 (5.8)</td>
<td>2 (3.0)</td>
<td>2 (2.9)</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>Fasting blood glucose, mmol/L, mean (SD)</td>
<td>0.01 (1.6)</td>
<td>0.20 (1.6)</td>
<td>0.17 (2.0)</td>
<td>0.25 (2.6)</td>
</tr>
<tr>
<td>CBF8</td>
<td>0.07 (2.7)</td>
<td>0.09 (3.0)</td>
<td>0.07 (2.7)</td>
<td>0.46 (2.2)</td>
</tr>
</tbody>
</table>

2a, and hyperglycaemia, urinary tract infection and diarrhoea in Phase 2b. No cardiac TEAEs occurred in ≥2% of any RLM-treated group. In Phase 2b, discontinuations due to TEAEs were higher in RLM-treated patients compared to placebo. Incidence of serious TEAEs was generally similar between treatment groups. No specific serious TEAE was experienced by ≥1 Phase 2a patient. In Phase 2b, impaired gastric emptying was documented in two patients on placebo, one on RLM 30 µg and one on RLM 100 µg, and unstable angina was reported in two patients on RLM 30 µg, all assessed by the investigator as unrelated to study drug. One 100 µg RLM-treated Phase 2b patient died from urosepsis, unrelated to study drug. Treatment-emergent diabetic ketoadocis (DKA) was experienced by three RLM-treated Phase 2b patients (one in each group), unrelated to study drug. In Phase 2a, one case of DKA occurred during the placebo run-in period (not considered treatment emergent). Over the Phase 2b study, the mean CBF was 12.4±1.1 volumes increased with RLM dose: mean (SD) values were -0.03 (0.86), 0.48 (1.03), 0.92 (1.53) and 0.81 (1.77) for placebo, 100 µg BID, 300 µg BID and 1000 µg BID respectively (test for linear trend p = 0.0043). No clinically relevant changes in weight were observed (Table).

Conclusion: Phase 2 results indicate that RLM 10–100 µg BID is generally safe and well tolerated in adults with DG. Proactive glycaemic management will be incorporated into the planned Phase 3 trial due to increased blood glucose and HbA1c levels observed in RLM-treated patients.

Disclosure: MC (with compensation to his employer) and AL have received research funds to study relamorelin and serve on the Rhythm Pharmaceuticals advisory board. RM has received grants and consulting fees from Rhythm Pharmaceuticals. ST, LK, MM, KB and AI are employees of Allergan plc and own stock and stock options in the company.

P1742 COLD SENSATIONS AND HEARTBURN EVOKED BY ESOPHAGEAL INFUSION OF L-MENTHOL INDICATE EXPRESSION OF THE TRPM8 RECEPTOR IN ESOPHAGEAL C-FIBERS IN HUMANS


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Introduction: The TRPM8 receptor is best known for its responsiveness to cold and menthol; however, TRPM8 was also implicated in amplification of nociceptive sensory signals. Recent studies in animals showed that C-fibers innervating the esophagus express TRPM8. Here we evaluated the translatability of this finding in humans.

Aims and Methods: We hypothesized that the infusion of the TRPM8 activator L-menthol into the esophagus induces cold sensation in healthy subjects and that this sensation is exaggerated in patients with chronic heartburn. We used L-menthol because of its higher potency on TRPM8 compared to R-menthol or racemic mix. L-menthol (3mM), vehicle (0.05% ethanol) or acid (HCl solution, pH = 1) was infused (8ml/min) into the esophagus via a transnasal tube with the opening placed 5 cm above the manometrically determined LES. The intensity of sensations was recorded every 2 min. by visual analogue scale (VAS, range 0–10).

Results: Esophageal infusion of L-menthol evoked a cold sensation behind the sternum in 11 of 12 healthy subjects (mild heartburn in the remaining subject). The intensity of sensations was relatively modest, it fully developed during the 10 min. and did not increase further during the rest of infusion. VAS score in healthy subjects at 20 min was 1.9±0.3 (N = 12). Surprisingly, in 11 of 12 patients with chronic heartburn, esophageal infusion of L-menthol evoked typical heartburn (cold sensation in the remaining one). The intensity of heartburn increased gradually during the whole duration of L-menthol infusion and the VAS score at 20 min was 6.8±0.7 (N = 12, P < 0.01 compared to healthy subjects). Infusion of vehicle failed to evoke similar sensations (N = 3). For comparison, in a separate group of patients with chronic heartburn (N = 12) the VAS score at 10 min of acid infusion was 7.1±0.8 indicating that the intensity of heartburn evoked by L-menthol is comparable to that evoked by acid infusion.

Conclusion: Cold sensations evoked by esophageal infusion of menthol in healthy subjects indicate the expression of TRPM8 in esophageal sensory nerves. A relatively intense heartburn evoked by menthol in patients with chronic heartburn indicates that TRPM8 is expressed in C-fibers and suggest that the role of TRPM8 in amplification of visceral painful sensations in humans deserves a closer look.

Disclosure: Nothing to disclose.

P1743 NEWLY DEVELOPED WIRELESS GASTROSTIMULATOR FOR MINIMALLY INVASIVE GASTRIC STIMULATION: IN VIVO PILOT STUDY


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Introduction: Gastric electrical stimulation (GES) via high-frequency, low-energy pulses can provide an effective treatment for gastroparesis and obesity; however, the current available device requires surgical implantation for long-term stimulation and repeated surgical procedure after a period of time. We aimed to describe test endoscopic implantation of newly developed wireless gastric electrical stimulator.

Aims and Methods: We developed a novel and miniature wireless gastric electrical stimulator. Endoscopic gastric implantation techniques were implemented on healthy weaner pigs under general anesthesia. We made endoscopic submucosal pocketing and inserted gastromotor as previously mentioned. In vivo gastric slow waves were recorded and measured during electrical stimulation. A multi-channel recorder (Acknowledge 4.4, MP150; Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study.

Results: Electrogastrogram recordings demonstrated that gastric slow waves became more regular and of constant amplitudes when stomach tissues were stimulated, in comparison with no stimulation. The frequency-to-amplitude ratio also changed significantly with stimulation.

Conclusion: Gastric electrical stimulation is feasible by our endoscopically implanted, wireless GES device. This technique may have the potential to increase the utility of GES as a treatment alternative.

Disclosure: Nothing to disclose.
P1744 OESOPHAGO-GASTRIC JUNCTION OUTFLOW OBSTRUCTION: OUTCOMES AND REASONS FOR 45 PATIENTS FROM A TERTIARY REFERRAL CENTRE
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Introduction: Oesophago-gastric junction outflow obstruction (OGJOO) is characterised by a raised integrated relaxation pressure (IRP) with preserved oesophageal peristalsis. Although in some series OGJOO is being reported more frequently than achalasia, challenges still remain understanding its aetiology, clinical significance, natural history and appropriate therapy.

Aim and Methods: From June 2015 to November 2017, a retrospective analysis of patients undergoing high-resolution manometry (HRM) using 36-channel solid-state catheter (Manoscan 360, Sierra Scientific Instruments) was performed in a tertiary referral centre in London. Patients who fulfilled the diagnostic criteria of OGJOO per version 3.0 Chicago Classification were included. 10 single water swallows were followed with 5 cm x 1 cm cubed of bread. Medical files of patients meeting the diagnosis were reviewed to determine patient demographics; clinical history, endoscopic and barium swallow findings as well as therapeutic interventions.

Results: 45 patients were included, 28 females (62%), mean age 56 ± 2 (range 33–83) years. Most patients (84%) reported symptoms of dysphagia and chest pain (Eckardt score ≥3), while the others complained of heartburn, epigastric pain and/or oesophagitis. 18 patients were diagnosed based on single water swallows alone (IRP >15mmHg), 7 based only on solid swallows and 20 on both. 43 patients had Oesophago-Gastro-Douenoseous (OGD) recorded, 3 had Endoscopic Ultrasound (EUS) and 10 had Timed Barium Swallow (TBS). 9 patients (21%) had possible explainable aetiology: 2 Schustski ring, 2 peptic strictures, 3 slipped fundoplication, 1 Esophagolipohlegy and 1 extrinsic compression at the OGJ (seen on EUS). The rest were idiopathic. 12 patients reported regular use of opioids, including morphine, codeine and/or tramadol. Thus far, 12 patients have been treated within the same tertiary institution: 9 had botulinum toxin (botox) injections into the OGJ and 7 had Rigiflex balloon dilation to 30 and/or 35mm (4/7 of who were previously treated with botox with no response). 4 of those who have undergone further Rigiflex dilatation reported improved significantly when assessed between 3 and 12 months following therapy. The median height of the barium column at 5 minutes prior to treatment was 8.2 cm (IQR = 6.11; 4.4) while the median height following treatment was 0.5 cm (IQR = 0.05; 0.04). Overall, mean Eckardt scores for the 12 treated patients dropped from 9 (range 4–12) prior to therapy to 2 (range 0–3) after treatment.

Conclusion: OGJOO is an increasingly recognised manometry-defined disorder.

Disclosure: None

P1745 OESOPHAGEAL APERISTALSIS IS UNDER INVESTIGATED IN THOSE WITHOUT ACHALASIA OR REFLUX
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Introduction: Aperistalsis (OA) is the absence of esophageal motility with water swallows at high-resolution manometry (HRM). Symptoms include dysphagia, regurgitation, globus, chest pain and heartburn. The main causes are achalasia and acid reflux although in many patients no cause is found. There is no consensus for the investigation of OA without achalasia; this will depend on how common the underlying aetiology is.

Aims and Methods: The objective of this study was to investigate the number of patients with an identifiable cause of OA and to investigate the number of investigations occurred in 50% of patients with NANRA, potentially losing the opportunity to identify other aetiologies. It is unclear whether NANRA patients with OA are under-investigated for AD or for EoE, or whether this should be done only in selected cases.

Disclosure: Nothing to disclose

P1746 RELATIONSHIP BETWEEN ESOPHAGEAL MOTILITY ABNORMALITIES AND SKIN INVOLVEMENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS: MULTIVARIATE ANALYSIS
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Introduction: Esophageal motility abnormalities (EMAs) are often seen in patients with systemic sclerosis (SSc). Several studies have shown a relationship between EMAs and skin involvements, while other studies have not. The objective of this study was to identify predictive variables for EMAs in patients with SSc. A total of 109 patients with SSc who underwent esophageal high-resolution manometry (HRM) between May 2009 and August 2016 at Gunma University Hospital were enrolled. Esophageal motility was assessed retrospectively according to the Chicago Classification v3.0. HRM and clinical data, including the presence of autoantibodies and skin involvements, were collected. The association between EMAs and skin involvements was evaluated. SSc was divided into two types, diffuse cutaneous SSc (dSSc) and limited cutaneous SSc (lcSSc), based on the presence or absence of the proximal extent of skin thickness. The severity of skin thickness was assessed by a modified Rodnan total skin thickness score. Chi-square or rank sum tests were used to compare variables between patients with EMAs and those without. Logistic regression analysis was performed. Data was expressed as median values (25%, 75%) unless stated otherwise.

Results: Forty-four patients had normal esophageal motility, eight had esophageal-gastric junction outflow obstruction, one had distal esophageal spasm, 27 had ineffective esophageal motility and 29 had absent contractility. Although the prevalence of dcSSc did not differ between patients with EMAs and those with normal esophageal motility (34% vs. 20%, respectively; p=0.19), patients with EMAs had a significantly higher skin score than those with normal esophageal motility (7.0 (4.0, 16.0) vs. 4.0 (2.0, 9.0), respectively; p<0.05; Table). Other variables such as age, sex, disease duration, and the presence of digital ulcers, Raynaud’s phenomenon, or autoantibodies did not differ between patients with EMAs and those with normal esophageal motility. Although a significant predictive variable for EMAs was not found by multiple logistic regression analysis, the presence of autoantibodies and skin thickness score was a significant variable for absent esophageal contractility.

Conclusion: A significant correlation between severe skin thickness and absent contractility was found in patients with SSc. Considering that, if such patients have a high skin thickness score, esophageal motility should be evaluated.
Introduction: Per-oral endoscopic myotomy (POEM) has revolutionized the management of esophageal achalasia and other spastic disorders of esophagus. In the absence of large studies with long-term follow-up, the role of POEM remains uncertain for the management of esophageal motility disorders. In this study, we aimed to analyse the safety and efficacy of POEM in a large cohort of patients with esophageal motility disorders.

Aims and Methods: The data of consecutive patients with achalasia and non-achalasia motility disorders who underwent POEM at a single tertiary care center from January 2013 to March 2018 were analysed. Technical and clinical success, adverse events, and operative time were analysed in all the patients.

Results: Overall, 775 patients (40.37±4.39 years, Males 428) with esophageal motility disorders underwent POEM during the study period. The type of achalasia as per Chicago classification were: type I (219), type II (481), type III (30). 15 patients were classified as esophageal achalasia spastic motility disorder including Jackhammer esophagus in 4 and diffuse esophageal spasm in 11 patients. Overall, 356 patients had history of prior treatment. Majority of patients (71.35%) underwent anterior POEM. POEM was successfully performed in 98.45% patients.

Discussion: POEM is safe, effective and durable for the treatment of esophageal motility disorders. However, gastroesophageal reflux disease occurs in a substantial number of patients and needs to be considered while considering POEM for the management of achalasia.

Disclosure: Nothing to disclose

P1747 PER ORAL ENDOSCOPIC MYOTOMY IN ESOPHAGEAL MOTILITY DISORDERS: OUTCOMES IN OVER 700 PATIENTS

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P1748 ABNORMAL DISTENDIBILITY ON ESOPHAGEAL ENDOLUMINAL FUNCTIONAL LUMEN IMAGING PROBE (ENDO-FLIP) TESTING PREDICTS ENDOLUMINAL FUNCTIONAL LUMEN OUTFLOW OBSTRUCTION AND DIRECTS MANAGEMENT WHEN INTEGRATED RELAXATION PRESSURE (IRP) ON HIGH-RESOLUTION MANOMETRY (HRM) IS NORMAL OR BORDERLINE

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Introduction: An important clinical role for esophageal outflow obstruction is typically identified when IRP is higher than the upper limit of normal. However, achalasia and esophageal outflow obstruction can manifest with IRP within the threshold of normal, and borderline elevated IRP may not be clinically relevant in some instances. Evaluation of EGJ distensibility and esophageal body contractility with endo-FLIP may refine diagnosis of esophageal outflow obstruction.

Aims and Methods: Our aim was to evaluate the value of endo-FLIP in identifying EGJ outflow obstruction when IRP values are normal or borderline on esophageal HRM. Adult patients undergoing both HRM and endo-FLIP testing at a tertiary care institution were eligible for inclusion. Patients with incomplete HRM or endo-FLIP data were excluded. Patients completed questionnaires defining presenting symptoms. Endo-FLIP was performed using sequential volumetric distention of a compliant balloon placed in the distal esophagus during sedated endoscopy. Primary metrics were distensibility index (DI) from endo-FLIP (≤ 2.8 mm2/mmHg = abnormal), and IRP from HRM (≥ 15 mmHg = abnormal; 15–20 mmHg = borderline). Chicago Classification 3.0 distinguishes provocative testing using IRP (rapid drink challenge or RDC, multiple rapid swallows or MRS), and esophageal body contractility were additionally assessed. Data was analyzed to assess concordance and discordance between HRM and endo-FLIP assessments of the EGI, and final diagnosis was made from each.

Results: Of 85 patients (61.4±1.6 yr, 61.2% F) identified over an 18-month period, 78 presented with dysphagia or suspected esophageal outflow obstruction, and the remainder had unexplained symptoms. Both IRP and DI were abnormal in 25 patients (29.4%); this was true for all patients with achalasia (6 patients). Among patients with a normal IRP, DI was normal in 21/53 (40%), while abnormal (discordant) in 32/53 (60%) (p = 0.0007). When IRP was borderline, DI was also abnormal in 9/12 (75%, p = 0.3 compared to normal IRP). In borderline and normal IRP cohorts, esophageal pressurization on provocative testing were more often abnormal on normal DI (69.4% 37.5%, p = 0.02); mean IRP (p = 0.6) and MRS IRP (p = 0.8) were not discriminative between abnormal and normal DI. High GERDQ scores suggesting reflux disease in the normal IRP cohort were associated with normal DI (p = 0.005), but other symptom assessments were not different between abnormal and normal DI cohorts. Of 10 patients with absent contractility and normal IRP, 5 patients (50.0%) had features of achalasia on endo-FLIP with mean DI 1.3±0.4 and mean IRP 6.8±0.6 mmHg, compared to true absent contractility (mean DI 5.4±6.0, p = 0.09, mean IRP 7.6±1.3, p = 0.6). Endo-FLIP findings resulted in a change in management in 67.8% with normal IRP, and in 75% with borderline IRP.

Disclosure: Nothing to disclose

P1749 FOOD RHEOLOGY AND NUTRITIONAL ASSESSMENT OF DYSPHAGIA IN ACHALASIA PATIENTS: AN OBSERVATIONAL STUDY

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Introduction: Esophageal Achalasia (EA) is a rare disease of still uncertain etiology, characterized by absence of peristalsis and absence or incomplete relaxation of the Lower Esophageal Sphincter (LES) in response to swallowing. Dysphagia, food stagnation and chest pain are the main symptoms, related with negative impact on the quality of life (QoL) and lead patients to limit food intake with possible nutritional consequences. There are no specific dietetic advice for this kind of dysphagia resulting in self-management.

Aims and Methods: Aims of the study was to evaluate diet, eating habits and nutritional status of achalasia patients, and to assess association, if any, between food rheology and symptoms. Twenty-five achalasia patients (F14, M11, mean age 53±18 yrs) were examined. The outpatient setting was chosen to study patients who did not yet undergone any treatment. Clinical data were collected using a symptom and QoL questionnaire, divided in two parts (MD Anderson Dysphagia Inventory and Modular Questionnaire Roma III). Patients filled in a diary for 15 days (a total of 990 meals), where they reported ingested food for each meal by simulating a meal in a typical day, and the presence of symptoms according to ESS. Estimated caloric intake and composition of macronutrient were compared to Mediterranean Diet. Patients with dysphagia were divided in 3 groups: (1) normal; (2) presence of symptoms according to ESS. Estimated caloric intake and composition of macronutrient were compared to Mediterranean Diet.

Results: Seventeen patients (68%) had a ESS>3 with dysphagia and chest pain as main symptoms, 16 patients (64%) reported no weight loss, 6 (24%) reported weight gain (5–10 kg). ESS score was higher in patients with weight gain (6.5±7.8) vs 5.0±1.3). The mean score of QoL was 19.08±12.94, corresponding to a mild degree of disability perception. Evaluation of the usual diet in comparison with estimated caloric need showed an intake of 1620±382 vs 2201±546 Kcal and in comparison with the recommended macronutrient assumption (the following subdivision: carbohydrates 45.4%±5.9 vs 55–59%, protein 20.3%±3.9 vs 15–18%, total fat 33%±3.8 vs 26–27% and fiber 14.9±4.2 vs 25–30 g. Solid food caused more frequently symptoms than semiliquid and liquid ones: dysphagia (26.2% vs 3.6% vs 1%), chest pain (13.6% vs 2.1% vs 0.5%), and regurgitation (7.8% vs 1.8% vs 0.5%). Spaghetti, pizza and bread were associated with dysphagia in >50% of the meals, dry foods and vegetables caused symptoms in ~30% of meals: 40% of patients reported a worsening of symptoms with cold foods, 36% of patient improvement with hot foods. Full meals were achieved by 68% of patients; 32% stopped meals for vomiting, chest pain or regurgitation (64%, 27%, 9%, respectively). The most frequent intervention to overcome symptoms was...
drinking (52%), followed by repeated swallowing (21%), waiting (14%), regurgitation (13%).

Conclusion: The results of this observational study suggest that dysphagia and chest pain are main symptoms in achalasic patients even after treatment and they affect mildly the QoL. However, patients conform their diet to avoid symptoms reducing the intake of solid food and food rich in carbohydrates, leading to a hypocaloric and unbalanced diet in favour of fat and protein.

Disclosure: Nothing to disclose

P1750 PYLORIC DISTENSIBILITY MEASUREMENT PREDICTS SYMPTOMATIC RESPONSE TO INTRA-PYLORIC TOXIN BOTULINUM INJECTION

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Introduction: Recent studies reported that pyloric distensibility is altered in 30–50% (1) of gastroparetic patients. Pyloric distensibility has also been shown to correlate with gastric emptying and symptom severity.

Aims and Methods: The aim of the present study was to assess whether pyloric distensibility measurement is predictable of the symptomatic response after intra-pyloric toxin botulinum injection in gastroparesis. Pyloric distensibility has been measured using the ENDOFLIP® system in 25 consecutive gastroparetic patients before intra-pyloric toxin botulinum injection (Botox, 200 UI). Altered pyloric distensibility was defined as a distensibility below 10 mm²/mmHg as previously reported (1). Dyspeptic symptoms and quality of life have been prospectively investigated before and 3 months after intra-pyloric toxin botulinum injection. Dyspeptic symptoms (vomiting, nausea, gastric fullness, early satiety, bloating, epigastric pain and regurgitation) have been evaluated using a 5 point likert scale (0 = non symptoms; 4 = most severe symptoms). Total symptomatic score (TSS) was defined as the aggregation of individual symptomatic scores. Quality of life was measured using the GIQLI score ranging from 0 (worst quality of life) to 144 (best quality of life). Gastric emptying was assessed using the C13 octanoic acid breath test.

Results: Using the threshold of 10 mm²/mmHg, 17/24 patients had altered pyloric distensibility. 10/8 patients had normal pyloric distensibility. In patients with altered pyloric distensibility, TSS dropped at 3 months from 13.6 to 11.0 (p = 0.02), while it remained unchanged in patient with normal pyloric distensibility (from 14.0 to 14.2; p = 0.77). Among dyspeptic symptoms, vomiting (from 1.3 to 0.5; p = 0.03) and gastric fullness (from 3.3 to 2.4; p < 0.01) were the only symptoms to be improved in patients with altered pyloric distensibility, while none of the dyspeptic symptoms were improved in patients with normal pyloric distensibility. GIQLI score improved from 65 to 74 in patients with altered pyloric distensibility (p = 0.06) while GIQLI score remained unchanged (from 70 to 70; p = 0.94) in patients with normal pyloric distensibility. In patients with altered pyloric distensibility, gastric emptying half time was 249 min before and 222 min 3 months after injection (p = 0.18). In patients with normal pyloric distensibility gastric emptying half time was 227min before and 214 min 3 months after injection (p = 0.93). When threshold was set at 9 or 8 mm²/mmHg, similar findings were observed.

Conclusion: Pyloric distensibility measurement before intra-pyloric toxin botulinum injection predicted symptomatic and quality of life response 3 months after injection in gastroparetic patients.

Disclosure: Nothing to disclose

Reference

P1751 PYLORIC DISTENSIBILITY MEASUREMENT AFTER GASTRIC SURGERY: WHICH SURGERY IS ASSOCIATED WITH Pylorospasms

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Introduction: History of gastric surgery is found in 10% of gastroparesis. A vagal lesion is often suspected to be responsible of pylorospasm, although there was until recently no routine test to diagnose such alteration. Recently, pyloric distensibility measurement using the ENDOFLIP® system showed that pylorospasm was found in 30-50% of gastroparetic patients.

Aims and Methods: The aim of the present study was to assess whether pylorospasm, diagnosed using the ENDOFLIP® system is observed in 3 different types of gastric surgeries, namely antireflux surgery, sleeve gastrectomy, and esophagectomy.

Pyloric distensibility and pressure were measured using the ENDOFLIP® system in 43 patients (19 antireflux surgery, 16 sleeve gastrectomy, and 8 esophagectomy) with dyspeptic symptoms after gastric surgery, and in 21 healthy volunteers. All patients had delayed gastric emptying, except in sleeve gastrectomy in the absence of normal values established in asymptomatic controls. Altered pyloric distensibility was defined as distensibility below 10 mm²/mmHg as previously reported (1). Results: Different groups patients were not different in demographic characteristics, except for body mass index that was increased in the sleeve gastrectomy group and age that was older in the esophagectomy group. Compared to healthy volunteers (distensibility: 25.2 ± 2.4 mm²/mmHg; pressure: 9.7 ± 4.4 mmHg), pyloric distensibility was decreased in the antireflux group (P = 0.065), in the esophagectomy group (P = 0.001) and esophagectomy (10.8 ± 2.1 mm²/mmHg; p < 0.05) groups, while pyloric pressure was only increased in the antireflux surgery group (18.9 ± 2.2 mmHg; p < 0.01). Pyloric distensibility and pressure were similar in healthy volunteers and the sleeve gastrectomy (distensibility: 20.3 ± 3.8 mm²/mmHg; pressure: 15.8 ± 1.6 mmHg) groups. Altered pyloric distensibility was found in 18% of patients from the sleeve gastrectomy group, 58% (p < 0.05) of patients from the antireflux surgery group and 67% (p < 0.05) of patients from the esophagectomy group.

Conclusion: Antireflux surgery and esophagectomy are associated with pylorospasm although pylorospasm is not found in all these patients. Sleeve gastrectomy was associated with altered pyloric distensibility nor altered pyloric pressure.

Disclosure: Nothing to disclose

Reference

P1752 BENEFIT OF SMALL-DOSE ANTIDEPRESSANTS FOR FUNCTIONAL DYSPEPSIA: EXPERIENCE FROM EASTERN CHINA

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Introduction: Traditional treatment of functional dyspepsia (FD) is unsatisfactory, and the potential role of antidepressant medications also hasn’t been definitely clarified.

Aims and Methods: This study aimed to evaluated the efficacy and safety of antidepressant medications for management of annoying symptoms of FD. Based on the Rome III criteria and the FD-related quality of life (FD-QoL) score, patients were divided into three subtypes at initial visit: postprandial distress syndrome (PDS), epigastric pain syndrome (EPS) or both. Patients were treated with different antidepressant agents and dosage according to individual illness features. An established 4-point Likert-type scale was used to measure the response of antidepressant therapy at follow-up according to the clinical records. Patient demographics, clinical symptoms, medication history, GI diagnostic tests, and antidepressant therapy were collected. Antidepressant treatment data extracted included the type and dose used, treatment response, and self-reported adherence.

Results: Among the total patients (n = 1524) referred to this specialist clinic because of refractory GI symptoms or asked for physical examination, 9.4% (n = 144) met the inclusion criteria for study cohort. Fourteen patients were subsequently excluded for failure to return after initiation of antidepressant therapy and 130 cases were left for analysis. The mean patient age was 50.5 years over a range of 18-83 years, and 88 patients (67.7%) were female. Thirty-eight patients (29.2%) had EPS, 64 (49.2%) had PDS, and the remaining 28 (21.6%) complained of both EPS and PDS. The mean duration of GI symptoms prior to initial evaluation was 3.8 years. Thirty-three patients (25.4%) of all had been treated with only one antidepressant; 91 (70%) were treated with two, and 6 (4.6%) had changed medication consecutively. Antidepressant agents, in descending order of frequency were: fluoxetine, fluvoxamil, metilatracen, sulpride, paroxetina, citalopram, mirtazapine, sertraline, duloxetine, amitriptyline, and venlafaxine. Following initiation of antidepressants, symptom improvement was attained follow-up visits (93.6%) at some time in 43% of symptoms (score = 3) occurred in 71 patients (54.6%), and the average time to obtain remission was 3.4 months; moderate improvement (score = 2) was obtained in 33 patients (26.2%). No significant difference was detected in remission rate in relation to symptom patterns and no antidepressant regimen was significantly different for management of three FD types. Complete symptom remission occurred in 46.9% of subjects with PDS vs. 57.9% for subjects with EPS and 67.9% with both. When subjects with symptom remission were compared with the reminder, young patients (P = 0.065) tended to lead a poor outcome. Furthermore, when given sulpride or fluoxetine, patients with younger age were associated with a poor outcome (P = 0.001 and P = 0.005, respectively).
However, there was no any association between gender, FD subgroups, or dyspepsia duration and response to antidepressants. A significant difference was observed in all FD subtypes in different subtypes (PDS, EPS) of FD between two criteria (p = 0.253, P < 0.01).

Conclusion: Rome IV criteria has more strict and accurate FGID definitions, allowing a more accurate identification of the disease and those patients who really need treatment, resulting in a more efficient and feasible application in clinical practice and scientific research. Disclosure: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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Introduction: Acid exposure time (AET) and reflux-symptom association (RSA) on pH-impedance monitoring can stratify esophageal syndromes into nonerosive reflux disease (NERD), and functional esophageal syndromes (FED), including reflux hypersensitivity (RH, normal AET with positive RSA) and functional heartburn (FH, normal AET and negative RSA). Low mean nocturnal baseline impedance (MBNI) is now a recognized marker of impaired mucosal integrity that can predict therapeutic outcome from antireflux therapy. We hypothesized that MBNI could differentiate between NERD and FED, particularly FH, allowing a more accurate identification of the disease and those patients who really need treatment, resulting in a more efficient and feasible application in clinical practice and scientific research. Disclosure: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

References
Conclusion: Recent years, functional dyspepsia is treated by two major cate-

Introduction: Autoimmune gastritis (AIG) is an organ-specific autoimmune

Conclusion: In this study, thiol/disulfide balance was shown to shift towards
disulfide form in AIG patients, compared to the control group. According to
these results, weakened thiol/disulfide equilibrium in AIG patients was thought
to be associated with autoimmunity and inflammation. Determination of abnor-
mal thiol/disulfide homeostasis in patients with AIG suggested that abnormal
thiol/disulfide homeostasis may be related to the pathogenesis of AIG.

Disclosure: Nothing to disclose

Reference


P1756 IMPROVEMENT OF MEAL-RELATED SYMPTOMS AND

EPIGASTRIC PAIN IN PATIENTS WITH FUNCTIONAL DYSPESPIA

TREATED WITH ACOTIAMIDE WAS ASSOCIATED WITH

ACYLATED GELIN LEVELS IN JAPAN

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Introduction: Recent years, functional dyspepsia is treated by two major cate-

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P1757 ASSESSMENT OF THIOL/DISULFIDE HOMEOSTASIS IN

PATIENTS WITH AUTOIMMUNE GASTRITIS

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Introduction: Autoimmune gastritis (AIG) is an organ-specific autoimmune and

inflammatory disorder. It is characterized by reduction and loss of parietal cells
and formation of autoantibodies against H+ K+-ATPase and intrinsic factor.

Oxidant radicals increase secondary to inflammation in autoimmune and auto-

inflammatory disorders. The increase in reactive oxygen species can react with
cellular macromolecules and causes in lipid peroxidation, nucleic acid damages
and protein modifications. Thios are functional sulhydryl groups and consist of
a sulfur atom and a hydrogen atom bound to a carbon atom and capable of
reacting with free radicals in order to provide protection against tissue damage
caused by reactive oxygen products. Thiol groups of proteins are oxidized by
oxygen molecules and are reversibly converted to disulfide bonds. These disulfide
bonds can be reduced to thiol groups in a condition of decreased oxidative stress.
In case of oxidative stress, thios form a number of products as a result of oxidative stress. These formed disulfide bonds can again be reduced to thiol

groups, and therefore thiol/disulfide homeostasis is maintained. An abnormality
in this homeostasis process may result in a variety of disorders. Since AIG is an
autoimmune and inflammatory disorder, abnormal thiol/disulfide homeostasis may
have a role in the pathogenesis of this condition.

Aims and Methods: Direct measurement of thiol/disulfide levels with a novel and
automated method is already available. Therefore, the aim of this study was to
investigate dynamic thiol/disulfide homeostasis in patients with AIG and identify
potential factors associated with this alteration. Also to determine whether
oxidation may have a role in the gastric emptying time in patients with AIG.
Forty-nine patients with AIG and 52 healthy volunteers were enrolled in the
study. Venous blood samples were collected from the subjects after overnight
fasting. Blood samples were separated and stored at 80 °C. Serum thiol-disulfide
homeostasis was determined with a colorimetric method recently developed
developed by Erel and Neselioglu (1). Native thiol and total thiol were measured
directly, and disulfide, disulfide/total thiol ratio, disulfide/native thiol ratio
were obtained with calculation.

Results: Mean native thiol (330.65 ± 33.43 mmol/L) vs 369.71 ± 21.73 mmol/L
and thiol/native thiol ratio total levels (90.61 ± 95.0:0:01) were determined lower in AIG patients, compared to the control group. Mean disulfide level (21.47 ± 4.50 mmol/L vs 16.73
± 2.4 mmol/L, respectively; P = 0.007), and disulfide/native thiol (5.1 ± 1.1 ± 1.2% vs 40 ± 1.2%, respectively, P < 0.001) were determined higher in AIG patients compared to the control group.

Conclusion: In this study, thiol/disulfide balance was shown to shift towards
disulfide form in AIG patients, compared to the control group. According to
these results, weakened thiol/disulfide equilibrium in AIG patients was thought
to be associated with autoimmunity and inflammation. Determination of abnor-
mal thiol/disulfide homeostasis in patients with AIG suggested that abnormal
thiol/disulfide homeostasis may be related to the pathogenesis of AIG.

Disclosure: Nothing to disclose

Reference


P1758 GASTRIC PH IN VITRO INFLUENCES LEVOTHYROXINE

SODIUM TABLET REQUIREMENT IN HYPOTHYROID PATIENTS

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Introduction: In vitro studies have highlighted that the dissolution of levothyrox-

ine tablets is linearly correlated to pH increase. An increased dose of

LT4 is needed to reach therapeutic target of serum TSH in different gastric
hypochlorhydric conditions as Helicobacter pylori infection, chronic autoimmune gastritis and chronic Proton pump inhibitors treatment. At present, a correlation between intragastic pH and therapeutic required therapy LT4 dose is lacking.

Aims and Methods: The aim of our study was to determine in vitro a correlation
between the pH of gastric juice and the effective dose of LT4 needed to restore euthyroidism.

Sixty-one dyspeptic hypothyroid patients (9M/52F; median age 51 yrs range 26–

73y) treated with LT4 were enrolled in this prospective study. In this cohort, 32 patients that required an excess of LT4 individually- tailored dose to normalize serum TSH value were screened for extraintestinal (drugs and food) and/or
gastrointestinal non-acid-related causes (celiac disease, Crohn disease, lactose intolerance, SIBO, gastric surgery) LT4 malabsorption. All patients underwent gastroscopy with sampling of gastric acid secretion and multiple gastric biopsies to assess Sydney System-related gastritis patterns. Chronic atrophic gastritis (CAG) was defined as the presence of oxyntic glandular atrophy in fundic gland mucosa (PGM) that was active and chronic in nature. The concentration of intragastric pH was determined by using a pH probe. The intragastric pH was measured in 30 minute periods for a total of 150 minutes. The study was conducted in a single-center setting in an outpatient gastroenterology practice. The study population consisted of 120 patients with non-cardiac dyspepsia (NCD) who were referred for evaluation of symptoms and were taking LT4 therapy. The patients were randomly assigned to one of two groups: the LT4 group and the placebo group. A total of 20 patients were included in each group. The primary outcome measure was the difference in the intragastric pH between the LT4 group and the placebo group.

Results: The intragastric pH was significantly higher in the LT4 group compared to the placebo group (p < 0.05). The mean intragastric pH was 1.5 ± 0.1 in the LT4 group, compared to 1.3 ± 0.1 in the placebo group. The difference in intragastric pH was maintained throughout the study period. No significant adverse events were reported in either group. Conclusion: Long-term LT4 therapy significantly improves the intragastric pH in patients with non-cardiac dyspepsia. This finding suggests that LT4 therapy may have a beneficial effect on the pathophysiology of dyspepsia. Further studies are needed to confirm these findings and to determine the long-term effects of LT4 therapy on the intragastric pH and the clinical outcomes of patients with non-cardiac dyspepsia.
Introduction: Eosinophilic oesophagitis (EO) is a chronic immunogenic-antigen mediated disease of the oesophagus, histologically defined by over 15 eosinophil counts seen in a high-power microscopic field, without gastro-oesophageal reflux disease. It causes symptoms including dysphagia, regurgitation and food bolus impaction. Oesophageal biopsies are necessary to diagnose EO. We evaluated the rates of repeat biopsies to investigate patients with dysphagia.

Aims and Methods: We studied the endoscopy records and oesophageal biopsy results of 160 consecutive patients who were referred with a new diagnosis of dysphagia to the endoscopy departments of East Sussex Healthcare NHS Trust, over a 3 month period. Data collection sources included the EndoBase reporting tool and patient case notes.

Results: 23 of the 160 patients had a diagnosis at endoscopy of oesophageal cancer or Barrett's oesophagus. These did not have routine biopsies taken for assessment of EO and were excluded from analysis. Of the remaining 137 patients, who had biopsies taken at different levels in the oesophagus to screen for EO, 5 were consistent with a diagnosis of EO, representing 3.6% of patients. 61.3% were normal and 35.1% showed changes of reflux related inflammation. The case notes of the patients with EO were reviewed. All revealed a history of either food bolus impaction or repeated episodes of dysphagia. Two patients had a history or family history of asthma and eczema.

Conclusion: In this series of 137 patients with symptoms of dysphagia who were diagnosed with EO, the cost of biopsies at two different levels in the oesophagus was £46.68 per patient. £1279 was spent to diagnose one case of EO. A selective strategy for taking oesophageal biopsies to diagnose EO would be more cost effective. This needs evaluation but restricting biopsies to a case with a history of episodic food bolus obstruction, a family or past history of asthma or atopy and endoscopic signs such as mucosal furrowing and prominent concentric rings merits further assessment.

Disclosure: Nothing to disclose.

P1762 VARIATION IN THE INVESTIGATION AND DIAGNOSIS OF EOSINOPHILIC OESOPHAGITIS IN DAILY CLINICAL PRACTICE

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Introduction: Eosinophilic oesophagitis (EOe) is a recognised cause of dysphagia, with an estimated annual incidence of 6–13 cases/100,000 persons. Diagnosis can only be definitively established by endoscopic biopsy and as such, societal guidelines advocate the acquisition of six non-targeted oesophageal biopsies. In this study, we aim to determine whether these recommendations are adhered to in routine clinical practice, and whether this practice is influenced by scope operator, patient age and referral pathway.

Aims and Methods: We performed a retrospective database review of all OGDs performed to investigate dysphagia or food bolus obstruction between 1st July 2016–31st June 2017, with three tertiary referral centres serving a total population of approximately 3.2 million people. We collected information on age, gender, endoscopy operator, referral pathway, endoscopic features and diagnosis, number of biopsies taken and histopathological diagnosis. Statistical comparisons were made using the Fisher’s exact test or Chi-square test with Yates’ correction.

Results: During this time period a total of 4056 (15.9% of total) OGDs performed to investigate dysphagia or food bolus obstruction between 1st July 2016–31st June 2017, with three tertiary referral centres serving a total population of approximately 3.2 million people. We collected information on age, gender, endoscopy operator, referral pathway, endoscopic features and diagnosis, number of biopsies taken and histopathological diagnosis. Statistical comparisons were made using the Fisher’s exact test or Chi-square test with Yates’ correction. Of these cases, the recommended 6 (or more) biopsies were taken in 923 (37.4%) of the cases. The recommended 5 (or more) biopsies were taken by histopathology in only 87 cases (9.43%). When specifically comparing gastroenterologists to surgeons (total of 2193 biopsies were received by histopathology), we noted that gastroenterologists were 5.6 times more likely to obtain biopsies than surgeons (46.7% vs 13.6%, p < 0.0001, Table 1). They were also 4.7 times more likely to obtain biopsies at different levels in the oesophagus to screen for EO, 5 were consistent with a diagnosis of EO, representing 3.6% of patients. 61.3% were normal and 35.1% showed changes of reflux related inflammation. The case notes of the patients with EO were reviewed. All revealed a history of either food bolus impaction or repeated episodes of dysphagia. Two patients had a history or family history of asthma and eczema.

Conclusion: In this series of 137 patients with symptoms of dysphagia who were diagnosed with EOe, the cost of biopsies at two different levels in the oesophagus to screen for EO, 5 were consistent with a diagnosis of EO, representing 3.6% of patients. 61.3% were normal and 35.1% showed changes of reflux related inflammation. The case notes of the patients with EO were reviewed. All revealed a history of either food bolus impaction or repeated episodes of dysphagia. Two patients had a history or family history of asthma and eczema.

Disclosure: Nothing to disclose.

P1763 BRAVO WIRELESS PH MONITORING CAN SAVE TIME WHEN INVESTIGATING PATIENTS WITH EOSINOPHILIC OESOPHAGITIS

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Introduction: The incidence of eosinophilic oesophagitis (EO) is increasing. Following diagnosis, the initial therapy is to place patients on protein pump inhibitors (PPI) and repeat oesophageal biopsies, as 30% of patients will be PPI responsive. As acid reflux is known to cause eosinophilic oesophagitis, pH impudence and manometry is also carried out to aid management. This is usually carried out as a separate hospital visit. An alternative test is wireless pH monitoring with a BRAVO device during which a pH monitoring chip is attached to the distal oesophageal axis at the same time as a gastroscopy. This is also an opportunity to take the repeated biopsies to assess PPI response; pH monitoring could therefore be integrated into the repeated endoscopic pathway and avoid the extra appointment for standard pH impedance. The fragile “crépe-paper” mucosa of EOe has been raised as a potential source of early detachment of BRAVO capsule thereby limiting their use in this condition.

Aims and Methods: We aimed to assess whether there is any difference in the detachment day of the BRAVO capsule in patients with EOe when compared to other conditions and thereby determine its use in the pathway for the investigation of EOe patients.

The electronic records of patients with EOe who also had a BRAVO were examined retrospectively between June 2008 and January 2018 at a single centre. The total number of recording of the BRAVO capsule was noted and whether reflux was significant. In addition the number of eosinophils per high field power on the oesophageal biopsies taken prior to or at the same time as the BRAVO study was recorded.

Results: Ten patients with EOe underwent 12 BRAVO studies (M: F 1:1, age range 18–56). One study detached within one day, three after two days and eight after four days. The patient whose capsule detached early went on to have a second BRAVO study lasting 4 days. Detachment times were compared to those for non-EOe in our department for a single calendar year (December 2016–December 2017). There was no significant difference in detachment rates between these two groups (p < 0.1). The range of eosinophils per HPF was 20 to 71 (average 38.1, standard deviation 20.5).

Conclusion: Bravo pH manometry is a useful investigation in patients with EOe and beneficial to the patient; reducing the number of invasive procedures by allowing the attachment of the BRAVO capsule at the same time as taking post-PPI biopsies. The detachment was not significantly greater in patients with EOe although the numbers are small. There was no correlation between eosinophil count per HPF and attachment times. The only drawback is that patients are expected to stop PPI 7 days prior to the BRAVO being placed with a theoretical risk of a recrudescence of oesophageal eosinophilia in that time although the standard time for redevelopment of EOe is around 6–8 weeks.

Disclosure: Nothing to disclose.
P1764 ESOPHAGEAL COMPLIANCE IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS BEFORE AND AFTER TREATMENT WITH TOPICAL BUDENSOIDE
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Introduction: Esophageal compliance is decreased in eosinophilic esophagitis (EoE). The reduction of compliance due to fibrosis has been shown to be a strong predictor of the risk of impaction and esophageal dilatation in patients with EoE. There is a lack of correlation between the eosinophil count and distensibility, revealing the dissociation that is sometimes observed between inflammatory and clinical activity. The reduced esophageal compliance correlates with the intensity of the endoscopic esophageal trachealization. The Functional endoluminal imaging probe (EndoFLIP®/C213, Crospon Ltd., Galway, Ireland) for the study of esophageal distensibility and diameter uses the impedance planimetry technique and allows the analysis of volume-controlled esophageal compliance, obtaining three-dimensional images of the esophageal light. The goal of the treatment of eosinophilic esophagitis is not only the clinical, endoscopic and histological improvement, but also the reduction in the degree of fibrosis, and therefore an improvement in esophageal compliance.

Aims and Methods: A pilot study to compare the esophageal compliance of patients diagnosed with active EoE before and after treatment with topical Budesonide.

We analyzed the esophageal compliance data of the first patients undergoing EndoFLIP at the Gastroenterology Department of the Hospital Universitario de La Princesa in Madrid. These patients presented active EoE and the esophageal compliance data were obtained before and after the treatment with Budesonide orodispersible tablets 1 mg every 12 hours for 6 weeks.

Results: Five patients were included in which clinical and histological improvement was observed (< 15 eos/hpf), as well as an increase in diameter and statistically significant esophageal compliance (p = 0.02) after 6 weeks of treatment with Budesonide. The functional endoluminal imaging probe EndoFLIP for the study of esophageal distensibility was performed during the same endoscopic procedure, under sedation, and there were no complications associated with the procedures in any patient.

Conclusion: With topical budesonide treatment, the clinical and histological response and increased compliance in patients with EoE are achieved. More studies are needed with a greater number of patients and comparing with control subjects to know the clinical benefit of EndoFLIP in the follow-up of patients with EoE, and thus be able to establish its usefulness in the diagnostic-therapeutic algorithm of EoE.

Disclosure: Nothing to disclose

P1765 UNRESPONSIVE DYSPHAGIA TO PROTON PUMP INHIBITORS IN EOSINOPHILIC ESOPHAGITIS PATIENTS SUGGESTS TO START STEROID THERAPY WITHOUT THE NEED OF PERFORMING A SECOND ENDOSCOPY
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Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune-mediated disorder characterized by symptoms of esophageal dysfunction due to an inflammatory eosinophilic infiltrate in the esophageal lamina propria. Currently, the endoscopic appearance of patients with EoE is defined by using the Endoscopic Reference Score (ERFS), whereas the eosinophilic infiltration is used to diagnose EoE (i.e. > 15 eos/hpf) and to estimate disease severity. The relationship between EoE and gastroesophageal reflux disease (GERD) has been demonstrated, although the magnitude of its is unknown and scant data have been published to date. Moreover, there is a lack of sufficient data evaluating the correlation of eosinophilic infiltrate with clinical presentation, endoscopic findings and reflux burden.

Aims and Methods: We aimed to correlate eosinophilic infiltration with clinical presentation, endoscopic findings as expressed by the ERFS score and reflux burden as assessed by impedance-pH studies. Patients with symptoms suggestive of EoE (i.e. dysphagia and bolus impaction) were prospectively enrolled in different Gastroenterology units in Italy. At baseline, an esophagogastroduodenoscopy (EGD) was performed to confirm the presence of inflammatory eosinophilic infiltrate (> 15 eos/hpf) in the proximal and distal esophagus and to establish the diagnosis of EoE. Then, patients referred to international EoE PPI therapy was administered b.i.d. for eight weeks and a second EGD with biopsies was repeated to assess the endoscopic and histological remission due to acid-suppressive therapy. Esophageal symptoms including dysphagia, bolus impaction, heartburn and regurgitation were assessed by means of a 4-point Likert scale before and after therapy by mean of a 4-point Likert scale from 0 (absent symptom) to 3 (severe symptom). Histological remission was considered if esophageal samples presented less than 15 eos/hpf. A value of zero for each symptom after PPI therapy was indicative of clinical remission.

Results: Thirty-one (25 Male; Age 18–68) patients with symptoms suggestive of EoE were enrolled. All of them presented dysphagia, 16 (52%) regurgitation and 19 (61%) heartburn. After 8 weeks PPI-therapy, 25 (74%) patients well tolerated the PPI b.i.d. therapy and 16 (51%) of the subjects did not. Dysphagia disappeared in all of the subjects with a positive response to PPIs and only in 4 out of 8 refractory to PPIs. Moreover, regurgitation and heartburn resolved in 14/15 (93%) and in 16/17 (94%) of patients responding to PPI, respectively (p = 0.031 and in 1/1 (100%) of patients resistant to PPIs, respectively. Using Fisher’s test, we calculated sensitivity, specificity, positive and negative predictive values (PPV and NPV) of symptom disappearance in order to segregate PPI responders from PPI-non responders without performing an EGD.

Disclosure: Nothing to disclose
Neither a correlation between pick of eosinophils count and value of EREFS score was observed (p > 0.05).

**Conclusion:** Eosinophils pick count in the esophageal mucosa of patients with EoE does not correlate with the severity of disease in term of endoscopic findings, symptomatic presentation and reflux burden. It seems that these factors are independently associated and additional phenomena are likely to be involved in determining the entity of eosinophilic infiltration.

**Acid Exposure Time (AET),%**

| 2 (0–8) |
| 41 (2–92) |
| 31 (1–69) |
| 9 (0–37) |
| 21 (6–65) |
| 1 (0.1–3.6) |
| 14 (4–35) |
| 30 (0–70) |

**Mean nocturnal baseline impedance (MBNI)**

1001 (237–3349)

**Disclosure:** Nothing to disclose

**P1767 COMPREHENSIVE ANALYSIS OF FACTORS DETERMINANT FOR EROUSIVE REFLUX ESOPHAGITIS: SIGNIFICANCE OF DEMOGRAPHIC/LIFESTYLE FACTORS IS EMPHASIZED IN HELICOBACTER PYLORI-NONINFECTED SUBJECTS**

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**Introduction:** The incidence of erosive reflux esophagitis has increased sharply in Japan, probably due to falling prevalence of **Helicobacter pylori** (HP) infection. HP-associated atrophic gastritis, which reduces gastric acid secretion, is known to be protective against erosive reflux esophagitis. However, both gastric acid secretion level and HP infection status should be taken into consideration when analyzing the risk factors of erosive reflux esophagitis. Pepsinogen I/II ratio is reported to correlate significantly with not only gastric atrophy grade but also gastric acid secretion level. Hence, we performed comprehensive analyses of the reported to correlate significantly with not only gastric atrophy grade but also HP-associated atrophic gastritis, which reduces gastric acid secretion, is known to be protective against erosive reflux esophagitis. Therefore, both gastric acid secretion level and HP infection status should be taken into consideration when analyzing the risk factors of erosive reflux esophagitis. Pepsinogen I/II ratio is reported to correlate significantly with not only gastric atrophy grade but also gastric acid secretion level. Hence, we performed comprehensive analyses of the risk factors of erosive reflux esophagitis by using pepsinogen I/II ratio as a surrogate marker of gastric acid secretion level.

**Aims and Methods:** A total of 959 consecutive subjects who underwent esophagogastroduodenoscopy and measurement of serum pepsinogen level at the same day were enrolled. The following subjects were excluded to avoid the influence on pepsinogen levels: 1) those who had received successful HP eradication therapy in the past, 2) those who had undergone gastrectomy, 3) those who were taking proton pump inhibitors for various reasons, and 4) those having renal failure (Creatinine > 3.0 mg/dl). HP infection status was determined by the titer of serum HP-IgG. Erosive reflux esophagitis was defined as grade M or more reflux esophagitis according to Los Angeles classification. Univariate and subsequently multivariate logistic regression analyses were performed to identify the factors of erosive reflux esophagitis. The following factors were evaluated: sex, age, body mass index (BMI), pepsinogen I/II ratio, drinking status, smoking status, and HP infection status.

**Results:** The 959 enrolled subjects comprised 466 males, with an mean age of 52. To neutralize an influence of HP infection status on erosive reflux esophagitis, the entire cohort was divided into 2, HP-infected (HP-IgG positive, n = 236) and HP-noninfected (HP-IgG negative, n = 723) subjects. In HP-infected subjects, univariate analysis showed that factors significantly associated with erosive reflux esophagitis were pepsinogen I/I ratio and BMI (OR 1.45, 95% confidence intervals (CI) 1.10–1.91) and BMI (OR 1.12, 95% CI 1.01–1.91). Multivariate analysis showed that pepsinogen I/I ratio was also a significant factor for erosive reflux esophagitis (OR 1.41, 95% CI 1.06–1.86). On the other hand, in HP-noninfected subjects, univariate analysis showed that male sex (OR 4.17, 95% CI 2.94–6.25), BMI (OR 1.13, 95% CI 1.07–1.19), everyday drinking (OR 3.38, 95% CI 1.26–8.51), and current smoking (OR 2.83, 95% CI 1.76–4.56) were associated with erosive reflux esophagitis. Multivariate analysis showed that male sex (OR 2.70, 95% CI 1.69–4.35), BMI (OR 1.07, 95% CI 1.01–1.13), and everyday drinking (OR 1.78, 95% CI 1.07-2.96) were statistically significant.

**Conclusion:** The factors for erosive reflux esophagitis differ between HP-infected and HP-noninfected subjects. In HP-infected subjects, pepsinogen I/I ratio was the only significant factor. On the other hand, in HP-noninfected subjects, demographic/lifestyle factors such as male sex, BMI, and everyday drinking were significant. These results suggest that although gastric acid secretion ability is reserved. In the era of falling prevalence of HP infection in Japan, lifestyle modification may be promising for preventing erosive reflux esophagitis.

**Disclosure:** Nothing to disclose

**P1768 GASTRIC BYPASS SURGERY IN THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE: A POPULATION-BASED COHORT STUDY**

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**Introduction:** Gastric bypass (GBP) is considered an effective surgical treatment option for co-existing gastroesophageal reflux and obesity. However, previous studies examining GBP and reflux have had small sample sizes, short follow-up, and substantial loss to follow-up. This study aimed to assess how GBP influences reflux in a large study with long and complete follow-up.

**Aims and Methods:** This nationwide and population-based cohort study included 2,805 obese individuals with preoperative reflux who underwent GBP in Sweden in 2006-2015, with follow-up until 2016. Reflux was defined as dispensation of > 6 months of antireflux medication, excluding other indications for such medication. Poisson regression was used to assess cumulative incidence and risk factors of postoperative reflux.

**Results:** Reflux re-occurred in 48.5% of patients within two years of GBP (48.5–100 person-years, 95% confidence interval [CI] 46.6–50.5). The re-occurrence of reflux remained stable around 50% during 3 to 10 years after GBP (yearly change in incidence rate [IRR] of 1.00, 95% CI 0.99–1.02). Risk factors for postoperative reflux were high preoperative dose of antireflux medication (IRR = 1.13, 95% CI 1.07–1.20) and female sex (IRR = 1.10, 95% CI 1.01–1.22 comparing age > 50 with ≤40 years), female sex (IRR = 1.16, 95% CI 1.15–1.39), and comorbidity (IRR = 1.13, 95% CI 1.11–1.15 comparing Charlson comorbidity index ≥ 2 with 0).

**Conclusion:** Reflux re-occurs in approximately half of patients after GBP, and the rate is higher in individuals using high preoperative dose of antireflux medication, and in those of female sex, older age, and with comorbidities. These results suggest that the treatment effect of GBP may have been overestimated.

**Disclosure:** Nothing to disclose
P1769 WAIST CIRCUMFERENCES IS THE INDEPENDENT RISK FACTOR OF GASTROESOPHAGEAL REFLUX DISEASE: A META-ANALYSIS

Introduction: Decrease in the lower esophageal sphincter pressure with increased gastro-esophageal pressure gradient and the hiatal hernia have been reported to be induced by high intra-abdominal pressure due to abdominal fat accumulation and obesity are related to the high prevalence of reflux esophagitis. Moreover, metabolic syndrome, characterized by the dyslipidemia, hypertension, and hyperglycemia, and all 4 factors have been suggested to correlate with the occurrence of GERD.

Aims and Methods: This study was performed to clarify the association between metabolic syndrome and erosive esophagitis and to find out which one of the diagnostic criterion of the metabolic syndrome is mostly correlate with erosive esophagitis. The study subjects were an adult population who visited a National Hospital for Gastrointestinal and Digestive Diseases.6–8 However, there is still no comprehensive article to assess the association between alcohol consumption and GERD (OR, 1.08; 95%CI, 0.73–1.60; P=0.69). The esophagitis group showed higher rate of obese subjects (28.9%) compared to the control group (20.8%). The odds ratio of obesity for esophagitis in women was 1.268; P=0.001).

Conclusion: Waist circumference, rather than metabolic syndrome is a reliable predictor for the prevalence and severity of erosive esophagitis.

Disclosure: Nothing to disclose

References

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P1770 ALCOHOL CONSUMPTION AND THE RISK OF GASTROESOPHAGEAL REFLUX DISEASE: A META-ANALYSIS

P1771 SMOKING AND ALCOHOL CONSUMPTION ARE ASSOCIATED WITH OESOPHAGEAL HYPOSensitivity

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Introduction: Alcohol-oesophageal reflux disease (GORD) is a common condition with a prevalence of up to 28%, often causing impaired quality of life [1]. Avoidance of lifestyle factors such as tobacco and alcohol is often recommended in GORD management; mostly on trial and error and only to some degree on epidemiological findings. Hence, smoking is associated with an up to two-fold increased risk of GORD as well as Barrett’s oesophagus (BO), whereas the effects of alcohol are less well known [1]. Physiologically, lower oesophageal sphincter pressure (LESP) decreases due to tobacco smoking and alcohol intake [1]. Correspondingly, smoking cessation has been shown to improve reflux symptoms, but only in normal-weight GORD patients, whereas the effect on acid exposure is less clear [1]. For alcohol, any immediate effect on oesophageal function in regard to reflux symptoms and/or reflux monitoring is doubtful [1]. In the long-term however, alcohol may lead to neuropathy [2] and possibly even have positive effects on chronic pain [3]. Only one study has addressed the impact of alcohol and smoking on oesophageal sensitivity, finding no relationship, likely due to the inclusion of only three smokers.

Aims and Methods: We aimed to characterize the impact of alcohol and tobacco consumption on experimental oesophageal sensitivity, and hypothesized that both of these are associated with hyposensitivity. Twenty-three patients with BO (mean age: 64.2±7.8 years) and 12 healthy controls (mean age: 54.9±10.8 years) were included. At baseline, all subjects reported consumption of alcohol (standard drinks per week) and tobacco (accumulated pack years). At a later visit, experimental oesophageal pain sensitivity was assessed by placing a multimoval stimulation probe in the lower oesophagus. The probe was then used to apply mechanical distension, thermal stimulation, electrical stimulation, and acid perfusion with 0.1 M hydrochloric acid (a Bernstein test). All stimulations were stopped when the subject felt moderate pain.

Results: Tolerated acid volume (hyposensitivity) increased with greater tobacco exposure and alcohol consumption in healthy controls (tobacco: P<0.001, alcohol: P=0.001), but not in patients with BO (all P>0.3). Concerning mechanical stimulation, no greater tolerance of stimulus volume was associated with tobacco or alcohol exposure only in patients with BO (P=0.02). For healthy controls in relation to tobacco smoking and for alcohol use in both groups, no significant associations with sensation to mechanical stimulation were found (all P>0.6). For electrical and thermal stimulation, neither alcohol nor tobacco use showed any significant associations in any of the groups (all P>0.1).

Conclusion: Oesophageal sensitivity decreased with greater reported consumption of alcohol and tobacco. Previous findings of a strong association to smoking in situational factors and volume was associated with tobacco exposure only in patients with BO (P=0.02). For healthy controls in relation to tobacco smoking and for alcohol use in both groups, no significant associations with sensation to mechanical stimulation were found (all P>0.6). For electrical and thermal stimulation, neither alcohol nor tobacco use showed any significant associations in any of the groups (all P>0.1).

Disclosure: Nothing to disclose

References
P1774 MONITORING RISK FACTORS FOR THE ONSET OF ESOPHAGITIS IN A LONG 15 YEARS FOLLOW-UP
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Introduction: Gastroesophageal reflux disease (GERD) is a disease determined by several concomitant factors. The pathophysiology is particularly linked to obesity, smoking habits and the secretory activity of the stomach; the variability of endoscopic findings depends on different resistance and sensitivity of the individual patient’s mucosa.
Aims and Methods: Aim of this study was to evaluate the influence of epidemiological risk factors (age, sex, obesity, smoking habits) and gastric acid secretion status in the development of esophagitis in a H pylori-negative population. A group of 320 patients (M = 234, F = 86, mean age = 42 ± 11.6 range = 18.80) with symptoms of the upper GI tract was recruited. They underwent gastroscopy in order to assess the presence of esophagitis: 150 had esophagitis (Group A) in comparison with 170 without lesions (Group B). All patients underwent to gastric acid aspiration test for measuring basal acid output (B.A.O.) and maximal acid output (M.A.O.) after stimulation with pentagastrin (i.m., 6 μg/kg). All of them underwent a blood sampling for serum pepsinogen I and G17 determination. Statistical analysis was performed by means of Mann-Whitney test for the comparison of demographic characteristics and endoscopic diagnoses. An univariate analysis was used to evaluate risk factors such as age, sex, smoking habit, BMI, M.A.O., PGI, G17. All patients underwent a 15 years follow-up using gastroscopy when symptoms occurred to assess the onset of a feature of esophagitis.
Results: Univariate analysis demonstrated a significant association between the feature of esophagitis, lasting the follow-up, and M.A.O. (p = 0.0001), PGI (p = 0.0001), G17 (p = 0.0014), while no association was found with age, gender nor smoking habit.
Conclusion: Our study demonstrated a positive association between high gastric secretion (M.A.O., PGI and G17) as well as BMI and the onset of esophagitis in an H.p. negative population lasting a 15-long years follow-up.
Disclosure: Nothing to disclose

P1775 LARYNGEAL MUCOSAL IMPEDANCE VALUES; A NEW DIAGNOSTIC TOOL FOR LARYNGOPHARYNGEAL REFLUX DISEASE
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Introduction: There are great difficulties for the diagnosis of laryngopharyngeal reflux disease (LPR). Reflux finding score (RFS) and reflux symptom index (RSI) were proposed for the diagnosis however their value is questionable. We propose a new diagnostic tool with the measurement mucosal impedance in different areas of larynx and pharynx in patients with LPR and controls.
Aims and Methods: The objective of the study was to assess the relation of laryngeal mucosal impedance values with LPR. In total 78 patients (38 female) were included who were operated for different ENT pathologies other than laryngeal diseases. Exclusion criteria: previous upper gastrointestinal or laryngeal surgery, on-going proton pump inhibitor treatment, other laryngeal disorders, previous radiotherapy in the head and neck, laryngeal carcinoma. Patients were divided into four groups according to LPR, RFS (Table). Normal values were accepted <15 for RSI and < 7 for RFS. After the general anesthesia and intubation, the mucosal impedance measurements of band ventricle, arytenoid, vallecula, posterior comissure, endolaryngeal surface of epiglottis and buccal area (as control) were recorded using Ohmega (Laborte) MIH-pH equipment with an impedance catheter (Unisensor). A mean value from a stabile measurement control) were recorded using Ohmega (Laborie) MII-pH equipment with an impedance catheter (Unisensor). A mean value from a stabile measurement was given in the table. A statistically significant difference was found for band ventricle, arytenoid, vallecula and endolaryngeal surface of epiglottis (p < 0.05) within all groups but especially between groups I (both RFS & RSI pathologic) and IV (both normal). 51 non-smokers exhibited higher but insignificant

References

Conclusion: There may be no little relationship between GERD and OSA. SSS, Epworth sleepiness scale (ESS) and IV (both normal), 51 non-smokers exhibited higher but insignificant
measurements compared to 27 smoker patients in all measured areas except band ventricle (1183 vs 779 ohms). Binary logistic regression analysis revealed that a model using measurements from band ventricular fold (OR 0.993, 95% CI 0.984–0.998), aetiology (OR 0.991, 95% CI 0.988–0.999) and endolaryngeal surface of epiglottis (OR 0.993, 95% CI 0.988–0.999) was able to distinguish especially between group I and group IV with a sensitivity of 93% and a specificity of 83%.

Conclusion: Mucosal impedance measurement of the larynx and pharynx can be used as a promising diagnostic tool. Smoking, as a possible strong confounding factor, has very limited impact on measurements. When our findings were evaluated with the parameters of RFS, posterior commissure hypertrrophy should not be taken into consideration however ventricular obliteration should be more emphasized. Considering the results of logistic regression more attention should be paid also to the aetynoids and endolaryngeal surface of epiglottis. It is possible to create a new diagnostic scoring system with this more objective technology. Outcome data and thinner catheters are needed for office-based measurements.

Disclosure: Nothing to disclose

### P1776 ON-THERAPY PARAMETERS RATHER THAN OFF- THERAPY IMPEDANCE-PH FEATURES BETTER IDENTIFY PATIENTS WITH NON-EROSSIVE REFUX DISEASE RESPONDING TO PROTON PUMP INHIBITOR THERAPY

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**Introduction:** Impedance-pH monitoring, providing a comprehensive assessment of reflux independently of the pH of refluxate, allows to reliably distinguish non-erosive reflux disease (NERD) from functional heartburn, and thus represents a valuable test for investigating proton pump inhibitor (PPI)-refractory patients.

**Aims and Methods:** We aimed to investigate whether impedance-pH off- or on-therapy may better identify patients with NERD responding to PPI therapy. In this prospective, multicenter study, 64 patients complaining of heartburn and with a negative upper endoscopy, underwent impedance-pH testing off-therapy. Then, patients with proven NERD based on traditional parameters (i.e. abnormal AET and/or positive symptom association association) were treated with PPI for 8 weeks and repeated the impedance-pH testing on-therapy. Tracings were blindly and manually reviewed and we measured conventional reflux testing parameters, such as esophageal acid exposure time (AET), number of reflux episodes and symptoms association analysis (symptom index, SI, and symptom association probability, SAP), and novel impedance-detected features, including the post-reflux swallow-induced peristaltic wave (PSPW) index and mean nocturnal baseline impedance (MNBI).

**Results:** Thirty-two individuals (16 male, mean age 48) had PPI-refractory heartburn (i.e.<50% of symptom relief after 8-week high-dosage PPI therapy), and thirty-two (18 male, mean age 56) had PPI-responsive heartburn. Demographic and clinical characteristics were not different between the two groups at baseline (P=ns). At off-therapy impedance-pH monitoring, no differences were found between PPI-refractory and PPI-responsive patients in terms of median AET, number of reflux episodes, symptoms association analysis, PSPW and MNBI, as illustrated in the Table. At on-therapy reflux testing, median esophageal AET and symptom association analysis did not differ between the two groups. However, the total number of refluxes, weakly acidic refluxes and bolus exposure were significantly higher, while PSPW index and MNBI were significantly lower in PPI-refractory cases (P<0.05), as shown in the Table.

**Conclusion:** Our data showed that only on-therapy impedance-pH monitoring is able to differentiate patients with NERD who are responding to PPI therapy from those who are refractory to acid-suppressive treatment. In particular, impedance-detectected characteristics (i.e. total number of refluxes, bolus exposure, PSPW index and MNBI) seem to better correlate with response to PPI therapy. This study provides additional evidence on the value of impedance-pH testing as compared to pH-metry alone in investigating reflux disease patients and evaluating therapeutic outcome.

Disclosure: Nothing to disclose

### P1777 MULTICHANNEL IMPEDANCE MONITORING FOR DISTINGUISHING NON-EROSSIVE OESOPHAGITIS WITH MINOR CHANGES ON ENDOSCOPY

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**Introduction:** There are reports about the relationship between baseline impedance level and oesophageal mucosal integrity by endoscopic findings such as erosive and non-erosive reflux oesophagitis. However, many children with symptoms of GORD have normal findings or minor changes on oesophagogastroduodenoscopy (OGD). We would like to examine whether trivial changes in OGD study can be evaluated by multichannel Impedance monitoring as an alternative measure.

**Aims and Methods:** Patients (ages 0–18 years) with symptoms related to GOR who underwent OGD and pH-MII monitoring in Women’s and Children’s Hospital in Adelaide, Australia, between 2014 and 2016 were retrospectively studied and the following data were collected: demographics (age, gender), pH-MII data (acid exposure (pH), included reflux index (acid exposure time)), mean acid clearance time, longest episode of acid exposure). Impedance data included: the number of acid and non-acid reflux events, and baseline impedance (distal channel 5, pH monitoring). It was objectively calculated using software created using Matlab (MathWorks, Natick, MA)). Endoscopic findings were classified by modified Los Angeles grading, LA-N as normal, LA-M as with a minimal change such as the reddish or whitish mucosa, or friability in the mucosa. Patients on proton pump inhibitors were excluded. Other exclusions were the presence of esophageal anatomical anomaly, eosinophilic esophagitis, and previous anti-reflux surgery.

**Results:** Seventy patients (43 boys 61%) were enrolled with a mean of age of 7.9 years (range 10 months to 17 years) in this study. Fifty-one patients (72.9%) were classified as the reddish or whitish mucosa, or friability in the mucosa. Patients on proton pump inhibitors were excluded. Other exclusions were the presence of esophageal anatomical anomaly, eosinophilic esophagitis, and previous anti-reflux surgery.

**Discussion:**
P1778 THE CONSISTENCY OF LOS ANGELES CLASSIFICATION OF GASTROESOPHAGEAL REFUX DISEASE ACCORDING TO THE INSERTION/WITHDRAWAL PHASES OF ESOPHAGOGASTRODUODENOSCOPY
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Introduction: During esophagogastroduodenoscopy (EGD), patients often belch and retch. Gastroesophageal junction (GEJ) is a narrow area easily affected by endoscopic manipulation and belching or retching during patients endoscopy. But there is no consensus on optimal timing of grading esophagitis during EGD, and no study was performed to assess the effect of these factors on the Los Angeles (LA) classification of reflux oesophagitis.

Aims and Methods: We performed prospective observational study to investigate the effect of endoscopic movement and patients’ belching/retching during EGD on the GEJ appearance. All images of GEJ were captured during both insertion and withdrawal phases of EGD and analyzed separately. All the image sets of GEJ (each subject has two image sets, one during insertion and the other during withdrawal) were mixed randomly, and reviewed by two expert endoscopists (who had performed more than 3000 upper gastrointestinal endoscopy), who were unaware of the relationship of mixed image sets. LA classification was recorded as normal, minimal change, A, B, C, and D. Simplified working definition of minimal change lesion (i.e., white turbid discoloration and Z-line blurring) was adopted in this study [1]. LA classifications determined by two reviewers were compared. For incongruent results, final grading was made by mutual agreement after discussion.

During EGD, patients’ belching and retching were scored by endoscopist as follows: none, mild (no significant but presence of any event), moderate (able to complete examination but difficult and prolonged examination due to the event), and severe (cannot evaluate completely due to the event).

Results: We prospectively enrolled 369 consecutive subjects, and 11 subjects were excluded due to unclear GEJ image for LA classification. Finally, 358 subjects (183 males and 175 females, mean age 59.6 years, range 17–87 years) were analyzed in this study. Belching occurred in more than 70% of subjects (none: 29.7%, mild: 52.1%, moderate: 15.7%, severe: 2.5%). Retching occurred in 7.5% of subjects (none: 92.4%, mild: 3.4%, moderate: 4.2%, severe: 0%). LA classifications graded from image sets during withdrawal phase were upgraded significantly compared to classifications graded from image sets during insertion phase (p < 0.001; Wilcoxon signed ranks test). Totally, LA classification change was occurred in BMI cohort (13.7%). The most common change between insertion and withdrawal phase was from ‘normal’ to ‘minimal change’ (Table 1).

Even though LA classification was not affected, there were several cases developing mucosal erosions and minor bleeding on GEJ during withdrawal phase (N = 12, 3.4%). Belching and retching was not significantly associated with LA classification change (p = 0.075 and p = 0.128 for each; Linear by linear association).

<table>
<thead>
<tr>
<th>Withdrawal phase</th>
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<th>LA-A</th>
<th>LA-B</th>
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</table>

[Relationship of LA classifications between insertion and withdrawal phase] Evaluation: LA classification of gastroesophageal reflux disease can be affected by endoscopic manipulation during EGD. We suggest taking pictures of GEJ during insertion phase rather than withdrawal phase for exact classification of reflux esophagitis.

Disclosure: Nothing to disclose

Reference

P1779 SYMPTOMS AND CLINICAL PRESENTATION ARE NOT PREDICTIVE OF ESOPHAGEAL REFUX BURDEN IN OBESE PATIENTS EVALUATED FOR BARIATRIC SURGERY
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Introduction: The spectrum of esophageal motor function, and reflux burden within obese subjects is not fully known. We compared esophageal questionnaire data, esophageal motor function and reflux metrics on pH-impedance monitoring among symptomatic and asymptomatic obese subjects presenting for bariatric surgery.

Aims and Methods: Our aim was to describe esophageal motor function and esophageal reflux metrics in symptomatic and asymptomatic obese subjects (BMI > 30). Patients undergoing esophageal function testing (HRM, pH-monitoring off medications) over 1.5 years prior to bariatric surgery were eligible for inclusion. Prior foregut surgery, lack of symptom data and incomplete esophageal tests were exclusion criteria. Patients completed standardized questionnaires evaluating reflux symptoms (GERDQ). HRM studies were evaluated using Chicago Classification 3.0 and GERD classification metrics; acid exposure time (AET, physiologic < 4%, pathologic > 6%), number of reflux episodes and mean nocturnal baseline impedance (MNBI, normal = 2292 ohms) recorded 5 cm proximal to the lower esophageal sphincter (LES), and post-reflux swallow-induced peristaltic wave index (PSWP index) were extracted from pH-impedance monitoring. Data were analyzed to determine the discriminative value of esophageal physiologic parameters in identifying patients with pathologic esophageal acid exposure in obese patients.

Results: 34 obese patients (43.0±2.3 yr, 85%F, BMI 49.6±2.7) fulfilled study inclusion criteria; 28 (82.4%) reported heartburn or regurgitation on questionnaires, and 17 had a positive GERDQ (>8). Demographics, esophageal motor diagnoses and esophageal pH-impedance metrics were similar regardless of symptom status. Using AET > 6% and MNBI < 2292 as indicative of pathologic reflux, the two metrics were concordant in 21/34 (61.8%), discordant in 11/34 (32.4%). When AET was borderline (<6%) or MNBI was low (<2292 ohms) (84.5% vs. 52.4%, p = 0.06), but similar BMI, symptom burden and motor characteristics. When the study cohort was segregated by MNBI, those with low MNBI (< 2292 ohms) had lower BMI, higher total AET, supine AET, and a lower PSWP index compared to patients with normal MNBI (84.5% vs. 52.4%, p = 0.06), but similar BMI, symptom burden and motor characteristics. In the normal MNBI cohort, there was 1 patient (8.3%) with AET > 4 and no patients with AET > 6%, compared to 10 patients (45.5%) with AET > 4 and > 6 when MNBI was low (p = 0.005). Symptom assessment (GERDQ, MDQ), EJG morphology and barrier function, esophageal body contraction vigor, and esophageal motor diagnoses could not differentiate AET-based or MNBI-based cohorts.

Disclosure: Nothing to disclose

Reference
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Introduction: Randomized controlled trials report ~30% of GERD patients complain of bothersome residual symptoms (heartburn/regurgitation) despite PPI. Some patients’ symptoms are caused by functional disease, however only a minority undergo anti-reflux surgery or formal evaluation. The LOPA (Lost Patients) studies of GERD patients in Germany revealed 46% of patients

Table 1

<table>
<thead>
<tr>
<th>Low MNBI (&lt; 2292 ohms)</th>
<th>Normal MNBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>46.5±1.61</td>
</tr>
<tr>
<td>Ineffective esophageal motility</td>
<td>23%</td>
</tr>
<tr>
<td>Number of reflux episodes</td>
<td>51.8±6.01</td>
</tr>
<tr>
<td>Total AET</td>
<td>4.93±0.91</td>
</tr>
<tr>
<td>Supine AET</td>
<td>4.22±1.09</td>
</tr>
<tr>
<td>AET &gt; 6%</td>
<td>45.5%</td>
</tr>
<tr>
<td>PSWP index</td>
<td>17.4±2.3%</td>
</tr>
</tbody>
</table>

[“p < 0.05 compared to normal MNBI]
experienced residual symptoms ≥2 days per week despite PPI but <10% received specific GERD. Reasons for dissatisfaction included: poor treatment alternatives.

**Aims and Methods**: The LOPA Brazil study is a prospective, multicenter, observational study conducted in 12 reflux specialty centers with 21 physicians (9 gastroenterologists, 12 surgeons). - Lost Patients – with chronic GERD, on PPI therapy for ≥1 year, and not satisfied with their therapy, were asked to complete a questionnaire. The physician was then asked to complete the patient’s physiological information and treatment recommendation following the visit.

**Results**: Responses were collected from 511 patients (42% male, mean age 46.7). Mean duration of GERD was 7.2 years; patients were prescribed PPI therapy on average 5.2 years.

Overall, 77% (n = 393) experienced heartburn and/or regurgitation ≥2 days per week (39% 4–7 days). More than half (54%) of patients were dissatisfied with their GERD condition (score 1–2 on an Likert scale 1–5). Reasons for dissatisfaction included breakthrough symptoms (88%), fear of risks associated with long-term medication (49%), inconvenience of daily medication (48%), and side effects from medication (5%). However, 62% of dissatisfied patients (166/265) and 66% overall (331/499) had never visited a surgeon for their GERD: 49% of patients said their doctor advised them against surgery.

pH or pH-impedance results were available for 56% (n = 288) of patients. In the GI and surgery groups, 51% (46/84) and 56% (113/206) had pathological 24-h pH (time pH <4.0 >6.0), respectively, and 65% (54/84) and 69% (143/206) with pathological DeMeester score (>14.7), respectively.

Despite similar patient-reported symptoms and physiological results, differences were seen in how patients were consulted. GI recommended 18% of patients to surgical consult, 79% to continue PPI therapy, 8% to try different reflux medication, and 7% to seek treatment for a non-GERD condition. Surgeons recommended consultation 63% for surgical consult, 20% to continue PPI therapy, 1% to try different reflux medication, and 9% to seek treatment for a non-GERD condition.

**Conclusion**: “Lost Patients” with bothersome GERD symptoms are frequently seen in routine care in both Germany and Brazil. The German patients suffered from GERD on average 9.4 years and were on PPI therapy for an average of 7.8 years; 72% were dissatisfied with their current condition, reasons for dissatisfaction, and perceptions about anti-reflux interventions.

**Disclosure**: All authors have worked as medical consultants for Endostim.

**References**


P1781 GERD PATIENTS ACROSS CULTURES HAVE SIMILAR CONCERNS: A COMPARISON OF “LOST” GERD PATIENTS IN GERMANY AND BRAZIL

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**Introduction**: The LOPA (Lost Patients) I Study in Germany revealed 46% of patients experienced heartburn and/or regurgitation symptoms at least twice per week despite PPI, 20% were dissatisfied with their treatment. Few patients had reported GERD symptoms on a GERD diaries or recommended treatment alternatives (<10%) despite breakthrough symptoms.

**Aims and Methods**: Follow-up studies to explore the perceptions of these GERD “Lost Patients” in Brazil. A screening tool could help identify and counsel these patients, and raise awareness in general practice of patients who could benefit from additional investigation and specialized treatment.

**Disclosure**: All authors have worked as medical consultants for Endostim.

**References**

Introduction: Chronic reflux patients with long-term PPI therapy frequently have persistent, at least 20% of the patients are unhappy with their therapy. Therapy options are limited. A critical source of the persistent acid reflux is the *acid pocket*, which can be treated effectively by the non-systemic reflux suppressing action of alginate.

Aim and Methods: Chronic GERD patients with at least one year of PPI long-term therapy, who were dissatisfied with their therapy, were treated over a period of 14 days with alginate as add-on and when required (up to 4 times daily) in a prospective, multi-centre observational study in GP practices. The frequency of symptoms and therapy were monitored with the validated GERD Symptom Score (GSS), as well as for four days at the second day of the study phase and the consumption of alginate. The validated GERD Q-score was also applied. The patients assessed satisfaction with the therapy on a five-point Likert scale (very unhappy = 1) before the beginning and at the end of the study. The primary endpoint of the study was improvement in satisfaction with the therapy by ≥ 1 point.

Results: 155 patients (53% women, median age 57 (18–85) years) entered the study. Six patients had to be excluded from the final efficacy analysis (no intake of study drug, lost to follow-up). The median duration of GORD was 8 (1–50) years and the median time on PPI therapy was 6 years. On average the patients took 3 sachets of alginate per day. The alginate therapy led to an improvement by at least 1 point on the Likert scale in 72% of patients (1 step n = 45, 2 steps n = 41, 3 steps n = 16, 4 steps n = 5). Patients with a Gerd Q score > 8 had a higher response rate at 81%. There was improvement in all typical reflux symptoms and sleep disorders. The treatment was generally well-tolerated.

Conclusion: Chronic GERD patients on long-term PPI therapy who are dissatisfied because of remaining troublesome symptoms an alginate as add-on and taken on demand is a new and effective option to improve patients satisfaction. Typical reflux symptoms are a valuable predictor of treatment success.

Disclosure: J. Labenz received speakers honoraria, consulting fees and an unrestricted grant from Reckitt Benckiser. G. Labenz received speakers honoraria from Reckitt Benckiser.
TABLES:

<table>
<thead>
<tr>
<th>Glucose (placebo)</th>
<th>Fructose</th>
<th>Fructans</th>
<th>p-value of the main effect</th>
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</thead>
<tbody>
<tr>
<td>TLESRs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.2 ± 6.7</td>
<td>27.0 ± 8.7</td>
<td>28.4 ± 7.4</td>
<td>0.006</td>
</tr>
<tr>
<td>Reflux</td>
<td>16.6 ± 8.0</td>
<td>15.9 ± 9.6</td>
<td>18.7 ± 8.3</td>
</tr>
<tr>
<td>Mixed + Gas</td>
<td>6.7 ± 5.9</td>
<td>7.1 ± 5.7</td>
<td>8.8 ± 7.1</td>
</tr>
</tbody>
</table>

The number of TLESRs and reflux episodes in the three different conditions (mean ± SD).

Disclosure: Nothing to disclose

P1778 RISK FACTORS FOR PATHOLOGICAL UPGRAADING OF ESOPHAGEAL LOW-GRADE INTRAEPITHELIAL NEOPLASIA DIAGNOSED WITH ENDOSCOPIC FORCEPS BIOPSY

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Introduction: Several studies have reported changes of the pathological analysis before and after endoscopic resection (ER) for esophageal intraepithelial neoplasia. We aimed to explore the risk factors for pathological upgrading after ER for lesions diagnosed as low-grade intraepithelial neoplasia (LGIN) with preoperative biopsy.

Aims and Methods: A total of 70 lesions which were initially diagnosed as esophageal LGIN by forceps biopsy and later underwent ER from November 2013 to July 2017 were included. They were divided into two groups according to pathological grading after ER. The risk factors for post-operation pathological upgrading were analyzed.

Results: The study enrolled 70 patients. The change of post-operation pathological diagnosis occurred in 30 (42.9%) patients (upgrade 28 (40.0%); downgrade 2 (2.9%). In the upgrading group, ER upstaged it to high-grade intraepithelial neoplasia (HGIN) for 20 (28.6%) lesions and to early esophageal cancer for 8 (11.4%) lesions. Univariate analysis showed that lesions >1/2 esophageal circumference (P = 0.006), maximal longitudinal-diameter ≥3 cm (P = 0.005), submucosal infiltration in endoscopic ultrasonography (P = 0.037), lesions based on depressed type (0-IIa) (P = 0.005) and reddish surface (P = 0.019) were factors for pathological upgrading compared with preoperative biopsy. Multifactor analysis indicated maximal longitudinal-diameter ≥3 cm (P = 0.008) and reddish surface (P = 0.013) were independent factors for pathological upgrading compared with preoperative biopsy.

Conclusion: Pathological upgrading of LGIN after ER was common, especially in large lesions with reddish surface. Endoscopic resection may be recommended for these lesions instead of follow-up observation.

Disclosure: Nothing to disclose

P1779 THE MID-TERM OUTCOMES OF ENDOSCOPIC TREATMENT FOR SUPERFICIAL CERVICAL ESOPHAGEAL CANCER

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Introduction: Cervical esophageal cancer (CEC) is a less common form of cancer. The survival rates of CEC patients remain poor because it is often locally advanced at the time of its diagnosis. With advances in endoscopy, more cases of superficial CEC are being treated endoscopically, and two required esophagectomy. Three patients developed local recurrence, and all cases were able to be retreated endoscopically. During the median follow-up period of 60 months (range 36-148), all the cases are still alive.

Conclusion: Planned semi-circular ESD for widespread superficial esophageal neoplasm may be an efficient strategy for preventing severe stricture formation.

Disclosure: Nothing to disclose
were mostly p16ink4a high, p53 low and wild-type TP53. There were more Tis/T1/2 tumours in HPV positive subjects as compared with HPV- patients (75.7% versus 54.3%, p = 0.02). Mean disease-free survival was superior in the HPV+ group (40.2 months versus 24.1 months, p = 0.003) as was overall survival (43.7 months versus 29.8 months, p = 0.02). Nevertheless, the prognostic significance of oesophageal tumour HPV status is unknown.

Introduction:

We hypothesized that HPV associated oesophageal tumours would show a favourable prognosis (as in viral positive head and neck cancers). Thus, we studied the association between HPV and related biomarkers of high-grade dysplasia (HGD)/OAC and survival. Pre-treatment biopsies were used for HPV DNA determination via PCR, in-situ hybridization for E6/E7 mRNA and immunohistochemistry for p16INK4A and p53. Sequencing of TP53 was also undertaken.

Results:

Amongst 142 HGD/OAC patients [M:F, 126 (88.7%): 16 (11.3%)] with HPV DNA determination via PCR, in-situ hybridization for E6/E7 mRNA and transcriptionally active virus positivity were both associated with a superior DFS (HR = 0.33, 95%CI: 0.16–0.67, p = 0.009) but not with OS (HR = 0.88, 95%CI: 0.49–1.63, p = 0.54). The FA score and the NLR were not significant risk factors on OS and DFS, such as ages and clinical stages (OS; HR 2.70, 95% CI: 1.08–6.76, p = 0.034; DFS; HR 2.16, 95% CI: 1.01–4.63, p = 0.046). The FA score and the NLR were not significant risk factors in multivariate analysis.

Conclusion:

High levels of mGPS were significantly prognostic factors in patients who had undergone esophagectomy for esophageal cancer. More patients for analysis are needed.

Disclosure: Nothing to disclose.

References

2. Wang B, Rajendra S, Pavey D, et al. Viral load and integration status of HPV+ cancers has been associated with Barrett’s dysplasia and oesophageal adenocarcinoma (OAC). Nevertheless, the prognostic significance of oesophageal tumour HPV status is unknown.

Conclusion:

HPV+ HGD/OAC is a distinct biological entity with a favourable prognosis as compared with viral negative oesophageal tumours. If these findings are confirmed in other centres with more advanced disease, it presents an opportunity for treatment de-escalation in the hope of reducing toxicity without detrimentally affecting survival.

Disclosure: Nothing to disclose.

References

P1793 ACCURACY OF ENDOSCOPIC TUMOR DEPTH PREDICTION IN SUPERFICIAL ESOPHAGEAL SQUAMOUS CARCINOMA

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Introduction: Even though the accurate prediction of tumor depth (T staging) for superficial esophageal squamous carcinomas (SESC) is essential for making the proper decision on treatment strategy, there are not enough studies about standard endoscopic criteria. In this study, we tried to know the diagnostic accuracy of conventional endoscopy for T staging in SESC and to make the conventional endoscopic criteria of mucosal and submucosal esophageal carcinoma (ESCC) easily obvious.

Aims and Methods: For first step, new endoscopic criteria of mucosal (T1m) and submucosal cancer (T1sm) were created by 2 experienced endoscopists with 60 randomly selected cases of pathologically proven SESC. For second step, endoscopic criteria of lesions, which were treated by surgical or endoscopic resection for SESCs between 1991 and 2010, were reviewed according to the new endoscopic criteria to predict the tumor depth. Results: The overall accuracy of new endoscopic criteria was 79.5% (232/292). The sensitivity, specificity, and positive and negative predictive values of mucosal cancers were 78.4%, 81.0%, 85.4%, and 72.6%, and those for submucosal cancers were 81.0%, 78.4%, 72.6%, and 85.4%. The prediction rate of mucosal cancers was high (95.9%) when the lesions were shown as flat or slightly elevated/depressed on a smooth/even surface regardless of size. And those of submucosal cancers were high (85.6%) when the lesions were irregular/nodular protrusion regardless of size. In multivariate analysis, tumor size less than 3cm (odd ratio 0.450, p = 0.014) was found as independent affect for the accuracy of endoscopic criteria.

Conclusion: The accuracy of endoscopic prediction for estimating T staging is acceptable in SESC. Careful endoscopic examination with new endoscopic criteria in SESC can provide more information and help to decided treatment methods between surgical and endoscopic resection.

Disclosure: Nothing to disclose

P1794 ARTIFICIAL INTELLIGENCE FOR AUTOMATED DETECTION OF EARLY OESOPHAGEAL SQUAMOUS CELL NEOPLASIA THROUGH CLASSIFICATION OF INTRAPAPILLARY CAPILLARY LOOPS

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Introduction: Intrapapillary capillary loop (IPCL) patterns provide an endoscopically visible marker of early squamous cell neoplasia (ESCN). Narrow-band imaging with magnification endoscopy (ME-NBI) allows detailed assessment of these microvascular patterns. The Japanese Endoscopy Society (JES) AB classification describes ESCN and predicts invasion depth based on the intrapapillary capillary loop (IPCL) pattern. Early lesions are amenable to endoscopic therapy (EET) so the prompt characterisation and identification of mucosal lesions is vital. Endoscopists, particularly those in areas with low ESCN prevalence, may not be familiar with the characterisation of ESCN. We have designed a novel deep convolutional network (CNN) able to classify IPCL patterns as normal (A) or abnormal (B1/B2/B3), in order to alert endoscopists to abnormal areas in ESCN during lesion assessment.

Aims and Methods: 17 patients were recruited at a referral centre in Taiwan. Endoscopies were performed using ME-NBI (Olympus). IPCLs were classified for each video by 2 experts as normal (type A), or abnormal (type B1/B2/B3), using the JES classification. Matched tissue was obtained by ESD for histologic evaluation of invasion depth. Images were quality controlled to remove uninformative (blurred) images. Our dataset consisted of 7046 images. A CNN was trained using a binary cross-entropy loss and evaluated on 1818 images for training, and 1637 unseen images (846 normal and 791 abnormal) for testing. Class activation maps were generated to provide a clinically interpretable network output. Accuracy, F1 scores, sensitivity and specificity for abnormal IPCL detection were calculated.

Results: 17 patients were included (10 had early neoplasia [1 high-grade intraepithelial neoplasia (HGIN) 4 carcinoma in situ (CIS) invading to the lamina propria, 4 to the muscularis mucosa and 1 to the submucosa] and 7 were normal). Our algorithm of lymph node involvement of early esophageal cancer, as well as the possibility of cheomoradation therapy or close follow-up needs to be assessed in multidisciplinary meetings before indicating esophagectomy after endoscopic resection.

Disclosure: Nothing to disclose

P1795 CHARACTERISTICS OF SYNCHRONOUS LESIONS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC EPITHELIAL NEOPLASIA

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Introduction: Since endoscopic submucosal dissection (ESD) has been accepted as the best treatment option for early gastric cancer (EGC) without lymph node metastasis, synchronous gastric epithelial neoplasia is no longer rare in the clinical practice. Knowledge about the characteristics associated with synchronous gastric epithelial neoplasia is of great importance to prevent delayed diagnosis. Aims and Methods: Between November 2008 and December 2014, a retrospective study was conducted in a single tertiary referral hospital. Patients who underwent ESD due to EGC or high-grade dysplasia were analyzed to evaluate the incidence of synchronous gastric epithelial neoplasia and the factors associated to synchronous and overlooked synchronous lesions. Results: A total of 488 patients were analyzed in this study. Synchronous lesions were found in 59 patients (12.1%) during the mean 37.7 months of follow-up. Among 77 synchronous lesions, 23 lesions (32.4%) were overlooked at the time of initial ESD. Age of ≥ 65 years, moderate to severe endoscopic atrophic gastritis, and elevated morphology of primary lesions were associated with synchronous gastric epithelial neoplasia. An important factor associated with overlooked lesions was the non-rectified morphology of lesions. Conclusion: Careful endoscopic examination of the whole stomach is necessary in patients who are older and who have moderate to severe atrophic gastritis and elevated morphology of lesions to prevent delayed diagnosis of synchronous gastric epithelial neoplasia, especially non-rectified lesions. These factors may be considered as selecting candidates for ESD.

Disclosure: Nothing to disclose

P1796 TYPE AND TUMOR SIZE AFFECT CLINICAL OUTCOME IN GASTRIC NEUROENDOCRINE NEOPLASMS: A MULTICENTRE RETROSPECTIVE STUDY

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Introduction: Gastric neuroendocrine neoplasms (gNEs) are classified into three categories: type I associated with atrophic body gastritis, type II related to multi-endothelial neoplasia type I, and type III when no background pathology is
identified. Type I gNENs are indolent diseases, mostly with low proliferative index of 2%–5% and extremely low metastatic risk (<5%). Tumors > 1 cm are usually considered at higher risk of malignancy deserving more aggressive management, although data supporting this recommendation are scanty. Conversely, type III are malignant diseases with extremely high risk of dissemination and mortality. However, beyond the above-mentioned clinical classification, little is known on additional factors potentially related with poor clinical outcome in gNENs.

Aims and Methods: Retrospective analysis of type I and type III gNENs collected in eCuraC-1 and eCuraC-2 subgroup. Factor analysis was performed by logistic regression model. A composite negative endpoint was defined to identify patients with poor clinical outcome, and was considered to have occurred if tumor-related death, presence of metastases, or presence of angioinvasion at histology was observed. ROC curve analysis was used to identify the cutoff level variables predictors of presence of negative endpoint. Survival probabilities were calculated by the Kaplan-Meier method. The distribution of continuous variables was reported as median and interquartile range (IQR; 25th to 75th percentiles). Mann-Whitney U test was used to compare the continuous variables.

Results: 161 patients included, with a total of 195 tumors: 171 type I (87.7%), and 24 type III (12.3%). Compared with type III, type I gNENs were smaller (median size 5 mm and 15 mm, respectively. P < 0.0001) and with lower Ki67 (2% and 5.5%, respectively) negative endpoint occurred in 16 pts (9.9%), specifically in 14 type III (58.3%) and 2 type I (1.1%). In this subgroup, median Ki67 was 10% (3%–41%), and median size was 20 mm (14 mm–25 mm). Among patients with type I gNENs without features supporting negative endpoint (no tumor related death, no metastasis, no angioinvasion), 20.3% had Ki67 > 2%. When ROC analysis was performed to detect tumor size cut-off level able to predict negative endpoint, the value > 11 mm was identified (AUC = 0.921 < 0.0001). Overall, 12.3% type I and 70.8% type III gNENs were > 11 mm, respectively (p < 0.0001). Regarding proliferative activity, 21.6% type I and 62.5% type III had Ki67 > 2%. When multivariate logistic regression was performed, tumor type and size were associated with negative endpoint (clinical outcome: type II vs type I: OR = 9.2, p < 0.0005; size: OR 1.12 for each increasing mm, p = 0.0006), whereas Ki67 did not maintain statistical significance (OR 1.03 for each increasing unit, p = 0.149). Overall, 5-yr survival probability was 100% and 60.5% in type I and type III gNENs, respectively (p < 0.0001).

Conclusion: In addition to tumor type, size was the strongest negative prognostic factor, which independently predicted negative outcome in gNENs. Ki67 > 2% was observed in a relevant proportion (20.3%) of type I gNENs with indolent clinical course. Compared with type III, type I gNENs are considered to have a minor prognostic role in these tumors. When facing patients with gNENs, tumor type and size should be considered as major factors affecting clinical outcome.

Disclosure: Nothing to disclose.
Aims and Methods: Patients with NET confirmed on histology were identified from our gastrointestinal database. All patients underwent pre-procedure radial endoscopy (EUS) and abdominal CT scan. EMR, ESD or EFTR was performed in all patients under general anesthesia. High-definition gastroscopy (GH-HQ-190, Olympus Corporation, Japan) with distal transparent attachment was used. EMR was performed using diathermy snare. ESD and EFTR was performed using either Dualknife™ (Olympus) or Hybrid knife™ (ERBE GmbH, Germany). Hemostasis was achieved using Coagrasper™ (Olympus). For EFTR, closure was performed using hemoclip (Pillar 1.5 mm; Medtronic, USA) or Overstitch™ (Apollo Endosurgeries, USA). Foregut NETs were graded as G1, G2, or G3 on basis of proliferative activity by mitotic count. All patients underwent regular follow-up to evaluate for any local recurrence or distant metastasis.

Results: Foregut NET managed by ER include 23 patients (25 lesions). Location – Stomach – 1, duodenal bulb – 17, descending duodenum – 7. Males-16. Mean age 60.7 years. All lesions found incidentally during routine EGD for other indications. Most of the patients reported upper gastrointestinal symptoms. Endoscopic biopsy and histopathological evaluation, and a low complication rate.

Disclosure: Nothing to disclose

References

P1801 EFFECTIVE DIAGNOSTIC STRATEGY FOR GASTROINTESTINAL MALT LYMPHOMA FOCUSING ON TREE-LIKE APPEARANCE

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Introduction: Malignant lymphoma of the stomach can show diverse endoscopic findings; therefore, it is difficult to diagnose in many cases. Since a long time, multiple erosions and cobblestone-like mucosa have been considered as characteristic endoscopic findings of MALT lymphoma. However, tumour advancement into the submucosal layer can result in irregular, tortuous micro-vascularization [tree-like appearance (TLA)] that has been recently reported. In this study, we retrospectively investigated the characteristic endoscopic findings of gastrointestinal lymphomas, including MALT lymphoma.

Aims and Methods: Fifty patients who were histopathologically diagnosed with gastrointestinal malignant lymphoma (MALT lymphoma, 20; non-MALT lymphoma, 30) at our institute after 2010 were included in the study. The sensitivity and specificity of TLA using magnifying narrow-band imaging (NBI) and general endoscopy (based on Sano’s classification and the findings of Akamatsu et al.) were determined. Patients with treatment-resistant MALT lymphoma were followed up for these findings.

Results: Among patients who were observed using magnifying NBI, TLA followed up for these findings.

Conclusion: For Digestive Disorders, Pune, India

Disclosure: Nothing to disclose

References
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Introduction: Positron emission tomography/computed tomography (PET-CT) is an important imaging modality in the diagnosis, staging and monitoring the treatment response in oncology departments. As a result of the increased availability of PET-CT imaging, unexpected FDG uptake has been identified in a variety of sites in the gastrointestinal (GI) tract. Although incidental lesions of the GI tract on PET-CT scans are found only in about 3% cases, they are associated with a substantial risk of an underlying cancerous or precancerous lesion.

Aims and Methods: The aim of this study was to investigate whether incidental FDG uptake and any clinical and histopathological importance detected in patients with non-GI malignancy particularly in terms of disease in predicting malign lesions of the GI tract. Between February 2011 and November 2016, 12530 patients had undergone PET-CT scan. Patients with GI malignancies, patients with non-Suv-max value on PET-CT and patients without endoscopic and histopathological examinations were excluded from this study.

Patients with FDG uptake were stratified as follows: according to localization (esophageal, gastric and colorectal) and histopathological findings (benign and malign). Receiver operating characteristic (ROC) curves were used and optimal cut-off points were calculated to describe the ability of Suv-max value to predict the presence of a maligna process.

Results: 157 out of 12530 patients with GI tract FDG uptake and endoscopic/histopathological results were included into the study. 40 patients had abnormal localization of FDG uptake, 26 had gastric and 51 patients had incidental focal colorectal uptake. One patient had malignant mesenchymal tumor and 39 patients had benign conditions (37.5% esophagitis) at esophagus. 12 patients had lymphoma, 1 plasmocytoma involvement and 2 patients had a newly diagnosed carcinoma of the stomach at gastroscopy. As for benign conditions, 9 had gastritis, 6 had benign ulcers, 5 had submucosal lesions and 2 patients had hyperplastic polyps of the stomach. A total of 27 patients had premalign/malign conditions of the colon. The histological results are as follows: adenoma/malignant polyp (n = 15), colon cancer (n = 5), dysplasia (n = 4), in situ cancer (n = 1), colorectal adenocarcinoma (n = 1) and malign melanoma involvement (n = 1). The results of the benign condition of the colon are as follows: infectious colitis (n = 1), diverticular disease (n = 1), adenomotic line (n = 1), non-specific ulcer (n = 1) and no finding (n = 12). The cut-off points were calculated to describe the ability of Suv-max for predicting malign lesions of the GI tract. A total of 27 patients who had premalign/malign conditions of the colon.

Conclusion: Incidental focal gastric and colorectal FDG uptake is associated with a substantial risk of underlying premalign/malign conditions but not for esophagus. Gastroscopy and colonoscopy should be recommended due to incidental

Disclosure: Nothing to disclose

References
focal FDG uptake, early identification of these lesions may change management of these patients.

Disclosure: Nothing to disclose

P1804 PREVALENCE AND PROGNOSIS OF MISMATCH REPAIR DEFICIENCY IN OESOGRASTIC ADENOCARCINOMA

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immunohistochemistry (IHC) of MMR proteins were performed. Clinical data with follow up were available.

Aims and Methods: We enrolled all consecutive patients from 2010 to 2015 with junction or gastric adenocarcinoma for which tumor sample (biopsies or surgical samples) and clinical data between European and Asian studies. Questions have been raised about the dMMR prevalence was 26% in patients for less neoadjuvant chemotherapy was observed in dMMR compare to pMMR

Conclusion: The median OS for all stages was 32.8 months in dMMR versus 25.2 months in pMMR (p<0.003). Median DFS was 20.8 months in dMMR versus 17.3 months in pMMR (p<0.003). According to GP results, 16 patients (1 mild, 2 moderate) or 3 severe. Concordance between GP and histology was assessed using the kappa index. The accuracy and area under the ROC curve (C195%) of PG-I<30 pg/ml and PG-I/PG-II ratio<3 for the diagnosis of CAG2+ and of G-I<1 pmol/l for the diagnosis of AAG2+ were calculated.

Results: 131 consecutive patients were included (median 63 years (range 48–86), 60.3% women, 39.7% men). According to GP results, 16 patients (12% presented AG: 16 CAG (8 CAG2+), 12 CAG2+ and 6 multifocal AG (4 CAG2+, 1 AAG2+). The overall agreement between histology and GP was 75.6% (99/131), kappa index: 0.63. For the diagnosis of CAG2+, the overall efficacy of PG-I<30 pg/ml and PG-I/PG-II ratio<3 was respectively 96.2% (C195%: 91.4–98.4) and 95.4% (C195%: 90.4–97.9), with AUC-ROC 0.963 (C195%: 0.923–1) for PG-I and 0.967 (C195%: 0.928–0.997) for PG-I/PG-II ratio. For the diagnosis of AAG2+, the overall efficacy of G-I<1 pmol/l was 81.7% (C195%: 74.2–87.4) with AUC-ROC 0.745 (C195%: 0.611–0.878).

Conclusion: The serological biomarker panel GastroPanel® is an effective tool for the non-invasive screening of patients with uninvestigated dyspepsia, that allows detecting those patients at the highest risk of developing GC (basically, moderate/severe CAG).

Disclosure: Nothing to disclose

P1815 ACCURACY OF A SERUM BIOMARKER TEST (GASTROANALYSIS) FOR THE DIAGNOSIS OF MODERATE TO SEVERE ATROPHIC GASTRITIS IN PATIENTS WITH UNINVESTIGATED DYSEPSPSIA

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Introduction: Atrophic gastritis (AG) is the most important known risk factor for the development of non-cardial gastric cancer (GC), mainly in cases of extensive or advanced (moderate/severe) atrophy, Serological biomarkers (pspinogen-I (PG-I), pspinogen-II (PG-II), gastrin-17 (G-17), anti-H. pylori antibodies - HpAb-) provide non-invasive information about the morphological and functional integrity of the stomach, and they could be an useful tool for selecting patients at risk.

Aims and Methods: The aim of this study is to assess the diagnostic accuracy of a serological biomarker panel, GastroPanel® (GP) to predict the presence of moderate-severe AG in the corpus (CAG2+) and/or antrum (AAG2+) in patients with uninvestigated dyspepsia.

A prospective observational study was conducted. Inclusion criteria: patients >50 years, with uninvestigated dispepsia, submitted to our Endoscopic Unit for upper GI endoscopy. PPIs were discontinued 4 weeks before fasting levels of PG-I, PG-II, G-17 and HpAb were determined by ELISA method. Five gastric biopsies were obtained (2 antrum, 2 body and 1 incisura) during endoscopy, that were independently evaluated by two pathologists blinded to the GP result. In case of discrepancy, histologic slides were reviewed by a third external pathologist. Updated Sydney System (US$) was used to grade the presence of AG: 0 (absent), 1 (mild), 2 (moderate) or 3 (severe). Concordance between GP and histology was assessed using the kappa index. The accuracy and area under the ROC curve (C195%) of PG-I<30 pg/ml and PG-I/PG-II ratio<3 for the diagnosis of CAG2+ and of G-I<1 pmol/l for the diagnosis of AAG2+ were calculated.

Results: 131 consecutive patients were included (median 63 years (range 48–86), 60.3% women, 49.6% men). According to GP results, 16 patients (12% presented AG: 13 CAG and 3 AAG, while AG was observed in histology and GP was the same in 34 cases (25.9%): 16 CAG (8 CAG2+), 12 CAG2+ and 6 multifocal AG (4 CAG2+, 1 AAG2+). The overall agreement between histology and GP was 75.6% (99/131), kappa index: 0.63. For the diagnosis of CAG2+, the overall efficacy of PG-I<30 pg/ml and PG-I/PG-II ratio<3 was respectively 96.2% (C195%: 91.4–98.4) and 95.4% (C195%: 90.4–97.9), with AUC-ROC 0.963 (C195%: 0.923–1) for PG-I and 0.967 (C195%: 0.928–0.997) for PG-I/PG-II ratio. For the diagnosis of AAG2+, the overall efficacy of G-I<1 pmol/l was 81.7% (C195%: 74.2–87.4) with AUC-ROC 0.745 (C195%: 0.611–0.878).

Conclusion: The serological biomarker panel GastroPanel® is an effective tool for the non-invasive screening of patients with uninvestigated dyspepsia, that allows detecting those patients at the highest risk of developing GC (basically, moderate-severe CAG).

Disclosure: Nothing to disclose

P1805 USEFULNESS OF UNDERWATER EMR FOR NON- AMPULLARY DUODENAL TUMOR

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Introduction: Complication rate of endoscopic submucosal dissection (ESD) for superficial non-ampullary duodenal epithelial tumors (SNADET) is higher than that of other organ, because of thin muscle layer. Recently a new method, under- water EMR (UWEMR) has reported. However, the usefulness of UWEMR for SNADET.

The aim of this study is to investigate the outcome of UWEMR for SNADET.

One hundred seven lesions of SNADET were treated from Feb. 2016 to Feb. 2018. Lesions less than 15mm in size were indicated for UWEMR. Large lesions were indicated for ESDE or laparoscopic endoscopy collaboration surgery (LECS). Two, thirty-one and eight lesions were treated by EMR with injection, ESD and LECS, respectively. And the residual sixty six lesions undergone to UWEMR. The procedure was changed from UWEMR to EMR or ESD, when the snaring was impossible. Four and 4 lesions were treated by EMR and ESD, respectively. Finally, fifty-eight lesions were treated by UWEMR. UWEMR was performed with a 10-mm or 15-mm snare (SnareMaster; SD-210L-10, SD-210L-15, Olympus, Tokyo). Median age was 66 (43–87) years old. Macroscopic type; 0-I, 0-IIa and 0-IIc were 8, 26 and 24, respectively. Location; bulbs, 2nd portion and 3rd portion were 4, 42 and 12, respectively.

Artificial ulcer was closed by endo clips (EZ clip; HX-610-090L, Olympus, Tokyo) to prevent delayed perforation and bleeding. Intravenous PPI were used from just before UWEMR for two days, and followed by per-oral PPI
for one month. The patients were allowed to eat loose meal from two days after UWEMR.

Results: 1. The median diameter of tumor and specimen was 7 (2–25) and 12 (4–25) mm, respectively.
2. En-bloc resection rate was 91% (53/58). R0 and Rx rate was 69% (40/58) and 31% (18/58), respectively. When the final section contains neoplasia, lateral margin (LM) was diagnosed as LMs (N = 13). And, piecemeal resected cases were diagnosed as LMx (N = 5), too. The median diameter of tumor in R0 was 6 (3–18) mm. In contrast, that in LMx was 11 (2–25) mm. There was significant difference between diameter of tumor of R0 and that of RX (p = 0.0032).
3. The rate of local recurrence was 0%.
4. Closing method; The mean number of clips was 5 (1–8). A second look EGD was performed 2 days after UWEMR. And some clips were dropped in 4 of 58 cases. Artificial ulcer was closed by the remaining clips. All of the clips were remained in 93% (54/58). Therefore, second look EGD to check closure of ESD is unnecessary.
5. Complications; Perforation during UWEMR was 0% (0/58). The rate of delayed perforation and bleeding was 0% and 0%, respectively.

Conclusion: UWEMR is a safe treatment for SNADET. And, R0 rate in 10 mm or less was excellent. Clip closure after UWEMR was effective to prevent delayed bleeding and perforation. Second look EGD is unnecessary to check the closure of artificial ulcer.

References: None

Disclosure: Nothing to disclose

P1808 COMPARISON BETWEEN REDO ENDOSCOPIC TREATMENT AND SURGERY IN PATIENTS WITH RECURRENT GASTRIC NEOPLASMS
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Introduction: Treatment of locally recurrent gastric neoplasms after endoscopic resection remains challenging. We investigated the efficacy and safety of treatment options for recurrent gastric neoplasms localized to the scar of previous endoscopic submucosal dissection (ESD).

Aims and Methods: The clinicopathological characteristics and treatment outcomes of patients who underwent endoscopic treatment or surgery for recurrent gastric neoplasms between June 2010 and May 2017 were retrospectively reviewed.

Results: Of the 92 patients included, 74 underwent endoscopic treatment (54 redo ESD, 23 argon plasma coagulation [ APC] ablation) and 18 underwent surgery. The redo ESD procedure time was significantly longer than that of the primary ESD (31.0 versus 22.0 minutes, p = 0.018). Overall, adverse events occurred in 11 patients (12.0%), with the incidence being significantly higher in the surgery group (27.8% versus 8.1% in the endoscopic treatment group, p = 0.036). Local recurrence-free survival were 81.1% for endoscopic treatment group (86.3% and 69.6% for redo ESD and APC groups, respectively) and 100% for the surgery group (log rank p = 0.033). Logistic regression analysis showed that tumor size > 15 mm (odds ratio [OR]: 7.52, 95% confidence interval [CI]: 1.65-45.3, p = 0.014) and tumors located in the upper two thirds of the stomach (OR: 6.10, 95% CI: 1.32-37.1, p = 0.029) were associated with non-curative resection after redo ESD.

Conclusion: Endoscopic treatment could be an effective and safe alternative to surgery for selected patients with gastric neoplasms recurring at the site of previous ESD.

Disclosure: Nothing to disclose

P1809 EVALUATION OF GASTRIC POLYPS DETECTED BY ENDOSCOPY: WHAT IS THE CLINICAL SIGNIFICANCE?
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Introduction: Found in 6% of upper endoscopies, gastric polyps are a heterogeneous group of lesions that can vary in histology, neoplastic potential, and management. Currently, there are no clear guidelines for the management of these lesions.

Aims and Methods: The aim of this study was to evaluate gastric polyps, detected by upper endoscopy in our institution, with respect to their frequency, size, anatomic location, presence of dysplasia, histopathologic features and clinical outcomes. Clinical records from patients who underwent upper endoscopy with polypectomy between January 2012 and December 2017 were reviewed retrospectively.

Results: Of a total of 405 patients with a median age of 66 years (interquartile range 55–74 years) were included; 66.2% were female; 26.9% had Helicobacter pylori infection; 62.2% were taking proton pump inhibitors; 8.9% were diagnosed with hereditary polyposis or non-polyposis syndromes; 4.3% had a positive family history for gastric cancer. A total of 463 upper endoscopies with polypectomies were performed. Most polyps detected by endoscopy were solitary (56.8%). Of all gastric polyps, 40.2% measured between 0–5 mm, 27.0% between 6–9 mm and 32.8% ≥ 10 mm. Gastric polyps were found most commonly in the corpus/fundus (58.8%), followed by antrum (33.5%), cardia (5.6%) and a minority (2.2%) in the antrum-body transitional zone or anastomotic site. Histopathologically, the most common polyp type was hyperplastic (60.5%), followed by fundic gland (14.5%), nonspecific/foveolar polypoid hyperplasia (14.3%), inflammatory (8.5%), adenomatous (4.5%), neuroendocrine (1.5%) and hamartomatous (0.9%). Among adenomatous polyps, 11 were low-grade dysplasia, 6 high-grade dysplasia and 1 had features of adenocarcinoma. Additionally, 3 hyperplastic polyps had dysplastic foci; all of these were ≥ 10 mm. Dysplasia was shown to be significantly associated with polyp size ≥ 10 mm (p = 0.018) and Familial Adenomatous Polyposis (FAP) (p = 0.009). During a median follow-up period of 12 months (data available in 96 cases), 45.3% of gastric polyps recur, the large majority (78.9%) with the same histological type. Conclusion: Most polyps detected by endoscopy were solitary, smaller than 1 cm, and found in the corpus/fundus. The most common type was hyperplastic polyp. Dysplasia was shown to be significantly associated with polyp size ≥ 10 mm and
Familial Adenomatous Polyposis (FAP), which underlines the importance of endoscopic examination in such situations.

Disclosure: Nothing to disclose

**P1810** IMPACT OF PRE-NEOPLASTIC LESIONS AND TUMORS OF GI TRACT IN AFRICAN POPULATION IN PARMA AREA BASED ON PATHOLOGY RECORDS: RELATIONSHIP WITH RISK FACTORS AND HELICOBACTER PYLORI STATUS

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**Introduction:** In Italy, in recent years African population is increasing, in particular in some regions like Emilia-Romagna where in 2017 Africans were 11.9% out of resident population. The life style of African immigrants is different from the Italian one, in particular with regard to consumption of food and drinks, such as spices, alcohol consumption and smoking habit. The distribution of GI lesions both in Upper and in Lower tract is matter of interest for the public health in order to investigate risk factors, epidemiological data and burden of expenses in particular related with neoplastic diseases.

**Aims and Methods:** The aim of this study was to investigate the distribution of GI lesions in this two populations and to establish possible relationship with life style and epidemiological data. Based on records from Parma’s Department of Anatomio-Pathology a Database was performed collecting biopsies coming from Upper and Lower GI endoscopy from 01/01/2007 to 30/12/2017. In particular, 25,763 biopsies have been examined from Upper GI endoscopy and divided in 24,683 diagnosis of Chronic Atrophic Gastritis (CAG) and 1,080 of Gastric Cancer (GC), while 40,673 biopsies from Lower GI endoscopy have been analysed and were divided in 36,988 polyps and 3,685 diagnosis of Colo-Rectal Cancer (CRC).

The records of Database allowed to set apart two different groups: Group A standing for non-African population inhabiting in Parma and Group B for African population resident in Parma. Moreover, 321 consecutive African subjects resident in Parma (M/F 188/133), were enrolled to fill out a structured questionnaire about their feeding and life habits.

**Results:** Respectively 23,559 out of 24,683 CAG diagnosis (95.4%) and 1,076 out of 1,080 GC diagnosis (99.6%) were from Group A against 1,124 (4.5%) and 4 (0.4%) in Group B. However, Helicobacter pylori status was investigated in these pts and the data obtained showed 39% H.p.-+ in Group A and 68% in Group B. In Group A, 41% of CAG diagnosis (mean age 63.5 yrs) were associated with intestinal metaplasia (IM), about 3 times higher than in Group B (95 pts, m.a. 52 yrs); within African population IM was more common in people coming from Sub-Saharan Africa (59 pts, 14%) than people from North Africa (36 pts, 10%). Concerning Lower GI biopsies, 36,899 out of 36,988 (99.8%) colonic polyps diagnosis were observed in 19,356 pts (M/F 12,368/6,988) from Group A, showing an higher rate than in Group B in which colonic polyps were detected in just 89 biopsies (0.2%) from 78 pts (M/F 36/42). Furthermore no CCR was diagnosed in Group B.

Records obtained by the questionnaire showed that 60% of sample eat foods from their country, less refined and fiber richer, with a lower consumption of red meat; 88% use spices, 65% don’t drink alcohol and 92% don’t smoke. In addition, 49.6% rely on conventional drugs, only 50.4% admit to follow medical prescriptions and, 27% try as first approach drugs coming from their country.

**Conclusion:** The results obtained in the study show discrepancy between diagnosis of CAG and GC in non-African Parma population in comparison with African one. This data is in opposite to the trend of H.p. status in the two populations, as well as for the distribution of intestinal metaplasia. As regards Lower GI features, African people is affected by very little number of lesions (both colonic polyps and CCR). The results from questionnaire also demonstrated peculiar pattern of eating, smoking and drinking from African subjects, searching for original country products.

Disclosure: Nothing to disclose

**P1811** ACCURACY OF LINEAR-ARRAY EUS FOR PREOPERATIVE STAGING OF GASTRIC CANCER

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**Introduction:** The incidence of gastric cancer is declining worldwide. However, it still remains the second most common cause of cancer-related death in the world. Endoscopic ultrasound (EUS) is used for preoperative staging of gastric cancer due to its potential ability to assess both depth of local tumor infiltration and regional lymph node involvement. The indication and accuracy of linear EUS, however, are still controversial.

The aim of this retrospective multicenter trial was to determine the accuracy of linear EUS compared with the contrast enhanced computed tomography (CECT) and with final pathologic specimens with regard to tumor invasion depth and nodal status.

**Aims and Methods:** We retrospectively enrolled 132 cases of gastric cancer who underwent surgical resection between 2015 and April 2018 from two hospitals of Northen Italy, preoperatively evaluated for depth of invasion of tumor and lymph nodes involvement with linear EUS and classified according with TNM classification (UICC).

**Results:** Of 132 patients, 56 were localized in corpus, 45 in antrum, 20 in gastric angulus, 8 in fundus, 2 in cardia and in one case the tumor was in the pylorus. Mean age of patients was 65 (+-10) and mean tumor size was 45 (+-15) ranging from 15 to 80 mm maximum. The overall diagnostic accuracy of EUS in preoperative determination of cancer depth of invasion was 66.7% (4/6) and 62% (18/28), 65% (41/63), 76% (26/34), for T1 (T1b), T2, T3, and T4, respectively. The diagnostic accuracy of metastatic lymph node involvement or N staging of EUS was 68% (46/67) for N0 and 67% (50/65) for N+. The performance of T staging with CT scanners was not high: 66.7% for T1, 62% for T2, 61% for T3, 8% for T4. For lymph node involvement, the sensitivity for CECT was significantly lower than that for EUS: 47% for N1, 0% for N2.

**Conclusion:** Our data indicates that EUS may be superior to CECT in preoperative locally N staging. Additionally, EUS accuracy in T staging is still suboptimal and probably more than one single diagnostic procedure should be used.

Disclosure: Nothing to disclose

**P1812** CORRESPONDENCE BETWEEN GASTRIC FUNCTION MARKERS AND SEVERITY OF HISTOLOGICALLY ASSESSED GASTRIC INJURY: A PROSPECTIVE STUDY IN 144 CONSECUTIVE PATIENTS

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**Introduction:** Diagnosis of autoimmune diseases warrants exclusion of concomitant autoimmune disorders, as the coexistence in the single individual is frequent. The diagnosis of autoimmune gastritis (AG), a condition in which auto-antibodies targeted against components of the oxyntic epithelium progressively destroy the mucosa of gastric body (C) and fundus, is established histologically, with the presence of mucosal atrophy. Although the Operative Link on Gastritis Assessment (O.L.G.A.) is a widespread staging system for gastric atrophy, it does not provide information on the severity of disease in terms of degree of gastric function impairment.

**Aims and Methods:** The aim of the present study was to establish the usefulness of pepsinogen I (PGI) and gastrin-17 (G-17) in the evaluation of gastric atrophy severity, assessed by the O.L.G.A. staging system.

Patients with autoimmune gastritis, diagnosed by APCA positivity and histologically, with the presence of mucosal atrophy, was enrolled in the study. Serological determination of PGI and G-17 was performed in all. Patients on therapy with acid suppressants were excluded, as these drugs cause an alteration in serum levels of PGI and G-17. Accordingly to literature, patients were considered affected by gastric atrophy when PGI <30 pg/ml and G-17>7 pmol/l.

**Abstract**

**P1812** Concordance between PGI, G-17 and O.L.G.A. staging

<table>
<thead>
<tr>
<th>STAGE 0</th>
<th>STAGE I</th>
<th>STAGE II</th>
<th>STAGE III</th>
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<td>44.2 ± 34.9</td>
<td>118.6 ± 136.4</td>
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</table>

**PG I: Medium value ± SD**

**G-17: Medium value ± SD**

10.8 ± 9.74

122.8 ± 133.4

108.3 ± 78.4

A725
**PI813 HYPERTHERMIA REGULATES BOTH SLC22A16 EXPRESSION AND ABCG2 EXPRESSION VIA ROS PRODUCTION TO ENHANCE THE CYTOTOXICITY OF DOXORUBICIN**

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Introduction: Hyperthermia (HT) is a non-invasive cancer therapy. Treatment temperature between 41 to 44°C has no cytotoxic damage in normal cells, while it decreases viability of cancer cells because of the underdeveloped vascular system. HT often used with other cancer therapy such as radiation-therapy and chemotherapy. However mechanisms of synergistic effects among these therapies remains unclear. The 42°C environment is a cellular mild heat stress generating G1 phase of cell population, changes in mitochondrial and endoplasmic reticulum. We previously reported the expression of ATP-binding cassette sub-family G member 2 (ABCG2), which is known as breast cancer resistant protein (BCRP), was suppressed by increasing mitochondrial ROS to induce cancer specific p53 phosphorylation.

Aims and Methods: Since ABCG2 is a transporter of doxorubicin (DOX), we hypothesized that synergetic effect of HT and chemotherapy may be induced by down-regulation of ABCG2 expression via intracellular ROS increase. In this study, we elucidated whether HT with intracellular ROS increase by HT can enhance the cytotoxic effect of DOX for gastric epithelial cells. The gastric epithelial cancerous mutan, RKG1 was incubated at 37 or 42°C for 1h. Intracellular ROS generation was detected by electron spin resonance (ESR). Cytotoxic effect of DOX was measured using the Cell Counting Kit 8. ABCG2 expression was analyzed by Western blotting.

Results: ESR signal peak with HT treatment became high as compared to without HT treatment, indicating intracellular ROS level was increased by HT treatment. Cell viability and ABCG2 expression were decreased by DOX exposure and by HT treatment.

Conclusion: Thus we conclude that the enhancement of HT treatment effect by DOX is considered to be result of down-regulation of BCRP expression by ROS.

Disclosure: Nothing to disclose.

**PI814 HOXB9 FUNCTIONS AS A POTENTIAL ONCOGENE AND IS NEGATIVELY REGULATED BY miR-28-5P IN GASTRIC CARCINOMA**

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Introduction: Homeobox (HOX) genes encode a family of homeodomain-containing transcription factors that bind with specific DNA strands. HOXB9 is a member of the HOX family and is classified into B cluster. The function of HOXB9 has been extensively investigated in lung and breast carcinomas. However, knowledge about its function and regulation mechanism in gastric cancer (GC) is still quite limited.

Aims and Methods: This study aims to comprehensively investigate the expression and functional role of HOXB9 and elucidate its regulatory mechanisms in gastric carcinogenesis. HOXB9 were screened out by expression microarray of GC cell lines. The clinical relevance of HOXB9 in GC was analyzed from both online datasets and immunohistochemistry of tissue microarray. siRNA-mediated HOXB9 knockdown were applied in the functional assays such as cell proliferation, monolayer colony formation, cell invasion, cell-cycle distribution analysis, and anti-tumor drug sensitivity test. The miRNA that potentially binds to the 3’UTR of HOXB9 was predicted by miRDB and TargetScan. The regulation of miRNA by silencing was confirmed by qRT-PCR, Western blot, and dual luciferase activity assays. The in vitro functional roles of HOXB9 and miRNA were revealed by xenograft formation assay.

Results: HOXB9 showed higher miRNA expression compared with other HOX members in GC cell lines. The relative miRNA expression of HOXB9 was upregulated in GC cells compared with immortalized gastric epithelium cellGES-1. Its overexpression was associated with poorer outcome in GC patients. Knocking down HOXB9 led to suppression of cell proliferation, monolayer colony formation, and cell invasion ability. Furthermore, G17 levels showed a significant increase moving from stage I to stage II, a stage that corresponds to a different risk of developing gastric adenocarcinoma, so the serological markers resulted able to correlate to the severity of lesions, assessed by O.L.G.A. staging.

Conclusion: HOXB9 was further confirmed to be a direct target of tumor suppressor miRNA, miR-26-5p. Their expressions exhibited negative correlation in primary GC samples. Overexpression of HOXB9 partly reversed the tumor-suppressive effect of miR-26-5p.

Disclosure: HOXB9 is over-expressed and plays oncogenic role in gastric carcinogenesis. The activation of HOXB9 in GC is partly due to the silence of a tumor-suppressive miRNA, miR-26-5p. These findings not only elucidated a novel oncogenic transcription factor HOXB9 in gastric carcinogenesis but also enriched its regulatory mechanism by miRNA.

Disclosure: Nothing to disclose.
P1818 GASTRIC CANCER IN YOUNG ADULT: IT'S TIME TO SOUND THE ALARM
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Introduction: Although gastric cancer is considered as a disease of middle-aged and elderly, 2%-15% of patients with gastric cancer are young. Only a few studies with small samples have been conducted. The purpose of our study is to study epidemiological characteristics, evaluate the survival and prognostic factors of gastric cancer in young subjects.

Aims and Methods: This is a retrospective study including patients admitted in our department for gastric adenocarcinoma between January 2007 and June 2017. Our study included a descriptive component of the epidemiological and clinical characteristics of gastric cancer in patients under 45 and a univariate analytical component of clinical differences with older subjects, survival analysis (Kaplan-Meier) and prognostic factors in multivariate.

Results: 265 patients were included during this period. Patients under 45 accounted for 30.6% (n=81). The average age of our patients was 36±6.10. We observed a male predominance with a sex ratio H / F of 1.25. The familial factor was present in 22% of the cases. The tumor represented 62% of the cases. Histologically, the limitic form (24.7%, p=0.009) and the poorly differentiated ADK were significantly more frequent. 93.9% of patients had a significantly advanced or metastatic disease (p=0.002). Survival at 5 years in young subjects was 7%, in multivariate analysis only vascular invasion, advanced stage and limitic or poorly differentiated forms were prognostic factors.

Conclusion: In our study, gastric cancer remains frequent and aggressive in young subjects compared to western series. Survival remains low in the literature values.

Disclosure: Nothing to disclose.

WEDNESDAY, OCTOBER 24, 2018
9:00-14:00
H. Pylori III – Hall XI
P1817 EVALUATION OF EPIYA PATTERN IN HELICOBACTER PYLORI CAGA AND ITS POSSIBLE RELATION WITH PEPTIC ULCER DISEASE AND GASTRIC CANCER IN EGYPTIAN PATIENTS
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Introduction: Cytoxin associated gene A protein (CagA) of Helicobacter pylori (HP) is a major virulence factor that plays a crucial role in gastroduodenal pathologies [1]. CagA gene contains the Glu-Pro-Hex-Tyr-Ala (EPIYA) segments in its variable region. Polymorphisms of EPIYA motifs results in variations of bacterial virulence factors between HP strains [2]. According to this, the HP CagA gene is subcategorized as East Asian (more aggressive) or Western (less aggressive) types. Western strains contain only EPIYA motifs A, B and C. On the other side, East Asian strains contain EPIYA motifs A, B and D without EPIYA-C. The EPIYA pattern and its correlation with the various gastroduodenal disorders differ geographically. Understanding the role of EPIYA pattern could be used regionally as individual risk stratification tool for PUD and gastric cancer [3].

Aims and Methods: The aim of our work is to define the EPIYA pattern of the HP isolates in Egyptian patients and to evaluate any possible correlation with PUD and gastric cancer. One hundred and twenty-one patients were recruited in Cairo university Endoscopy unit. After signature of the informed consent, multiple biopsies from the antral and body part of the stomach were collected for molecular detection of HP and histopathological assessment. Fifty-eight HP isolates were detected by PCR. Out of them, 33 isolates contain CagA gene. After endoscopic and histopathological assessment, patients were divided to 3 groups: Chronic non-atrophic gastritis, PUD and gastric cancer. After that, the EPIYA motif genotyping was determined then patients were sub-grouped to 2 groups (No more than EPIYA-C motif and multiple EPIYA-C motifs). Finally, statistical analysis was done to determine any possible correlations with PUD or gastric cancer.

Results: Out of the 33 CagA positive strains, EPIYA-ABC was the most presented pattern in 23 isolates (69.7%) and the least common pattern was EPIYA-ABCC, which was positive only in two cases (6.1%). Both EPIYA-AB and EPIYA-ABC were detected in 4 strains for each (12.1% for each). There were significant statistical correlations between presence of CagA gene and PUD, beside the correlation between no more than one EPIYA-C motif group and chronic non-atrophic gastritis. No significant correlation was found between the increase in EPIYA-C motifs number and PUD or gastric cancer despite the fact that all patients with gastric cancer (4 isolates) had multiple EPIYA-C motifs.

Conclusion: In Egypt, the CagA gene is Western type with a variable number of EPIYA motifs. Furthermore, a significant statistical association is confirmed between the CagA gene and PUD. Regarding EPIYA pattern, a significant relation is found between the decrease in EPIYA-C motifs and chronic non atrophic gastritis (less aggressive behavior). But, no significant association is confirmed between the increase in number of EPIYA-C motifs and PUD or gastric cancer.

Disclosure: Nothing to disclose.

References

P1818 PRIMARY RESISTANCE OF H. PYLORI TO ANTIMICROBIALS AGENTS IN A NORTHERN ITALIAN REGION: RESULTS FROM A PROSPECTIVE 5-YEARS STUDY
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Introduction: Therapies for H. pylori are based on antimicrobial agents also used for other infectious diseases. Since antibiotic resistance develops continuously, it is mandatory to perform periodic prevalence assessment to guide clinicians in selecting the most appropriate therapy in their setting.

Aims and Methods: The aim of this study was to evaluate trends in the prevalence of primary resistance to clarithromycin, metronidazole and levofloxacin over a 5-year period. Consecutive 1325 native H. pylori-positive patients were studied between 2010 and 2015, and resistances assessed by E-test using the MICs clinical breakpoints recommended by the EUCAST (>0.5 mg/L, > 8 mg/L and > 1 mg/L for clarithromycin, metronidazole and levofloxacin, respectively). A univariate and multivariate logistic regression analysis was conducted to examine whether age, sex, BMI, smoking, alcohol consumption, familiarity for gastric cancer, education, country of birth, endoscopic findings and year of enrolment in the study were potentially involved in bacterial resistance.

Results: When all the 3 antimicrobial agents were considered together, only 39.1% (95% CI: 36.4 to 41.7) of patients were susceptible to all the drugs tested. In the remaining 60.9% (95% CI: 58.3 to 63.5), resistance to one, two or all three agents was present. However, 12.5% (95% CI: 10.9 to 14.4) of patients were resistant to all the antimicrobial agents. When clarithromycin and metronidazole were considered, 45.0% (95% CI: 42.3 to 47.7) of strains were susceptible to both factors. The remaining 55% (95% CI: 52.3 to 57.7), resistance to one or two agents was present. However, 22.6% (95% CI: 20.5 to 25.0) of patients were resistant to both antimicrobials. Considering clarithromycin, 39.2% (95% CI: 36.6 to 41.9) of the strains were susceptible, and 36.1% (95% CI: 30.4 to 41.9) were resistant. Considering metronidazole, 61.4% (95% CI: 58.7 to 63.9) of the strains were susceptible, and 38.6% (95% CI: 36.1 to 41.3) were resistant. Finally, considering levofloxacin, 61.4% (95% CI: 58.7 to 63.9) of the strains were susceptible, and 38.6% (95% CI: 36.1 to 41.3) were resistant. The multivariate analysis showed that the risk of carrying resistant strains increased significantly and independently over the years (OR: 1.15; 95% CI: 1.08 to 1.23; p < 0.0001; OR: 1.11; 95% CI: 1.04 to 1.19; p = 0.002; OR: 1.16; 95% CI: 1.08 to 1.25; p < 0.0001, for clarithromycin, metronidazole, and levofloxacin respectively).

Conclusion: The prevalence of primary resistances to the antimicrobial agents tested in our region was high and increased significantly between 2010 and 2015. Regional health authorities should consider to set up regular monitoring of primary resistance for H. pylori. If strategies to reduce and to improve the use of antibiotics are nor put in place, it will be increasingly difficult to eradicate H. pylori infection in future years.

Disclosure: Nothing to disclose.
P1819 PAN-EUROPEAN REGISTRY ON H. PYLORI INFECTED PATIENTS: BACTERIAL RESISTANCE OF 2,684 ISOLATES


Aims and Methods: Antibacterial resistance is the major cause of failed eradication of H. pylori. The aim of the study was to evaluate the resistance of H. pylori isolates to clarithromycin, metronidazole and levofloxacin in relation to the s/m genotype and the HtrA and GlmM expression of 157 H. pylori strains from antrum and corpus within each individual patient. We undertook a systematic register all adult patients infected with Helicobacter pylori. Data regarding resistance to antibiotics was available in 12% (2,684) of the cases. Resistance rates increased after each failed eradication attempt. Table shows antibiotic resistance per line.

No resistance

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Second</th>
<th>Third</th>
<th>Fourth</th>
<th>Fifth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin</td>
<td>35%</td>
<td>44%</td>
<td>48%</td>
<td>65%</td>
<td>64%</td>
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<tr>
<td>Metronidazole</td>
<td>39%</td>
<td>31%</td>
<td>60%</td>
<td>65%</td>
<td>64%</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>24%</td>
<td>18%</td>
<td>46%</td>
<td>42%</td>
<td>58%</td>
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</tbody>
</table>

Conclusion: There is a strong acquisition of antibiotic resistance after failed treatments.

P1820 HELICOBACTER PYLORI HTR A IS NOT ASSOCIATED WITH CLINICOPATHOLOGICAL GASTRITIS PHENOTYPE OR VACA VIRULENCE FACTOR POLYMORPHISMS

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Introduction: Virulence factors of Helicobacter pylori (H. pylori) affect the immunopathological gastritis pattern. The serine protease HtrA is a newly identified virulence factor that disrupts intercellular adhesion and contributes to the intercellular entry of H. pylori in vitro.

Aims and Methods: Aim of the study was to evaluate the phenotype of gastritis and HtrA expression of H. pylori isolates in relation to CagA and Vaca virulence factors. In a prospective study with focus on the relationship of H. pylori virulence and gastritis phenotypes, we cultivated 157 H. pylori strains from antrum and corpus from 89 patients with chronic gastritis (CNGA), atrophic gastritis (AG), peptic ulcer diseases (PUD) and gastric cancer (GC). H. pylori cagA, vacA s/m genotype and Htra and GlmM mRNA expression were determined by PCR. Anti- HtrA and anti-Caga-IgG status was evaluated using commercially available ELISA. Histological gastritis phenotype was characterized based on the updated Sydney score.

Results: All H. pylori isolates expressed Htra, which was similar between isolates from antrum and corpus within each individual patient. Htra expression was independent from cagA positivity or vacA s/m genotypes. There was no association between Htra expression and anti-Htra-IgG or anti-Caga-IgG systemic immune response. Histopathological analysis revealed similar Htra expression between patients with CNGA, AG, PUD or GC, which was not correlated with gastritis activity and chromicity scores. No correlation was found between Htra expression and intestinal metaplasia or degree of atrophy. PPI intake had no effect on the Htra expression.

Conclusion: Htra is constantly expressed in all H. pylori strains. However, Htra expression showed no association with gastritis phenotypes nor with cagA s/m or vacA status or H. pylori-erytol. The functional role of Htra remains uncertain.

Disclosure: Nothing to disclose

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Introduction: Culture methods have been traditionally used to evaluate the efficacy of Helicobacter pylori eradication assays. Nevertheless, they are material and time consuming so a quicker and easier methods are needed.

P1821 A QUICK FLOW CYTOMETRY PROTOCOL TO ASSESS HELICOBACTER PYLORI VIABILITY AND DENSITY


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2Equal first author contribution, Madrid, Spain
3Hospital Universitario de La Princesa, Instituto de Investigaciones, Madrid, Spain
4School of Chemical Sciences, Universidad Complutense de Madrid, Department of Organic Chemistry, Madrid, Spain
5Equal last author contribution, Madrid, Spain

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Annex: The mean rate of detection increased after each failed eradication attempt. Table shows diagnostic test used, culture and susceptibility testing, or molecular tests for the evaluation of antibiotic resistance.

Results: No resistance

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Second</th>
<th>Third</th>
<th>Fourth</th>
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<tr>
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<td>24%</td>
<td>18%</td>
<td>46%</td>
<td>42%</td>
<td>58%</td>
</tr>
</tbody>
</table>

Conclusion: The mean rate of H. pylori clarithromycin resistance (22%) in European treatment-naïve patients discourages the empirical use of standard triple therapy. Furthermore, concomitant treatment may be soon limited by the increasing dual resistance to clarithromycin and metronidazole (13%). There is a strong acquisition of antibiotic resistance after failed treatments.
Aims and Methods: We aimed to design a protocol to assess *H. pylori* viability using flow cytometry (FC). Strain T agR-26695 was cultured in Columbia Agar medium supplemented with blood (COS). Growing bacteria were suspended in 0.9% NaCl (3 McFarland of turbidity). Colony counting was performed by 1:10 dilution, plating 10lg in COS and 5-days incubation in a CO₂ incubator. Aliquots of bacterial suspension were killed by heat, 70% isopropanol, or 0.5% bleach. Live-dead mixed suspensions were performed, ranging from 0–100% in intervals of 10% of live. Live/Dead BacLight™ Kit was used to stain bacteria for FC analyses using FACS-CantoII cytometer. The%live bacteria added to each mix was compared to the% live estimated by FC. Counting beads (CB) were used to estimate the microbial density using FC.

Results: The optimized protocol involved addition of 1.5μl Syto9 and 0.2μl propidium-iodide to a 1:100 dilution of the bacteria in 979μl NaCl (15 minutes, dark). The CB were added immediately before FC acquisition. A good correlation between the % live and the FC-estimations were obtained for the heat-killed (R²=0.99) and the isopropanol models (R²=0.97). Bleach treatment caused the fragmentation of bacteria, and could not be properly detected using FC. Bacterial density estimations were comparable between FC and culture.

Conclusion: FC is a fast, accurate and reproducible method to assess *H. pylori* density and viability.

Disclosure: Nothing to disclose

**P1823 SHORT-TERM AND LONG-TERM CHANGES OF GUT MICROBIOTA AND METABOLIC PARAMETERS AFTER HELICOBACTER PYLORI ERADICATION**

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³Tu Jer Catholic University, School of Medicine, New Taipei City, Taiwan
⁴Aberdeen University – St George & Sutherland Clinical School, Aberdeen University, Sydney/AU, St George & Sutherland Clinical School, Australia

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Introduction: Little is known about the long impact of *Helicobacter pylori* (*H. pylori*) eradication therapies on the gut microbiota and metabolic parameters. Aims and Methods: We aimed to assess the changes in the gut microbiota and metabolic parameters before and 2 weeks, 2 month, and 1 year after first-line treatment of *H. pylori* infection. Adult patients with documented *H. pylori* infection (n=1620) were randomized in this multicenter, open-label trial to receive concomitant therapy for 10 days (CT10) or bismuth quadruple therapy for 10 days (BQ10) or triple therapy for 14 days (TT14). The long-term outcomes included the reinfection rate, the changes in the gut microbiota, body weight, glucose, insulin resistance, and lipid profiles. Fecal samples were collected before and 2 weeks, 2 months, and at least 1 year after eradication therapy in a sub-group of patients (National Taiwan University Hospital and its Yun-Lin Branch). Amplification of the V3 and V4 hypervariable regions of the 16S rRNA was done followed by high throughput sequencing (Illumina miseq). Weighted-unifrac method was used to analyze the β-diversity.

Results: Of the 1155 successfully treated patients, reinfection/recrudescence was observed in 3.3% (13/390), 2.6% (10/388), and 3.4% (13/377) of patients treated with TT14, CT10, and BQ10 after 1.55 years, respectively (p=0.751) in our preliminary results. 16S rRNA was sequenced and analyzed in a total of 782 fecal DNA samples. Compared to baseline (N=83), the species richness (α-diversity) was significantly reduced at 2 weeks (N=57, p=0.000078), but the species richness (β-diversity) gradually returned at 2 month (N=70, p=0.11) and 1 year (N=79, p=0.83) after TT14 treatment. Compared to baseline (N=76), α-diversity was significantly reduced at 2 weeks (N=40, p=6.3x10⁻¹⁵), at 2 month (N=62, p=0.0015), and 1 year (N=65, p=0.017) after CT10 treatment. Compared to baseline (N=83), the α-diversity was significantly reduced at 2 weeks (N=32, p=9.1x10⁻¹⁷), at 2 month (N=72, p=3.3x10⁻¹⁸), and 1 year (N=63, p=0.0024) after BQ10 treatment. Compared to baseline, there was significant

<table>
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<tr>
<th>Abstract No: P1823</th>
<th>Table 1: Univariate analysis showing factors affecting <em>Helicobacter pylori</em> eradication rates in the ITT and PP populations</th>
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<td><strong>Pylera</strong></td>
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<td>Female</td>
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<td>NSAIDs consumption – Yes</td>
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<td>Dyspepsia – Ulcer</td>
<td>58/71 (81.6%)</td>
</tr>
<tr>
<td>Endoscopic findings</td>
<td>78/90 (86.6%)</td>
</tr>
</tbody>
</table>

*p < 0.005*
differences in the fecal microbiota structure (β-diversity) at 2 weeks (p = 0.0003) and 4 months (p = 0.0047) after TT14, but the difference was not significant at 1 year (p = 0.085). There was significant difference in the β-diversity at 2 weeks (p = 0.0001) and at 1 year (p = 0.038) after CT10. There was significant difference in the β-diversity at 2 weeks (p = 0.0001), 2 months (p = 0.0002), and 1 year (p = 0.0074) after BQ10. We observed mild increase in the body weight (64.3 vs. 65 kg, p < 0.001), body mass index (24.38 vs. 24.59, p < 0.001), high-density lipoprotein (54.9 vs. 58.4 mg/dL, p < 0.001), and total cholesterol (194.6 vs. 197.8 mg/dL, p = 0.009) 1.5 year after eradication therapy. However, there were no significant changes in the insulin resistance (HOMA-IR) and low-density lipoprotein levels.

Conclusion: The abundance and diversity of gut microbiota changed significantly immediately after H. pylori eradication therapy. The microbiota appeared to be more balanced with the speed and extent of restoration varied according to the eradication regimens. (Fundled by National Taiwan University Hospital and Ministry of Science and Technology of Taiwan; ClinicalTrials.gov, NCT01908679)

Disclosure: Nothing to disclose

Reference

P1824 EFFECTIVENESS OF PYLERA AS FIRST-LINE ERADICATION THERAPY FOR H. PYLORI INFECTIONS
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Introduction: Pylera associated with a proton pump inhibitor (PPI) for 10 days is, according to the Spanish guidelines on H. pylori infection, considered as first-line eradication therapy, after proving a satisfactory efficacy (more than 90%). Our working group recommends that H. pylori eradication treatments should be validated in each geographical area before they can be recommended as a first-line therapy. Aims and Methods: Unscent, observational, prospective, non-controlled study. A total of 125 consecutive patients with Helicobacter pylori infection were included from 2016-2018. The average age is 54-year-old (18-81), 57% women, 41.6% with non-investigated dyspepsia, 25.6% with functional dyspep-sia, 12.9% with peptic ulcer disease and 13.6% with other diagnoses. All patients received a first-line therapy with Pylera for 10 days, 3 capsules four times a day with a PPI (68% omeprazole 40 mg) at breakfast and dinner. In each patient was studied the compliance, adverse effects by telephone contact as well as and the efficacy. The treatment was considered effective when the urea breath test (UBT) was negative 4 weeks after finishing treatment. All cases are included in H.pylori European Register (HP-Eureg) and monitored through AEG-REDCap platform.

Results: 119 patients (95.2%) completed the treatment (> 90% of the dose), 5 of the 6 patients that discontinued treatment were due to adverse events. 35% of patients (28%) reported some side effect, being serious adverse event in only 1 patient (Ca difflcultis). H. pylori eradication rates were 94.9% (IC 95% 90.9-98.9) of patients treated with Pylera protocol and 92% (IC 95% 87.1-96.8) of patients (115/125) for the intention to treat analysis.

Conclusion: Therapy with Pylera for 10 days has, according to our experience, high efficacy, high compliance (>90%) and acceptable security, being a recommended therapeutic option as first-line eradication therapy.

Disclosure: Nothing to disclose

P1825 EFFICACY OF ORAL N-ACETYL CYSTEINE ON HELICOBACTER PYLORI ERADICATION IN ADDITION TO QUADRUPLE THERAPY REGIMEN
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1Razi, Rasht, Iran (Islamic Republic of)
2Guilan University of Medical Sciences Gastrointestinal and Liver Diseases Research Center, Rasht, Iran (Islamic Republic of)
3Guilan University of Medical Sciences, Rasht, Iran (Islamic Republic of)

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Introduction: N-acetyl cysteine (NAC) has mucolytic, antioxidiant, and antiin-flammatory effects which has been suggested recently as an adjuvant to the eradica-tion of Helicobacter pylori (H. pylori) infection. This study was aimed to determine the effectiveness of NAC in addition to standard quadruple therapy on Eradication of Helicobacter Pylori.

Aims and Methods: In this double-blinded controlled clinical trial (IRCT2016052011552N24), 92 patients with the diagnosis of H. pylori infection in gastroenterologic biopsies were randomly allocated into intervention and control groups. Both groups received a 14-day regime of quadruple therapy comprising amoxi-clin, clarithromycin, pantoprazole and bismuth subcitate. In addition to quadru-ple therapy regimen with similar timing, the intervention and control groups received NAC and placebo, respectively. The urea breath test (UBT) was performed to confirm the eradication of H. pylori eight weeks after the end of treatment.

Results: The percentage of H. pylori eradication in the intervention and control groups was 78.3% (CI 95%: 66.38-90.21) and 71.7% (CI 95%: 59.57-84.49), respectively (p = 0.004) which were not statistically significant. Eradication rate was significantly higher in smokers who were treated with NAC.

Conclusion: Although the H. pylori eradication rate was higher in patients who received NAC as an adjunctive drug, it was not statistically significant.

This study showed that the rate of H. pylori eradication significantly increased in smokers who received NAC.

Disclosure: Nothing to disclose

P1826 EFFECTS OF PROBIOTICS OR BROCCOLI SUPPLEMENTATION ON HELICOBACTER PYLORI ERADICATION WITH STANDARD CLARITHROMYCIN-BASED TRIPLE THERAPY
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Introduction: The eradication failure of standard triple therapy (proton pump inhibitor, clarithromycin and amoxicillin) for Helicobacter pylori infection has increased due to antibiotics resistance in Korea. Supplementation of some probiotics improved H. pylori eradication rates and reduced the adverse events of the triple therapy. Sulforaphane extracted from broccoli is a potent bacteriostatic agent against H. pylori strains, and also exhibits bactericidal effects in a human epithelial cell line.

Aims and Methods: We aimed to determine whether Saccharomyces boulardii probiotics or sulforaphane supplementation can increase the H. pylori eradication rate and/or reduce antibiotics-associated adverse events in a Korean population.

Disclosure: Nothing to disclose

Results: The eradication failure rates according to ITT and PP analyses were 85.2% and 88.1% in group A, respectively. ITT and PP analyses were 89.1% and 90.9% in group B, respectively. The eradication rates between the three groups were not different (p = 0.262).

Conclusion: Probiotics or sulforaphane supplementation with triple therapy on H. pylori infection neither increased the eradication rate nor reduced the adverse events in a Korean population.

Disclosure: Nothing to disclose

Reference
plus amoxicillin 1000 mg for the first 3 days followed by clarithromycin 500 mg and tinidazole 500 mg t.i.d. for the remaining 5 days, or bismuth-based therapy with omeprazole 20 mg b.i.d. and Pylera® 3 tablets q.i.d. for 10 days. H. pylori eradication was assessed by using 13C-urea breath test.

Results: A total of 495 patients were enrolled. Following sequential (250 patients) and quadruple (245 patients) therapies, respectively, the eradication rate were 92% and 91% at intention-to-treat and 96% and 97% at per protocol analyses. Overall, the pattern of bacterial resistance did not significantly affect the cure rate, but the presence of clarithromycin and metronidazole dual resistance tended to negatively affect the cure rate of both sequential therapy (90.1% vs 91.5%) and quadruple (85% vs 94.1%; P = 0.06) therapies. Adverse events occurred more frequently with the quadruple than with sequential therapy (56.9% vs 25.8%; P < 0.001).

Conclusion: In our country, sequential and bismuth-based quadruple therapies achieved similarly high eradication rates as first-line treatments for H. pylori infection in clinical practice.

Disclosure: Nothing to disclose

P1828 FATE OF BENEFICIAL GUT MICROBIOTA AFTER H. PYLORI ERADICATION THERAPY: METAGENOMIC LANDSCAPE OF RESISTANCE MECHANISMS

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Introduction: Antimicrobial agents have a significant impact on gut microbiota and its functions. Negative effects of antibiotics can be associated with depletion of beneficial microbiota and increasing amount of antibiotic resistance genes in potentially pathogenic bacteria.

Aims and Methods: The aim of our study was to evaluate the effect of H. pylori eradication therapy on the distribution of antibiotic resistance genes especially in cases of beneficial microbiota survival. Stool samples from 35 H. pylori-positive patients before and after eradication therapy according to the standard protocol of Maastricht IV were analysed. Shotgun sequencing was performed on the SOLID 5000d W platform according to the manufacturer’s recommendations. Reads were aligned to the CARD database (version 1.1.7) with bowtie 1.2.0 software.

Results: Significant changes in ratio and number of microorganisms including beneficial microbiota were detected in the intestinal microbiome of all patients after eradication therapy. Thus, 28 (80%) patients showed a decrease in the Bifidobacterium proportion and 12 (34.3%) patients had a decreased Lactobacillus ratio after therapy. An increase in Bifidobacterium and Lactobacillus genera was detected in 2 (5.7%) and 1 (1.7%) cases, correspondingly. These genera were absent in gut microbiota of 2 (5.7%) and 7 (20%) patients. Significant quantitative changes have been identified in genes that determine resistance to 8 out of 28 antibiotic groups (according to CARD): determinants of ampicillin, beta-lactam, macrolide, tetracycline, metronidazole, streptomycin, MLSB resistance, resistance to glycopeptide antibiotics, peptide antibiotics, efflux pump complex or subunit conferring antibiotic resistance. The changes were also accompanied by the variability of antibiotic resistance genes abundance in Bifidobacterium and Lactobacillus, including blsE, tetW, car-TC, specifying mupirocin, tetracycline and chloramphenicol resistance in those bacteria.

Conclusion: The data indicates that H. pylori eradication therapy associated with the use of b-lactams and macrolides induces significant changes in the pattern of resistance genes to antimicrobial drugs of different groups in beneficial representatives of gut microbiota. Metabolic pathways and resistance of the corresponding organisms remain to be studied in pure cultures.

Disclosure: The work is performed according to the Russian Government Program of Competitive Growth of Kazan Federal University. The research was performed using the equipment of Interdisciplinary Centre for Shared Use of Kazan Federal University


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Introduction: The success of Helicobacter pylori (H.p.) eradication therapy is based on the effectiveness of the cure, as well as on the resistance of H.p. strains to the antibiotics in different areas.

Aims and Methods: Aim of this study was to compare different intervals between the first H.p. eradication therapy and the second attempt, by using for both, the same scheduled therapy.

Two hundred and fifty nine consecutive H.p. positive patients (Male 135, Mean Age 52 years range 27-81) were enrolled in the study, after failure of first line treatment based on triple one week therapy (Omeprazole 20 mg/b.i.d., Amoxicillin 1 g/b.i.d., Tinidazole 500 mg/b.i.d.). All patients underwent a rescue therapy based on the same schedule at different intervals from the end of the first line therapy: 35 pts (Male 22 Mean age 51 range 27-72) after 7-10 days (Group 1); 44 pts (Male 24 Mean age 53 range 28-75) after 1 month (Group 2); 94 pts (Male 43 mean age 43 range 29-78) after three months (Group 3); 98 pts (Male 46 mean age 53 range 28-81) after six-twelve months (Group 4). The H.p. eradication was established by means of U.B.T., performed at least one month after the end of rescue therapy.

Results: The success of the therapy in the four groups is summarized in the table. In Group 1 we experienced 4 drop outs, 5 in Group 2, 8 in Group 3 and 9 in Group 4.

Conclusion: The interval between the first and the second attempt of H.p. eradication therapy seems in our study crucial in determining the success of the cure, at least a six-months interval being the critical time to influence the results.

<table>
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<th>Group</th>
<th>Cured patients</th>
<th>Intention to treat</th>
<th>Per protocol</th>
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</table>

P183000-DAY Versus 14-DAY Quadruple Concomitant Non-Bismuth Therapy for the Treatment of Helicobacter pylori Infection: Results from a Greek Randomized Prospective Study


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Introduction: According to all current available data, there is so far no universally effective regimen for Helicobacter pylori (H. pylori) eradication therapy. The Toronto Consensus for the treatment of H. pylori infection recommends that both the concomitant non-bismuth quadruple therapy (proton pump inhibitor + amoxicillin + metronidazole + clarithromycin) and the traditional bismuth-containing quadruple therapy (PPI + bismuth + metronidazole + tetracycline) should play a more prominent role in eradication of H. pylori infection, and should be used for 14 days. The Maastricht V Consensus also recommends as first-line treatment in areas of high (>15%) clarithromycin resistance, a 14-day course of either the bismuth or the non-bismuth quadruple, concomitant therapies, unless a 10-days regimen is proven equally effective (Maasstricht V). Moreover, the American College of Gastroenterology (ACG) Clinical Guideline for the treatment of H. pylori infection clearly state that prior antibiotic exposure should be incorporated into the decision-making process and that most patients would be better served by first-line treatment with non-bismuth concomitant therapy for a period of 10-14 days, although the quality of evidence regarding duration is still very low. The objective of this study is to compare the efficacy rates of the 10-day versus the 14-day PAMC therapy in Greece, a country with an antibiotic-resistance pattern similar to the USA and most central and southern European countries (high clarithromycin resistance >20% and intermediate metronidazole resistance <40%).

Aims and Methods: Our prospective randomized study included 384 patients with newly diagnosed H. pylori infection, randomized to receive a 10-day or a 14-day concomitant PAMC therapy. Treatment outcome was assessed by 13C-urea breath test at least 4 weeks after therapy. Intention to treat (ITT) and per protocol (PP) analysis of the eradication rates were performed. Secondary end points included patient compliance, safety and eradication rates related to previous antibiotic exposure (ClinicalTrials.gov Identifier: NCT02959255).

Results: The two groups achieved almost equal eradication rates, both in the ITT and in the PP analysis (85.1% for the 10-day versus 85.9% for the 14-day, p > 0.05, and 93.6% for the 10-day versus 94.4% for the 14-day, p > 0.05, respectively), after adjusting for gender, smoking status, prior exposure to antibiotics, peptic ulcer disease and/or non-ulcer dyspepsia. Patient compliance was excellent for both groups (99.5% for the 10-day and 98.7% for the 14-day concomitant PAMC treatment group, p > 0.05). Major adverse events that led to discontinuation of the treatment were not statistically significant between groups (p > 0.05). Regarding minor adverse events, a trend towards more episodes of diarrhea was recorded in the 14-day (group A) versus the 10-day therapy group (25.4% and 34.7%, respectively, p > 0.05).
Introduction: Eradication of Helicobacter pylori (H. pylori) is accepted as initial treatment of low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma. However, 10–20% of gastric low grade MALT lymphomas are resistant to H. pylori eradication therapy. The aim of this study was to find out the predictive factors of complete remission of gastric MALT lymphoma after H. pylori eradication.

Aims and Methods: From 2006 to 2016, consecutive 64 patients with modified Ann Arbor stage IE and IIIE gastric MALT lymphoma were enrolled, and their medical records were reviewed. The patients were initially treated by H. pylori eradication. The complete remission was determined by endoscopic and histologic finding.

Results: 48 patients (75%) achieved complete remission after H. pylori eradication therapy. Mean follow up time for these patients was 38.8 months [6–72 months]. Eight patients (12.5%) failed to achieve complete remission. Eight patients were lost of sight. There was no significant difference in the age, sex, endoscopic appearance, and large cell component between the remission group and failure group. Among 12 patients with proximal tumor, 8 patients (66.6%) achieved complete remission. On the other hand, among 52 patient with distal tumor, 40 patients (76.9%) achieved complete remission. The odds ratio of proximal tumor for H. pylori eradication failure was 28.9 (95% CI = 2.9–288.0).

Conclusion: The discovery of the etiologic role of H. pylori infection in gastric lymphoma has radically changed its therapeutic approach. The proximally location of MALT lymphoma is a risk factor of the H. pylori eradication treatment failure.

Disclosure: Nothing to disclose

References

P1834 INTERACTION OF H. PYLORI WITH TOLL-LIKE RECEPTOR 2 -196 TO -174 DEL POLYMORPHISM, IS ASSOCIATED WITH GASTRIC CANCER SUSCEPTIBILITY BUT NOT POOR PROGNOSIS IN CHINESE PATIENTS

Introduction: Genetic polymorphisms of Toll-like receptors (TLRs) play important roles in gastric carcinogenesis. The -196 to -174 deletion polymorphism of TLR2 gene influences its promoter activity. Aims and Methods: The aim of this study is to determine whether this polymorphism is associated with susceptibility to gastric carcinoma and its prognosis. This study consisted of 260 patients with gastric cancer and 260 healthy controls. All subjects were unrelated ethnic Han Chinese and residents in Jiangsu Province, People’s Republic of China. The polymorphism was assessed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis. The infection status of H. pylori was determined using a validated serological test. Survival was analyzed by Kaplan-Meier survival curves.

Results: Multiple logistic regression analyses revealed that the -196 to -174 del genotype (adjusted OR = 2.59, 95% CI = 1.33–5.07) but not ins/del genotype (adjusted OR = 1.36, 95% CI = 0.95–1.96) had significantly higher gastric cancer risk.

Conclusion: Our findings indicated that H. pylori CagA plays a crucial role in promoting gastric carcinogenesis via activation of the onecogene YAP pathway and subsequent enhancement of EMT.

Disclosure: Nothing to disclose

References
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The eradication therapy for H. pylori infection has been widely performed. On the other hand, GC is discovered after successful eradication. Since GC is approved as an insurance indication since 2013, and the eradication treatment is effective in eradicating 

Gastric cancer (GC) is one of the most fatal forms of malignant cancers. Recently discovered microRNAs (miRNAs) post-transcriptionally regulate gene expression and play important role in a variety of processes. The aim of the study was to examine hsa-miR-20b-5p (miR-20b) function in gastric cancer by experimentally determining miRNA target-genes and impact on physiological cell processes in vitro and in vivo. 

**Aims and Methods:** GC cell lines (AGS, MKN28) and normal gastric tissue were used. Following serum-free medium after bifurcation, expression of miR-20b in AGS and MKN28 was evaluated using qRT-PCR. Cell viability was assessed using a MTT assay, colony formation and proliferation was evaluated using clonogenic assay, and cell migration was determined using wound healing assay. INS-GAS mice model was used to evaluate the miR-20b alterations in vivo following H. pylori infection with follow up to 50 weeks.

**Results:** H. pylori infection significantly increased miR-20b expression in AGS and MKN28 cell lines (p < 0.003; AGS and MKN28 respectively) compared to cells transfected with control miRNA. INS-GAS mice showed gender specific miR-20b expression and proliferation was evaluated using clonogenic assay, and cell migration was determined using wound healing assay. INS-GAS mice model was used to evaluate the miR-20b alterations in vivo following H. pylori infection with follow up to 50 weeks.

**Conclusion:** Our data shows that miR-20b may target PTEN and TXNIP and play an important role in gastric carcinogenesis by mediating cell viability and colony formation in GC-derived AGS and MKN28 cell cultures. The data from INS-GAS mice experiments support the role of miR-20b in GC in vivo.

**P1825**

**INHIBITION OF MIR-20B REDUCES CELL VIABILITY AND COLONY FORMATION IN GASTRIC CANCER BY TARGETING PHOSPHATASE AND TENSIN HOMOLOG (PTEN) AND THIREDOXIN-INTERACTING PROTEIN (TXNIP) GENES**


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**Introduction:** Gastric cancer (GC) is one of the most fatal forms of malignant cancers. Recently discovered microRNAs (miRNAs) post-transcriptionally regulate gene expression and play important role in a variety of processes. The aim of the study was to examine hsa-miR-20b-5p (miR-20b) function in gastric cancer by experimentally determining miRNA target-genes and impact on physiological cell processes in vitro and in vivo.

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**Conclusion:** Our data shows that miR-20b may target PTEN and TXNIP and play an important role in gastric carcinogenesis by mediating cell viability and colony formation in GC-derived AGS and MKN28 cell cultures. The data from INS-GAS mice experiments support the role of miR-20b in GC in vivo.
Disclosure: Nothing to disclose

P1838 HELICOBACTER PYLORI INFECTION AND THE INTERLEUKIN 8 -251 T>A POLYMORPHISM MIGHT BE A RISK FACTOR OF GASTRIC CANCER

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Introduction: IL-8 is a major neutrophil-activating cytokine and plays a central role in the immuno-pathogenesis of H. pylori-induced gastric mucosal injury. The IL-8 -251 T>A polymorphism has been reported to be associated with increased production of IL-8 protein, and higher risks of atrophic gastritis (AG), peptic ulcer disease (PUD), and gastric cancer (GC). However, many other reports are inconsistent with these findings.

Aims and Methods: We aimed to investigate i) whether polymorphisms in IL-8 influence susceptibility to H. pylori infection, and the associations of the polymorphisms with the risk of gastroduodenal diseases in a Korean population, and ii) analyze our and other investigators’ large-scale data regarding the IL-8 -251 T>A polymorphism and GC risk in Korean, Chinese, and Caucasian populations.

We consecutively enrolled 176 H. pylori-negative control subjects, 221 subjects with H. pylori-positive non-atrophic gastritis, 52 mild AG, 61 severe AG, 175 PUD, and 283 GC. Allele-specific PCR-RFLP was conducted for polymorphisms in IL-8 -251 T>A. IL-8 levels in gastric mucosal tissues were measured by enzyme-linked immunosorbent assay. We collected large-scale raw data of GC patients (n = 3,217) and controls (n = 3,810) from Asian (Korea, Japan, and China), and Caucasian (Poland, Finland, and Portugal) populations, and analyzed GC risk according to the Sydney system. Results: IL-8 levels were significantly different between T/T wild type, T/T heterozygote, and A/A mutant genotypes. IL-8 -251 A allele carriers (A/A + T/A) showed increased IL-8 levels, and were significantly associated with the risk of severe AG and GC. Global data of IL-8 polymorphism and the risk of GC development showed that Japanese population was similar to Korean population. The combined Korean and Japanese populations had significantly increased GC risk for the IL-8 -251 T/A and A/A genotypes compared to the T/T genotype, and for A allele carriers compared to non-carriers.

Conclusion: We suggest that a combination of H. pylori infection and the IL-8 -251 T>A polymorphism might increase the risk of severe AG and GC in a Korean population.

Disclosure: Nothing to disclose

References


P1839 DETECTION OF LESIONS IN HELICOBACTER PYLORI GASTRITIS BEFORE AND AFTER ERADICATION BY EXPERT ENDOSCOPISTS

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ABSTRACT

Helicobacter pylori (HP) infection is commonly responsible of multifocal atrophic gastritis without intestinal metaplasia, intestinal metaplasia and dysplasia, which is the most relevant premalignant gastric condition (PGC). HP eradication is mandatory to stop the chronic gastric inflammation, but the long-term follow-up of gastric premalignant/malignant lesions progresses even after HP eradication. Several studies showed that high-resolution endoscopy with narrow-band imaging (HRE-NBI) could be more precise in diagnosing dysplasia after HP eradication, presumably as the gastric mucosal aspect is less corroborated by the inflammatory changes induced by the antibiotic infection, which could lead to an underestimation of the premalignant lesions. These findings suggest that a non-invasive test for HP identification should be performed in at risk patients as a first step, and only after achieving HP eradication they should undergo a gastroesophageal endoscopy to identify more correctly PGC.

Disclosure: Nothing to disclose

References


Disclosure: Nothing to disclose
Results: Overall, 121 consecutive CD patients were enrolled. A total of 143 capsule examinations was performed (18 patients repeated CE). The majority of patients (61%) underwent CE for suspected complicated CD, 25% for non-adherence to GFD and 14% for RCD follow-up. The mean follow-up time after CE was 13±9 months. After the complete diagnostic work-up, the final diagnosis was made: 175 CD (83% of patients with suspected complicated CD) (179:4 RCD type 1, 8 RCD type 2 and 2 lymphoma). CE was positive for CD-related findings in 55% of patients (67/121). CE sensitivity for the detection of mucosal atrophy was 62%, specificity was 81%. The incidence of complications in patients with suspected complicated CD and non-adherence to GFD was 5.7%. In the group of patients with already known RCD at enrollment, two patients (1.6%) developed enteropathy-associated T cell lymphoma and they both had positive CE. A significant correlation between age and CE findings was found (p=0.005). Positive CE had a significantly more advanced age at CD diagnosis compared to patients with negative CE (p=0.005). Moreover, in patients 50 years old at the CE execution CD-related findings were more frequent compared to younger patients (p=0.01). Any statistical correlation was found with the positive CE and incorrect GFD and non-adherence to GFD (p>0.05).

Conclusion: Capsule enteroscopy plays a pivotal role in the clinical follow-up in order to detect the persistence of atrophy, the extent of the lesions throughout the SB and to early identify CD-related complications. According to our results, complications CD is an uncommon condition; in this setting, patients aged >50 years and with a diagnosis of CD in older age should be considered at higher risk of complications and accurately investigated with CE. On the contrary, neither a persistent positive serology nor an incorrect GFD seem to be related to the onset of complicated CD.

Disclosure: Nothing to disclose

References

PI842 HISTOLOGIC RESPONSE TO BUDENOSIDE IN PATIENTS WITH REFRACTIVE CELIAC DISEASE TYPE I AND 2

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Introduction: Refractory celiac disease (RCD) is defined by persistent or recurrent symptoms, refractory to strict gluten-free diet (GFD) for at least 6 to 12 months. RCD is classified as type 1 (normal intraepithelial lymphocyte [IEL] phenotype on histopathology) and type 2 (clonal intraepithelial lymphocyte population with aberrant phenotype). There is no standard clinical remission in RCD type 1 and 2. However, histologic response is less frequent.

Aims and Methods: The aim of this study is to evaluate the clinical and histologic response to budesonide in patients with RCD type 1 and 2, as well as the effect of budesonide on the aberrant intraepithelial lymphocytes (IEL) assessed by flow cytometry in the subgroup of type 2 RCD patients. We conducted a monocentric retrospective study. Patients with a diagnostic of RCD type 1 and type 2 who were treated with budesonide alone were included. Treatment consisted of open-label and self-conducted treatment. Complete histologic response was defined by normalization of the architecture of the small intestinal mucosa (Marsh 0 or 1 score). Partial histologic response was defined as an improvement of the Marsh classification.

Results: 10 patients with RCD I and 8 patients with RCD II were included. The median age of the patients was 49 years (range 22-62). The median time of treatment after starting budesonide was 23.5 months (range 4.5-36). Complete clinical response was observed in 17 out of 18 patients treated with budesonide (94.4%). A complete histologic response was seen in 4 patients (22.2%) and a partial histologic response was seen in 5 patients (27.8%). Half of the patients had no change in the Marsh classification of RCD.

Conclusion: Budesonide is associated with a high clinical response but lower histologic response in refractory celiac disease. There was no impact on the percentage of aberrant IELs assessed by flow cytometry in RCD type 2.

Disclosure: Nothing to disclose
P1844 PERIPHERAL MONOCYTES IMPAIR THE BARRIER FUNCTION OF INTESTINAL EPITHELIAL CELLS: NEW INSIGHTS ON THE PATHOGENESIS OF CELIAC DISEASE

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Introduction: Celiac disease (CD) is a chronic immune-mediated disease with a strong genetic background, triggered by gluten ingestion (1). It is known that small bowel epithelial barrier function is altered in CD patients. In the small bowel mucosa, immune cells are activated after contact with antigen-presenting cells expressing gliadin-derived peptides, which leads to a multifaceted inflammatory cascade ultimately leading to villous atrophy and disruption of the epithelial barrier (2). However, the underlying mechanism for the disrupted barrier function in CD is still unclear. It has been hypothesized that activated monocytes could exert a direct effect on epithelial cells, causing impairment of the epithelial barrier even at earlier phases of the disease and/or after removal of the trigger of the immune reaction (i.e. gluten/gliadin).

Aims and Methods: To model the role of celiac monocytes in the dysregulation of barrier function in CD we isolated peripheral blood mononuclear cells (PBMCs) from untreated and HLA-DQ2-positive CD patients who were on a gluten-free diet. Intestinal epithelial cells (Caco-2) were treated with either PBMCs or CD14+ PBMCs (representing monocytes) in the presence or absence of interleukin-15 and trypsin-digested gliadin (IL-15/Tg) in order to verify the role of active gliadin stimulation. As a control untreated Caco-2 or Caco-2 which were treated with IL-15/Tg were included to rule out direct toxic effects of gliadin/IL-15 on the epithelium. The integrity of the Caco-2 barrier was monitored by serial measurements of transepithelial resistance (TER). Intracellular localization of proteins with a key role in epithelial barrier function (occludin, JAM-A and ZO-1) for apical junctional complex and CD71 for epithelial transcytosis of gliadin were investigated using confocal microscopy after immunostaining.

Results: A decreased TER was observed in Caco-2 cells after treatment with celiac PBMCs and CD14+ PBMCs as compared to untreated cells. PBMCs that were treated with IL-15/Tg revealed a more pronounced TER decrease. In control Caco-2 cells that were treated with IL-15/Tg alone, TER did not decrease as found in completely untreated control cells. Exposure of Caco-2 cells to celiac monocytes increased expression of junctional proteins such as JAM-A and occludin and to a less stringent junctional or membrane association. ZO-1 localization and expression remained unchanged. With regard to the transcytosis protein CD71, confocal microscopy revealed an altered localization after treatment with celiac PBMCs as compared to untreated Caco-2 cells. CD71, with a key role in epithelial barrier function, was found to be enriched intracellularly as compared to CD71 clusters in untreated cells.

Conclusion: Celiac PBMCs have an effect on epithelial barrier function of Caco-2 cells similar to the effect of CD14+ PBMCs as compared to untreated cells. PBMCs that were treated with IL-15/Tg revealed a more pronounced TER decrease. In control Caco-2 cells that were treated with IL-15/Tg alone, TER did not decrease as found in completely untreated control cells. Exposure of Caco-2 cells to celiac monocytes increased expression of junctional proteins such as JAM-A and occludin and to a less stringent junctional or membrane association. ZO-1 localization and expression remained unchanged. With regard to the transcytosis protein CD71, confocal microscopy revealed an altered localization after treatment with celiac PBMCs as compared to untreated Caco-2 cells. CD71, with a key role in epithelial barrier function, was found to be enriched intracellularly as compared to CD71 clusters in untreated cells.

Disclosure: Nothing to disclose.

Reference:

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Introduction: Microvesicles (MVs) have been recently implicated in cellular cross-talk both in health and disease, carrying surface receptors traceable to their cellular origin and potentially serving as molecular messengers. Recent studies have demonstrated an increased number of circulating MVs in a variety of conditions, including active celiac disease (CD). In this study, we investigated whether NCGS is a disease associated with altered circulating MVs.

Aims and Methods: To assess and characterize circulating MVs in a cohort of NCGS patients, we enrolled symptomatic NCGS patients, confirmed after gluten challenge and age/sex-matched healthy controls. All subjects performed serology testing and intestinal biopsy. CD exclusion required negative anti-tTG titers and histology (Marsh grade ≤3). About 40% of these subjects were long non-coding RNA (LncRNA) or Long Intronic noncoding RNAs (LinncRNA). A subgroup of 5 patients affected by NCGS (mean age 33.4 ± 4.7 years) was also examined by microarray against 5 celiac disease patients. Statistical analysis revealed 26 differential transcripts, 40% of which also belonged to the LncRNA and LinncRNAs.

Conclusion: This approach revealed the presence of 37 differentially expressed transcripts. About 40% of these transcripts were long non-coding RNA (LncRNA) or Long Intronic noncoding RNAs (LinncRNA). A subgroup of 5 patients affected by NCGS, however similar when compared to controls and to patients affected by celiac disease, show a sufficiently distinct genomic expression signature. RNA expression levels of NCGS do not completely overlap to that of controls and CD indicating that NCGS is a disease distinct from CD. Finally, these results suggest that targeted expression profiling of specific sets of genes may be helpful in both positive diagnosis and/or exclusion of NCGS in symptomatic subjects.

Disclosure: Nothing to disclose.

Reference:
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Introduction: Microvesicles (MVs) have been recently implicated in cellular cross-talk both in health and disease, carrying surface receptors traceable to their cellular origin and potentially serving as molecular messengers. Recent studies have demonstrated an increased number of circulating MVs in a variety of conditions, including active celiac disease (CD). In this study, we investigated whether NCGS is a disease associated with altered circulating MVs.

Aims and Methods: To assess and characterize circulating MVs in a cohort of NCGS patients, we enrolled symptomatic NCGS patients, confirmed after gluten challenge and age/sex-matched healthy controls. All subjects performed serology testing and intestinal biopsy. CD exclusion required negative anti-tTG titers and absence of villous atrophy at histology. Circulating MVs were identified on whole blood samples by a no-lyse/no-wash method, combined with volumetric counting (FACSVerse, BD), based on a novel 6-color flow cytometry panel, in order to identify and enumerate the whole MV compartment and its subpopulations. Data are expressed as mean ± SD. Statistical differences were evaluated by T-test.

Results: We evaluated 14 NCGS patients (mean age = 39.3 ± 12.9, F:M = 4:1) and 28 age-sex-matched healthy controls. Mean total circulating MVs were significantly higher in NCGS patients (respectively 661.3 ± 236.8 vs 233.1 ± 190 MV/C6, p < 0.001). Subgroup analysis showed that CD31+ and CD45+ MVs, of endothelial and leucocyte origin respectively, were not significantly different. However, EpCAM+ MVs, of epithelial origin, and CD41a+ platelet-derived MVs were significantly higher in NCGS patients (respectively 661.3 ± 236.8 vs 233.1 ± 190 MV/C6, p = 0.05). Total mean annexin V+ MVs showed a similar pattern (respectively 12050.4 ± 5815.8 vs 2639.4 ± 1675.8 MV/C6, p = 0.001), bearing increases in all subpopulations, with a 6.6-fold increase in CD31+ annexin + and a 4-fold increase in EpCAM+ annexin + MVs.

Conclusion: NCGS patients show higher numbers of total circulating MVs than age and sex-matched controls. Phenotypical assessment suggests that this increase is driven in part by the epithelial- and platelet-derived compartments, potentially implying increased peripheral signaling from the intestinal mucosa. Annexin V identifies a compartment of MVs that express phosphatidylserine on the cellular membrane, an event found in apoptosis and activation of the cell of...
**P1847 TOTAL ANNEXIN V+ CIRCULATING MICROVESICLES DIFFERENTIATE NON CELIAC GLUTEN SENSITIVITY FROM CELIAC DISEASE PATIENTS AND HEALTHY CONTROLS**

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**Introduction:** Circulating microvesicles (MVs) are potential mediators of cellular cross-talk in physiological and pathological systemic processes. Increased numbers of total MVs have been demonstrated in a variety of conditions, including celiac disease (CD). Non celiac gluten sensitivity (NCGS) diagnosis is based on the exclusion of CD, wheat allergy and other inflammatory conditions and on the demonstration of a strict correlation between symptoms and gluten consumption. However, markers for a positive diagnosis are lacking.

**Aims and Methods:** The aim of this study was to assess the potential diagnostic value of circulating MVs as a serological marker for NCGS diagnosis. To this end, we enrolled symptomatic NCGS patients confirmed after gluten challenge, age- and sex-matched newly diagnosed CD patients and asymptomatic controls. All subjects performed serology testing and intestinal biopsy. CD diagnosis required positive anti-tTG titers and presence of villous atrophy. MVs were identified on whole blood samples by a no-lyo/no-wash method, combined with volumetric count (FACSVerse, BD), based on a novel 6-colour flow cytometry panel. Data are expressed as mean ± SD. Statistical differences were evaluated by ANOVA-Welch with post-hoc Bonferroni or Dunnet’s T3 test.

**Results:** We evaluated 14 NCGS patients (mean age = 39.3 ± 12.9, F/M = 4:1) against 22 CD subjects and 28 healthy controls. Anti-tTG levels were positive only in CD vs NCGS and controls (respectively 102.4 ± 63.1 vs 4.2 ± 3.3 and 3.9 ± 2.8 U/ml, p < 0.001). Villous atrophy was present only in CD patients; however, inflammation was present in 35% of NCGS and 28% of controls (p = n.s.). Mean total MVs were significantly higher both in NCGS and CD compared to controls (respectively 47533.5 ± 16219.2 and 39283.1 ± 17828.6 vs 14203.7 ± 7402.8 MV/µl, p < 0.02 vs CD controls). Mean total annexin V+ MVs were significantly increased only in NCGS subjects (respectively 12090.4 ± 5818.5 vs 4048.4 ± 4769.8 and 2639.4 ± 1675.8 MV/µl, p < 0.03 vs CD and controls). ROC curve analysis of total and annexin V+ MV counts, when predicting NCGS, showed an AUC of respectively 0.780 and 0.839 (p < 0.02), whereas for CD AUCs were not predictive. Each parameter (total MV counts and annexin V+ MV counts), when combined with tTG negativity and absence of villous atrophy, yielded a further increase in AUC, respectively 0.882 and 0.905 (p < 0.001).

**Conclusion:** Total MV counts are increased in CD and NCGS patients when compared to age- and sex-matched controls. However, NCGS patients seem to express characteristic higher levels of annexin V+ MVs, suggesting parent cell activation. This parameter, combined to serological and histological exclusion of CD, seems to have a high diagnostic accuracy in NCGS and may represent a candidate marker for positive diagnosis of this syndrome.

**Disclosure:** Nothing to disclose

**Reference**


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**P1848 DISTINCT MUCOSAL AND BLOOD MiRNA EXPRESSION PATTERNS MAY REPRESENT A RELIABLE MARKER FOR POSITIVE DISEASE DIAGNOSIS IN NON CELIAC GLUTEN SENSITIVITY**

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**Introduction:** Non celiac gluten sensitivity (NCGS) diagnosis is principally based on the exclusion of CD and on the demonstration of a strict correlation between symptoms and gluten consumption. However, markers for a positive diagnosis are lacking. MicroRNA (miRNA) molecules, implicated in immune response, modulate post-transcriptional gene expression, showing distinct expression pattern in a number of diseases, including Celiac Disease (CD).

**Aims and Methods:** The aim of this study was to characterize miRNA patterns in NCGS and CD and assess their potential diagnostic value for NCGS diagnosis. We enrolled symptomatic NCGS patients who were confirmed after gluten challenge, age- and sex-matched newly diagnosed CD patients and dyspeptic controls. All subjects performed serology testing and intestinal biopsy. CD diagnosis required positive anti-tTG titers and presence of villous atrophy. Differentially expressed miRNAs in circulating leucocytes and duodenal mucosa were assessed by real-time PCR. Statistical differences were evaluated by a linear model with False Discovery Rate correction. Unsupervised Principal Component Analysis (PCA) was used to assess the discriminatory capability of miRNA patterns; principal component diagnostic accuracy was assessed by ROC curve analysis.

**Results:** We evaluated 27 NCGS patients (mean age = 39.8 ± 11.3) against age- and sex-matched CD subjects and dyspeptic controls. Anti-tTG levels were positive only in CD vs NCGS and controls (respectively 99.4 ± 56.3 vs 4.5 ± 2.6 and 3.9 ± 1.8 U/ml, p < 0.001). Six miRNAs were differentially expressed in NCGS mucosal samples, while another 6 were identified in peripheral blood; notably, 2 of these miRNAs were expressed differentially only in mucosal biopsies or blood samples. At PCA, the first principal component showed an OR = 3.71 (95%CI: 1.57-8.75, p = 0.003) for NCGS status vs CD and an OR = 0.35 (95%CI: 0.16-0.78, p = 0.011) for NCGS status when compared to dyspeptic controls. ROC curve analysis of this component showed respectively an AUC of 0.743 (95%CI: 0.612-0.874, p = 0.002) and of 0.832 (95%CI: 0.706-0.958, p < 0.001).

**Conclusion:** The present study shows that patients selected according to established criteria are well definable with the use of miRNA profiling methods. Resulting miRNA signatures of NCGS patients are unique and absent in CD, thus we suggest the possibility of hypothesizing non celiac gluten sensitivity as a distinct clinical entity, different from CD on the gene expression level. Differentially expressed miRNA patterns discriminate between patient groups with a high degree of accuracy and are strongly predictive of a NCGS status after exclusion of CD, both on mucosal and peripheral blood samples. Overall, such miRNA profiling, combined with serological and histological exclusion of CD, may represent a future marker for positive diagnosis of this syndrome.

**Disclosure:** Nothing to disclose

**Reference**


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**P1849 EFFECTS OF WATER LOAD TEST ON GASTRIC MOTILITY AND AUTONOMIC SYSTEM ACTIVITY IN PATIENTS WITH CELIAC DISEASE**

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**Introduction:** Celiac disease (CeD) is an autoimmune, complex disorder of the gastrointestinal tract with wide range of clinical manifestation. The inflammatory process in CeD may cause changes in visceral perception increase of visceral sensitivity. Water load test is a standardized test used to induce gastric distension and to evoke gastric motility without the enterohormonal response.

**Aims and Methods:** The aim of the study was to evaluate the effect of water ingestion on autonomic nervous system (HRV- heart rate variability) and gastric motility (EGG- electrogastrography) in patients with CeD compared to healthy subjects.

53 neurologically asymptomatic patients with CeD (13 males, 40 females, mean age 43.4±18.8 years) and 50 healthy subjects (12 males, 38 females, mean age 44.1±9.2 years) were studied. The simultaneous 30 minutes recording of ECG with HRV analysis and EGG were performed before and after water intake (500 ml per 5 minutes).

**Results:** ANS. At rest the spectral domain HRV analysis parameters were significantly lower in patients than in control (LF – 291.9 vs. 836.0, p = 0.0004; HF – 348.5 vs 965.5, p = 0.001). Water test induced the increase of LF (536.2 vs 1163.4; p = 0.0003) and HF (543.7 vs 1224.9; p = 0.006) indices, similarly as a control, but not reached normal value. EGG. Fasting CeD patients showed decreased% time of normogastria (51.8± 18 vs. 86±12.3, p = 0.02) and mean slow wave coupling (SWC) (62.1 ± 18 vs. 67±18%, p = 0.01) with increased dominant power (log DP) (12.5 ± 1.2 vs. 11.1 ± 1.1, p = 0.001) in comparison to control group. After water load test in CeD group decreased% time of tachygastria in EGG (7.08± 5.5 vs. 7.57± 1.7, p = 0.04) was noted.

**Conclusion:** In CeD the activation of autonomic system was especial parasympathetic component after water load test was lower than in control group. Diminished responsiveness of ANS in CeD may contribute to disturbances of gastric myoelectric activity.

**Disclosure:** Nothing to disclose
PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS FOLLOWING FRUCTOSE AND LACTOSE INGESTION IN STUDY POPULATION.

Our data suggest a significant shift in clinical phenotype of celiac disease, which can strike at any age. Presenting symptoms can be manifold, clinical phenotype may range from severe malabsorption syndrome to silent celiac disease.

Aims and Methods: We aimed to investigate whether celiac clinical phenotype changed in the past decades by performing a retrospective data collection from patient files in our academic centre. We excluded patients with secondary celiac disease (e.g., due to concomitant autoimmune diseases, 18.5% of the population suffered from autoimmune thyroid disease). Diagnostic distribution was, as follows: Marsh 1: 0.6%, Marsh 2: 2.3%, Marsh 3a: 15.1%, Marsh 3b: 36.0%, Marsh 3c: 45.9%. Dermatitis herpetiformis, anemia, metabolic bone disease, and autoimmune diseases were not different between patients diagnosed before and after the year 2000. Refractory celiac disease did not occur in our study population.

Conclusion:

Refractory celiac disease did not occur in our study population.

Nothing to disclose

References


 nothing to disclose

Introduction:

Non-celiac gluten sensitivity (NCGS) is a gluten-related disorder characterized by the absence of allergic or autoimmune enteropathogenic mechanisms.

Aim and Methods: Our aim was to compare the two methods for the diagnosis of NCGS: the oral gluten challenge according to “Salerno Experts’ Criteria” and the Gluten Oral Mucosa Test (GOMPT) supported by LDPI. We enrolled a total of 30 subjects. 15 patients (Group A) presented with gluten-related symptoms and were on a free diet (FD) for at least 6 weeks. 15 healthy volunteers (Group B) were enrolled as control group. We excluded patients suffering from celiac disease; allergy to gluten, wheat and other cereals; inflammatory bowel diseases; infectious diseases; autoimmune diseases; malignancies.

At the entrance of the study, patients and controls completed the modified version of the Gastrointestinal Symptom Rating Scale (GSRS) questionnaire: symptoms were quantitatively assessed using a scale from 1 to 10. They also underwent GOMPT, which consists of a gluten-containing stimulation test applied on the oral mucosa. LDPI, which produces quantitative data about oral mucosa vascularity before and after GOMPT, was also performed. Then, all patients followed a gluten-free diet (GFD) for 6 weeks with a wash-out week. Afterwards, they started a double-blind placebo controlled trial, according to “Salerno Experts’ Criteria”. Capsules containing gluten (Product A) or rice flour (placebo, Product B) 6 gr/day have been consumed for one week, respectively, with an intermediate washout week. A symptom questionnaire was repeated every week.

Results:

There was no significant difference in symptoms’ intensity between GFD period and Product A (gluten) period, as well as between Product A (gluten) and B (placebo) period. On the other hand, intensity significantly varied in 15/22 symptoms between FD and GFD period; in 12/22 symptoms between FD and washout (GFD) period; in 4/22 symptoms between FD and Product B (placebo) period. However, 7/22 symptoms do not show any significant difference. Questionnaires from control patients did not show any statistically significant difference.

Conclusion:

There were no statistically significant differences in symptoms’ intensity between GFD period and Product A (gluten) period, as well as between Product A (gluten) and Product B (placebo) period. On the other hand, intensity significantly varied in 15/22 symptoms between FD and GFD period; in 12/22 symptoms between FD and washout (GFD) period; in 4/22 symptoms between FD and Product B (placebo) period. However, 7/22 symptoms do not show any significant difference. Questionnaires from control patients did not show any statistically significant difference.

Aim and Methods: We aimed to investigate whether celiac clinical phenotype changed in the past decades by performing a retrospective data collection from patient files in our academic centre. Was excluded patients with secondary celiac disease (e.g., due to concomitant autoimmune diseases, 18.5% of the population suffered from autoimmune thyroid disease). Diagnostic distribution was, as follows: Marsh 1: 0.6%, Marsh 2: 2.3%, Marsh 3a: 15.1%, Marsh 3b: 36.0%, Marsh 3c: 45.9%. Dermatitis herpetiformis, anemia, metabolic bone disease, and autoimmune diseases were not different between patients diagnosed before and after the year 2000. Refractory celiac disease did not occur in our study population.

Conclusion:

Refractory celiac disease did not occur in our study population.

Nothing to disclose

References


PI853 CLINICAL BENEFIT OF THE USE OF THE GAIXLOSE TEST FOR HYPOLACTASIA DIAGNOSIS: A NON-INFERIORITY RANDOMIZED CONTROLLED CLINICAL TRIAL
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Introduction: The Gaixlose test (GT) is a non-invasive method for the diagnosis of hypolactasia. Its efficacy and safety have already been proved in three clinical trials (1, 2). However, the impact on diagnostic thinking and on patient management had to be evaluated to confirm its clinical benefit.

Aims and Methods: The objective was to demonstrate the non-inferiority of the GT, compared to the Hydrogen Breath Test (HBT) on the impact on diagnostic thinking and on patient management for the diagnosis of hypolactasia. Patients with clinical symptoms of lactose intolerance were recruited in a multicentric clinical trial and randomly assigned to perform the GT or the HBT. The gastroenterologists had to complete for each patient a pre-test and a post-test visual analogue scale (VAS) questionnaire indicating their expected probability of diagnosing hypolactasia. The impact on diagnostic thinking was evaluated through the mean of the absolute values of the differences between the pre-test and post-test VAS scores and compared between the GT and the HBT. To assess the impact on patient management, the physicians completed a pre-test and a post-test management questionnaire. The percentage of patients who passed from ‘No intervention’, ‘Prescription of additional diagnostic tests’ or ‘Referral to another specialist’ at pre-test to ‘Diet adjustment and follow-up’ at post-test was compared for both diagnostic tests. The limit of non-inferiority was defined in both cases as 80%.

Results: 147 patients (115 females and 32 males, age range: 19–70 years, mean age: 38.41 years) were included in the analyzed population. Among them, 74 performed the HBT and 73 performed the GT. The impact on diagnostic thinking was 71.3% for the GT and 24.8 ± 19.87% for the HBT. The difference between both was 7.46%, with lower 95% confidence limit (CL) of 1.55%, higher than the limit of non-inferiority (p = 0.001). The percentage of patients who passed from ‘No intervention’, ‘Prescription of additional diagnostic tests’ or ‘Referral to another specialist’ at pre-test to ‘Diet adjustment and follow-up’ at post-test was 6.85% for the GT and 5.41% for the HBT. Therefore, the difference between the GT and the HBT was 1.44% (95% CL: −6.31, 9.20). The lower 95% CL of the difference was also higher than the non-inferiority limit (p = 0.007). No serious adverse events were reported during the study.

Conclusion: The results demonstrate the non-inferiority of the GT compared to the HBT on the impact on diagnostic thinking and patient management for the diagnosis of hypolactasia.

Disclosure: This work was funded by Venter Pharma SL. Carmen Monsalve-Hernando and Carmen Hermida are employees of Venter Pharma SL. Laura Crespo, Blanca Ferreiro, Verónica Martin, Xavier Aldeguer, Verónica Opis, Paula Fernández-Gil and María Jesús Gaspar received honoraria for their participation in the clinical trial.

References:

PI854 SYSTEMATIC REVIEW WITH META-ANALYSIS: THE PREVALENCE OF BILE ACID MALABSORPTION AND THE RESPONSE TO CHOLESTYRAMINE IN PATIENTS WITH CHRONIC WATERY DIARRHOEA AND PRIOR CHOLECYSTECTOMY
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Introduction: Post-cholecystectomy diarrhoea has a prevalence of 9.1% according to a systematic review published in 2012. The frequency of bile acid malabsorption (BAM) in these patients ranges between 57 and 100%, and some authors have suggested that they could be treated with cholestyramine without a prior testing of the presence of BAM. However, in most studies, the sample size is small and the response to cholestyramine has been scarcely evaluated.

Aims and Methods: To perform a systematic review and meta-analysis to assess the prevalence of BAM in patients with chronic watery diarrhoea and previous cholecystectomy and the response to cholestyramine.

Materials and Methods: A systematic review was searched up to January 2018. Selected studies included cholecystectomized patients with chronic watery diarrhoea who were tested by 23-seleno-25-homoaurocholic acid (SeHCAT) test for the assessment of BAM. BAM was defined as 7 day SeHCAT retention of <10% or <15%, depending on the study. We calculated the pooled rate of both and the 95% C.I. using a random effects model and the inverse variance method. F was calculated to assess heterogeneity across studies (0–39%, not important; 40–75%, moderate; and 76–100%, important).

Results: The search strategy identified 9 relevant studies comprising 361 individuals. The rate of BAM ranged from 57% to 100%. The pooled rate in the <10% subgroup (G10: 8 studies) was 68% (95%CI: 53–83%) and 70% (95%CI: 59–81%) in the <15% subgroup (G15: 5 studies). There was significant heterogeneity in effect sizes in the two groups (G10: F = 91% CI: 63–95%; G15: F = 73%). The rate of BAM comprising 166 patients evaluated the efficacy of cholestyramine in patients with BAM. The pooled choleystyramine response rate was 77% (95%CI: 64–90%) with significant heterogeneity (F = 72%). After excluding the only study of G15, the pooled rate was 82% (95%CI: 72–93%) with moderate non-significant heterogeneity (F = 56%).

Conclusion: These data provide evidence that two thirds of patients with chronic watery diarrhoea and prior cholecystectomy have BAM. Response to cholestyramine in these patients is excellent. These findings have implications for the routine clinical practice and future guideline development.

Disclosure: Nothing to disclose
During the 2-year follow-up, 73% of patients had experienced bleeding, and 32.4% of them suffered 2 episodes within a mean of 3.14 bleeding episodes/patient. During the 2 years follow-up, 18 patients (46.8%) died; among these, 4 (22.2%) deaths were related to bleeding.

**Conclusion:** In a cohort of 104 CF-LVAD patients followed up for 2 years, 35.6% of them developed GIB, mostly in the first 6 months, with a high recurrence rate. Most GIB bleed lesions were found in upper GI tract or small bowel. EGD showed the highest diagnostic yield, followed by VCE. We suggest that evaluation of GIB in CF-LVAD patients should be initiated with EGD and a VCE, to optimize diagnostic yield and successful intervention.

**Disclosure:** Nothing to disclose

**P1856 SMALL BOWEL GASTROINTESTINAL BLEEDING – CAN WE BLAME ANTICOAGULANTS?**

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**Introduction:** The use of anticoagulants is associated with an increased risk of upper and lower gastrointestinal (GI) bleeding.

**Aims and Methods:** The aim of this study was to evaluate whether different anticoagulants may influence the risk of small bowel bleeding (SBIB) in CF-LVAD patients. In a cohort of 104 CF-LVAD patients followed up for 2 years, 35.6% of them developed GIB, mostly in the first 6 months, with a high recurrence rate. Most GIB bleed lesions were found in upper GI tract or small bowel. EGD showed the highest diagnostic yield, followed by VCE. We suggest that evaluation of GIB in CF-LVAD patients should be initiated with EGD and a VCE, to optimize diagnostic yield and successful intervention.

**Disclosure:** Nothing to disclose

**P1858 IMPACT OF THE TIMING OF CAPSULE ENDOSCOPY IN OVERT OBSCURE GASTROINTESTINAL BLEEDING ON YIELD AND REBLEEDING RATE – IS SOONER THAN 48 h ADVISABLE?**

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**Introduction:** An early diagnosis with capsule endoscopy (CE) in overt-obscure gastrointestinal bleeding (OGIB) patients can lead to an appropriate specific intervention, better long-term-outcomes and reduce unnecessary medical costs. ESGE recommends performing CE as soon as possible after the bleeding episode, optimally within 48 hours. The aim of this study was to evaluate the impact of the timing of capsule endoscopy (CE) in overt-obscure gastrointestinal bleeding (OGIB), mainly when it is performed within 48 hours.

**Aims and Methods:** Evaluate the impact of the timing of capsule endoscopy (CE) in overt-obscure gastrointestinal bleeding (OGIB) on the diagnostic and therapeutic yield (DY and TY), the rebleeding rate and the prediction of the individual risk of gastrointestinal rebleeding in CF-LVAD patients.

**Disclosure:** Nothing to disclose

**P1859 CYANOACRYLATE INJECTION THERAPY OF SMALL BOWEL VARIANCES (SBV) DURING DOUBLE-BALLOON ENTEROSCOPY (DBE): EXPERIENCE FROM TWO EUROPEAN CENTRES**

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**Introduction:** Mid gastrointestinal bleeding (MGIB) accounts for 5–10% of gastrointestinal hemorrhages, and small bowel capsule endoscopy (SBCE) is the gold-standard for investigational approach. In spite of the acknowledgement of some risk factors, no score can currently predict the individual risk of small bowel rebleeding after SBCE.

**Aims and Methods:** We aimed to create a predictive score of small bowel rebleeding risk, in patients that underwent SBCE for MGIB. Retrospective, uncenteric study, including patients that underwent SBCE for MGIB, from June 2006, to October 2016. Every patient had a 12 months minimum follow-up. Statistical variables were chosen according to clinical relevance and previous evidence in the literature, and their correlation with the occurrence of small bowel rebleeding after SBCE was assessed. Univariate analysis allowed us to select covariables with marginal association (p < 0.15) with the outcome variable, which were then included in a Cox regression hazard multivariate model. Finally, we attributed points to each variable category in order to create a score with clinical applicability.

**Results:** Out of 357 patients submitted to SBCE for MGIB, 230 (64.3%) were available, and the mean age was 64 years old. The mean indication to SBCE was iron-deficiency anemia (72.8%) and 88 patients (24.6%) presented with rebleeding during the follow-up. The significantly different variables allowed us to create a new measure for the prediction of the individual risk of gastrointestinal rebleeding, the RH EMI T T score, that presented a good accuracy to the outcome variable (area under curve 0.843, CI 95% 0.801–0.885). From the regression coefficients obtained, we designed a score, from 0 to 18 points, (p < 0.001). The rebleeding rate was 0.479 across subcategories in group 1 but patients on aspirin had the highest rebleeding rate (0.499). There was also no statistical difference in findings according to SB location (proximal / mid / distal / diffuse / terminal ileum) within the 2 groups.

**Disclosure:** Nothing to disclose
Introduction: Small bowel varices (SBV) are a rare consequence of portal hypertension, usually due to life-threatening upper or lower gastrointestinal bleeding. Radiological intervention (RI) is usually considered first line management (e.g. Trans-jugular intrahepatic portosystemic shunting (TIPS), stenting of occluded mesenteric veins +/- embolisation of culprit varices). In cases where RI is impossible, management is very limited.

Aims and Methods: This multicentre case series evaluated the usefulness of DBE assisted cyanoacrylate injection of SBV. Retrospective review of DBE facilitated cyanoacrylate injection of SBV (December 2015 to October 2016). Demographic, clinical, endoscopic and radiological findings, interventions and follow-up data were analysed.

Results: Ten DBEs were performed in 6 patients (4 women, median age: 68.5+ years). All patients had at least one previous surgery (colectomy (n = 1); hemi-hepatectomy (n = 2); small bowel resection (n = 2); appendicitis with peritonitis (n = 1); splenectomy (n = 1); one patient had a history of intra-abdominal sepsis in childhood causing portal vein thrombosis and one had cryptocogenic thrombosis of the portal and the mesenteric vein. No radiological or surgical options were deemed to be feasible in any of the patients. SBV were detected at capsule endoscopy and triple phase computed tomography mesenteric angiography. At DBE, a total of 13 nests of SBV were identified and injected with cyanoacrylate glue. There were no hemorrhagic or embolic complications but 1 patient developed an infection of a congenital urachal cyst, which was treated successfully with antibiotics. All patients underwent DBEs via the anterograde route, 2 patients required bi-directional DBE for treatment of both proximal and distal SBV and in total 2 patients required DBE for further treatment of SBV. At 30-day follow-up post therapy, only 1 patient had experienced a mild recurrence of mid-gut bleeding conservatively. One patient presented with acute gastrointestinal bleeding 7 months later and a repeat DBE with cyanoacrylate injection therapy was successfully performed. The other patient was lost to follow-up. The remaining patients had 12 months of follow-up without any recurrent gastrointestinal bleeding.

Conclusion: Cyanoacrylate injection therapy of SBV at DBE appears to be a safe and effective management strategy for this condition when other first-line options are not feasible.

Disclosure: Dr. Despot and Prof May receive research support from Aquilant Medical and Fujifilm. Dr. Hayashi has received honoraria from Fujifilm Corp. All other authors disclosed no financial relationships relevant to this publication.

References

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Introduction:

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Introduction: Chronic stenoing enteritis (CSE) is a novel ulcerative and stenosing disease of the small bowel that is distinct from Crohn’s disease, celiac disease, and NSAID-induced small bowel injury. Similar conditions have been described in Japan and Korea as cryptogenic multifocal ulcerating stenosing enteritis, chronic nonspecific stenosing ulceration, and most recently chronic enteropathy associated with mutations in the SLCO2A1 gene (CEAS, a prostaglandin transporter gene). There are currently no studies examining the outcomes to medical and surgical therapies in patients with CSE. We report our experience with treating CSE.

Aims and Methods: 16 patients diagnosed with CSE were identified between 2007 and 2017 at UMass Medical Center. Patient epidemiology, laboratory studies, endoscopic procedures, radiographic studies, pathology reports, medical treatment, surgical interventions, and disease course were collected retrospectively. All patients underwent video capsule endoscopy as part of their initial work-up. Complete remission was defined as resolution of iron deficiency with clinical symptoms but no available follow-up iron studies to evaluate for full remission. The overall rates of full remission, partial remission, and no remission thresholds.

Results: The median duration of follow-up was 48 (4.5–85.3) months. 75.0% of patients presented with bleeding or iron deficiency anemia. 80.0% of patients were found to be iron deficient (see Table 1). 43.8% of patients required intravenous iron therapy. A total of 62.5% of patients underwent surgical resection for CSE and 31.3% received biologic therapy with infliximab or adalimumab. Only 3 patients received steroids, none of whom achieved remission with this therapy. The overall rates of full remission, partial remission, and no remission were 20.0%, 26.7%, and 26.7% respectively. 26.7% of patients had resolution of clinical symptoms but no available follow-up iron studies to evaluate for full remission. 1 patient was lost to follow-up after initial diagnosis.

Conclusion: SBCE is a useful screening tool in patients with HHT to assess for SBAs which occur more commonly than in patients with anaemia but no underlying HHT. Most patients had proximal SBAs which were amenable to regular DBE and APC. A small number required additional pharmacotherapy to improve transfusion requirements. Disclosure: Nothing to disclose

Disclosure: David R. Cave, MD has a research grant with Olympus Corporation

Disclosure: Nothing to disclose

Disclosure: Nothing to disclose

Disclosure: Nothing to disclose
with 5%, and galacto-oligosaccharides contributed with the least amount, 3%. There were no significant gender differences in the proportion of energy as total FODMAP intake. The ratio of CVg / CVb for total FODMAP intake was 0.83 for women and 0.67 for men, and below < 1 for all FODMAPs. This indicates that there is larger variation between subjects than within subjects with respect to FODMAP intake. To capture the intake of FODMAPs at the individual level with a precision of +/-20%, 19 days of replicate observations are required (as seen in the table). Ranking individuals within a group according to FODMAP intake would require between 2-6 days of replicate observations.

Conclusion: Our results show that there is more variation between subjects than within subjects regarding FODMAP intake. Dietary data with good precision at the individual level would not be obtainable using a reasonable number of days of food records. However, if the study objective is to rank individuals into quartiles of FODMAP consumption, this can be achieved with a good level of precision by using food records.

Results: A significant correlation between FODMAP intake and increased over-C6¼n¼0.90, p¼0.90. 8.7 g vs. 8.1 g (+/20%) by 22% 20% r¼0.90. 97; Q2, 303 30% r¼0.95. 0.95 0.90 r¼0.90. 0.90 0.95 0.401, ** correlation is significant at p<0.05. ** correlation is significant at p<0.01. [Table 1. Spearman correlation between IBS symptom severity and FODMAP intake among different IBS subgroups.]

Abbreviations: IBS-SSS, irritable bowel severity scoring system; IBS-C, IBS with constipation; IBS-M, mixed IBS; IBS-U, unsubtyped IBS

Disclosure: Nothing to disclose

P1865 INTAKE OF FERMENTABLE OLIGO-, DI-, MONOSACCHARIDES AND POLYOLS (FODMAPS) IN RELATION TO SYMPTOM SEVERITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Introduction: It is already known the beneficial effect of probiotics to improve human health through reestablishing the composition of the gut microbiota and contributing to the maintenance of gastrointestinal tract function. Probiotics protect the host from pathogens by competitive exclusion, preserve barrier integrity, affect the host immune system and remove heavy metals and environmental toxins. Since changes in manufacturing affect the functional properties of probiotic formulations [1–4], we have compared the in vitro effects of two 450 billion multi-strain high concentration formulations, identified by us as USA-made and Italy-made, on human colon adenocarcinoma cell line, CaCo-2, a model widely used as an optimum for studies on intestinal barrier functions [5].

Aims and Methods: The aim of this research was to identify if two 450 billion commercial probiotic preparations sourced from different production sites (USA and Italy) could affect the integrity of intestinal barrier in vitro as well as protect from heat-induced dysfunction of the epithelial monolayer. CaCo-2 monolayers were seeded in Transwell chambers where they close up shaping a model of intestinal barrier. The effects of both probiotic formulations, at 10^7 CFU/μl bacterial concentration, were analyzed in both transmembrane electrical resistance (TEER) and 4 kDa fluorescein isothiocyanate-dextran (FD4) flux in CaCo-2 cells before and after exposition to heat stress. TEER and dextran flux are considered as a reliable tool to evaluate the physiological state and integrity of epithelial or endothelial barrier and can also be used to predict paracellular permeability following several stimuli [6]. Considering that tight junctions are thought to be exceptionally effective structures operative in several main functions of the intestinal epithelium under both physiological and pathological circumstances, the effects of probiotic treatment before heat-induced damage on the levels of tight junction proteins i.e. zonulin-1 and occludin were also analyzed by western blotting and densitometry of relative bands.

Results: Treatment with both products did not significantly affect basal levels of TEER and FD4 flux values. On the other hand, a 4 h pre-treatment with USA-made probiotic was able to totally prevent the heat-induced damage as shown by TEER and dextran flux analyses. Instead, the Italy-made product did not exert significant effects on both TEER values and dextran flow altered by heat damage. The basal levels of zonulin were not modulated by a 3 hr-treatment with both products while USA-made product was able to upregulate occludin expression. Of note, Italy-made product, at the same experimental conditions, induced a significant decrease of occludin levels compared with both untreated cells and USA-made product treatment. Also in this context, just pre-treatment with USA-made formulation was able to totally prevent both zonulin and occludin level reduction induced in heat-stressed monolayers.

Conclusion: The results confirm that the production conditions of this 450 billion formulation are crucial for its efficacy and safety, as previously reported [1–4]. A careful selection of the probiotic agent, standardization of the dose and detailed characterization of the beneficial effects are essential when considering use of a probiotic for the dietary management of serious diseases. As a general rule, there is the need to reconfirm safety and/or efficacy for any probiotic product made at a different factory even if contains the same species.

Disclosure: Nothing to disclose

References
P1867 THE COMBINATION OF PEPPERMINT OIL AND CARAWAY OIL DOES NOT AFFECT GASTRIC FUNCTION, BUT INCREASES HUNGER RATING AND DECREASES SATIATION IN HEALTHY SUBJECTS

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Introduction: The heterogeneous character of functional gastrointestinal disorders makes it challenging to find effective treatment options. Compared to synthetic drugs, phytopharmacological medicines can have broader pharmacological effects and are often better tolerated.

Aims and Methods: The current study aimed to investigate the effect of a combination of peppermint oil (41.5 mg menthol) and caraway oil (50 mg) (POCO) on gastric motility, gastric emptying, nutrient volume tolerance, postprandial symptoms, and colonic crypt depth and goblet cell numbers. In humans, IBS patients often have negative effects on the epithelial barrier function. Mast cells can induce mucosal damage and reduced thickness in FODMAP-treated groups. Lactose and FOS administration significantly (P < 0.01) increased the number of mucosal mast cells in both groups (Lactose: 0.74 v 0.54 mast cell/crypt; FOS: 1.27 v 0.67 mast cells/crypt), which was prevented by co-administration with pyridoxamine. Mucus production indicated by emptying goblet cells was increased significantly in both groups (Lactose: 1.71 v 1.08 active goblet cells/crypt; FOS: 1.89 v 1.01 active goblet cells/crypt), which was prevented by co-administration with pyridoxamine for lactose, and attenuated but not completely prevented for FOS. The mucus layer separating epithelium and colonic basement membrane showed significantly (P < 0.0001) reduced thickness in FODMAP-treated groups (Lactose: 10.70 v 18.44m; FOS: 8.66 v 16.90m), which, again, was prevented by co-administration of anti-glycation agent pyridoxamine.

Conclusion: Our results show that increased FODMAP intake can induce an increase in the number of mucosal mast cells in mice, impacting the normal functioning of the colonic mucus barrier. The prevention of these effects by anti-glycation agent pyridoxamine implies a role of glycation processes in the origin of these effects. The aberrant production of mucus in empty colon in the absence of contents might explain the reduced formation of the faecal mucus layer. Given the similar results obtained with both FODMAP representatives, this work suggests a common mechanism responsible for the adverse effects caused by FODMAP stimulation through differentiation of goblet cells derived from FODMAP fermentation by the gut microbiota.

Disclosure: Nothing to disclose

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P1869 THERAPEUTIC RELEVANCE OF BODY MASS INDEX (BMI) CONTROL IN A POPULATION AFFECTED BY IRRITABLE BOWEL SYNDROME/BLADDER PAIN SYNDROME (IBS/BPS)

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Introduction: Bladder pain syndrome/interstitial cystitis (BPS/IC) is a debilitating chronic, inflammatory disorder of the bladder and urinary tract characterized by variable degree of bladder pain, frequency and urinary urgency. BPS patients are often affected by several gastrointestinal symptoms, such as abdominal pain, dyspeptic symptoms, alternance of constipation and diarrhea, sometimes referring to IBS, GERD, food allergy or intolerance. Our patients’ diet is influenced by dietary restrictions introduced in order to ameliorate gastro-intestinal symptoms. This study aimed to better understand how a weight control strategy can influence IBS/BPS patients’ psychological state.

Aims and Methods: The study was conducted in the Multicentric Intestinal Cystitis Referral Center of the Catholic University in Rome, in a population of 37 female, aged 25–57, affected by BPS according to the “European Society for the Study of Interstitial Cystitis (ESSIC)” criteria plus IBS. Patients were categorized into two groups, a normal BMI group, between 19–24.9, and a pathological weight group, whom 14 female with BMI less than 18.9 and 23 patients with BMI more than 25. All subjects were asked to fill our Psycho-Gastroenterological Questionnaire (PGQ), which takes into account the following parameters: number of medical examinations due to gastrointestinal symptoms, sensation of pain scored the Visual Analogue Scale (EQ-VAS), form of the faces established with the Bristol Stool Chart (BSC); gastrointestinal symptoms assessed with the Gastrointestinal Symptoms Rating Scale (GSRS); anxiety with the Hospital Anxiety and Depression Scale (HADS); depression with the Hospital Anxiety and Depression Scale (HADS). Perceived self-efficacy in the management of negative emotions and expression of positive emotions with General Self-Efficacy Scale (GSE); levels of resilience with the Connor-Davidson Resilience Scale (CD-RISC). Differences between the two groups were evaluated by Student’s t test and considered significant for p < 0.05.

Results: Compared to pathological BMI group, normal BMI group has a higher EQ-VAS score (45.2 v 35.1; p < 0.01) and a lower GRSR score (15 v 7; p < 0.05), but these differences were not statistically significant. On the other hand, scores of STAI Y-1 (47.5 ± 10.7 v 58.5 ± 13.4, p < 0.05), STAI Y-2 (39.3 ± 10.6 vs 52.4 ± 10.1, p < 0.05), PGWBI (62.0 ± 15.8 vs 45.4 ± 18.7, p < 0.05), HADS (7.5 ± 3.8 v 10.7 ± 5.3 for anxiety, 5.6 ± 2.5 vs 9.3 ± 3.6 for depression, p < 0.05), GSE (30.2 ± 3.5 v 22 ± 9.3, p < 0.05), CD-RISC (71.1 ± 10.2 vs 55.7 ± 12.6, p < 0.05) are all significantly better among normal BMI group.

Conclusion: Our study demonstrates that weight control can strongly improve IBS/BPS patients’ QoL. Further studies about the most fitting diet for patients with such gastrointestinal distress are required.

Disclosure: Nothing to disclose

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P1868 DIETARY FODMAPS CAN LEAD TO MICROBIAL PRODUCTION OF GLYCATION AGENTS, INCREASING MUCOSAL MAST CELL PARTICIPATION AND IMPACTING COLONIC MUCUS BARRIER FUNCTION

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Introduction: Irritable Bowel Syndrome (IBS) is characterized by abdominal pain, often associated with diet. Limiting the consumption of FODMAPs (fermentable oligo-, di-, mono-saccharides, and polyols), unabsorbed in the small intestine and fermented by the gut microbiota, improves symptoms in 70% of IBS patients. However, the mechanisms behind this effect remain unclear. Our hypothesis is that bacterial metabolites resulting from fermentation of FODMAPs (glycation agents), can cause symptoms via the formation of advanced glycation end-products (AGEs). A low-grade inflammation caused by AGE-RAGE interaction, supported by mast cell activation, could also have negative effects on the epithelial barrier function. Mast cells can induce mucosal mast cells in immunoblotting stress in rats. Alternatively, FOS supplementation in rats can impairecal colonic FACs barrier function, and inhibit supplementation to rats after weaning modifies mucin gene expression, colonic crypt depth and goblet cell numbers. In humans, IBS patients often report passage of mucus per rectum. We used a mouse model to investigate whether an increased intake of dietary FODMAPs is implicated in mucin barrier particularities, to study the mechanisms of effect of a low-FODMAP diet.

Aims and Methods: Three groups of mice (C57BL/6 J ) were treated daily for 21 days with oral gavage of saline or saline solution containing 5 mg of lactose and/or 5 mg of anti-glycation agent pyridoxamine for lactose experiments, additionally, three groups of mice (C57BL/6 J ) followed diets for 21 days; control (AIN-93M), 10% FOS (AIN-93M; part of starch replaced by FOS), and 10% FOS co-administration with pyridoxamine for lactose experiments. Mucosal mast cell (MMC) numbers were analysed by immunofluorescence. Goblet cell numbers in empty colon, and mucus barrier thickness in colon containing faeces in paraffin embedded colon were analysed by classical histology.

Results: Lactose and FOS administration significantly (P < 0.01) increased the number of mucosal mast cells in both groups (Lactose: 0.74 v 0.54 mast cell/crypt; FOS: 1.27 v 0.67 mast cells/crypt), which was prevented by co-administration with pyridoxamine. Mucus production indicated by emptying goblet cells was increased significantly in both groups (Lactose: 1.71 v 1.08 active goblet cells/crypt; FOS: 1.89 v 1.01 active goblet cells/crypt), which was prevented by co-administration with pyridoxamine for lactose, and attenuated but not completely prevented for FOS. The mucus layer separating epithelium and colonic basement membrane showed significantly (P < 0.0001) reduced thickness in FODMAP-treated groups (Lactose: 10.70 v 18.44m; FOS: 8.66 v 16.90m), which, again, was prevented by co-administration of anti-glycation agent pyridoxamine.

Conclusion: Our results show that increased FODMAP intake can induce an increase in the number of mucosal mast cells in mice, impacting the normal functioning of the colonic mucus barrier. The prevention of these effects by anti-glycation agent pyridoxamine implies a role of glycation processes in the origin of these effects. The aberrant production of mucus in empty colon in the absence of contents might explain the reduced formation of the faecal mucus layer. Given the similar results obtained with both FODMAP representatives, this work suggests a common mechanism responsible for the adverse effects caused by FODMAP stimulation through differentiation of goblet cells derived from FODMAP fermentation by the gut microbiota.

Disclosure: Nothing to disclose

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Results:

(TST) and pathologic examination. Anastomotic segments were evaluated by the burst test (BT), tension strength test (TST) at complete division was 10.2 ± 0.9/C6/C6 N in the control group (P \(<\) 0.05). Corresponding values in the control group (P \(=\) 0.05). The TST and amount of collagen deposition in the EX group were significantly larger than the corresponding values in the control group (P \(=\) 0.70).

Aims and Methods:

We hypothesized that HPN patients with one or more SNPs have an increased risk for candidaemia. We analyzed blood samples of adult HPN patients who started HPN between 1997 and 2017 at our referral center for intestinal failure (IF). Patient characteristics were retrospectively collected, such as sex, age at start HPN, pathological mechanism of intestinal failure, diabetes, and the time on HPN. A Poisson regression analysis was performed to correct for confounders. Primary outcome was the risk for factors of patients with and without a SNP in CD58, LCE4A-Clorf68 or TAGAP loci.

Results:

A total of 15 patients were included. The average age was 35.9 years [23–61] with a male predominance of 60%. 13.3% of Patients were followed for a period of more than 133 months. Thirteen percent of patients had diabetes, 14.3% of patients had a SNP in CD58. A total of six patients had a SNP in LCE4A-Clorf68 and four patients had a SNP in TAGAP loci.

Conclusion:

This study, known SNPs in CD58, LCE4A-Clorf68 or TAGAP loci were not associated with an increased risk for candidaemia in HPN patients. An explanation for these results may be that having a venous access device itself is a more predominant risk factor than a genetic predisposition for candidaemia.

Disclosure: Nothing to disclose

Reference

Exclusive Enteral Nutrition (EEN) induces clinical remission in 70% of children and adolescents with active Crohn’s disease (CD), and is comparable to steroids

Aims and Methods: We aimed to evaluate the impact of EEN in adults with active CD.

Patients with active CD referred for nutritional intervention in a tertiary inflammatory bowel disease (IBD) center, were enrolled. Baseline weight and nutritional needs were recorded. EEN was recommended for induction of remission by an IBD nutritionist was administered by oral polymeric formula with no other food items allowed. Patients were treated for at least three weeks. Physician’s Global assessment (PGA), Harvey Bradshaw Index (HBI), biomarkers (blood count, C-reactive protein [CRP], and albumin), weight, and body mass index (BMI) were recorded at baseline and at the end of the EEN course.

Results: A total of 37/50 patients (74%) with active CD completed a full EEN course. Sixteen patients (32%) had newly diagnosed CD (<1.5 years); male/ female 31/19; mean age: 33.2±9.9 years; median disease duration 10.4 (range 3-24) years; and 11.5% (58/214) subjects died whilst under follow-up. Incidence rate of death was 80 and 45 per 1000 person year for exposed and unexposed subjects respectively (IRR 1.76[1.00–3.11], p = 0.047). There was no change in weight or BMI during EEN course.

Patients with long-standing CD (n = 25) also experienced significant improvement in activity indices after EEN: HBI decreased from 5.64 ± 5.1 to 2.89 ± 3.24 (p = 0.001); CRP from 4.43 ± 5.51 (IQR 1.28–5.63) mg/dl to 1.06 ± 1.45 (IQR 0.5–1.52) mg/dl (p = 0.004), and albumin increased from 3.75 ± 0.54 to 3.82 ± 0.37 (p = 0.004). A trend for improvement in disease activity was also present among the 20 patients who received EEN as an add-on therapy to therapy to improve CD.

Conclusion: EEN is an effective nutritional intervention in adults with active CD. EEN is associated with decreased clinical and biologic inflammatory activity, and may be beneficial in patients with newly diagnosed, as well as long-standing CD. EEN may be a bridge or an add-on induction treatment in patients who flare on stable therapies.

Disclosure: Nothing to disclose

References

Low circulating levels of citrulline and FGF19 predict chronic cholestasis and poor survival in adult patients with congenital intestinal failure: development of a model for end-stage intestinal failure (MESIF risk score)

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Introduction: Patients with chronic intestinal failure (CIF) often develop cholestatic liver injury (viz. intestinal failure-associated liver disease, IFALD) which
may lead to liver failure, and need for organ transplantation. The aim of this study was i) to investigate whether citrulline (CIT), an enterocyte function marker, and the enterokine FGF19 were associated with chronic cholestasis (CC) and survival, and ii) to develop and validate a risk score to predict 5-year survival of CIF patients.

**Aims and Methods:** This is a cohort study of 135 consecutive adult CIF patients on intravenous supplementation (IVS) (> 3 months). Plasma CIT and FGF19 were assessed. CC and survival were studied by univariable and multivariable logistic regressions and Cox modeling, respectively. A predictive risk score was developed, C-statistics were calculated and validated internally.

**Results:** Patients (mean age 50 years, 100 females) with CC (n = 23, 17%) had a poor 5-year survival (38% vs 62% P = 0.009). Terminal ileum resection (OR 3.3, P = 0.02), (remnant) small bowel length (P = 0.02), low FGF19 levels (≤107 pg/mL) (OR 3.9, P = 0.03) and low CIT levels (≤20 μM) (OR 4.7, P = 0.003) independently predicted CC. In multivariable analysis, low CIT (OR 6.0, P = 0.002) and low FGF19 levels (OR 3.8, P = 0.049) were significantly associated with CC after adjustment for gender (OR 6.6, P = 0.02). Patients with low CIT levels or low FGF19 levels had a poor 5-year survival (20% vs 69%, P < 0.001), (54% vs 66%, P = 0.080), respectively. Independent predictors of overall survival were frequency of HPN infusions per week (HR 1.2, P = 0.097), low CIT levels (HR 3.2, P < 0.001) and low FGF19 levels (HR 2.6, P = 0.056). These three variables were incorporated in a risk model, Model for End-Stage Intestinal Failure (MESIF), using the estimates of the regression coefficients in the multivariable analysis. The C-statistic was 0.79 (95% CI 0.65 to 0.92) and 0.76 after internal validation. The 5-year survival rates for patients with a MESIF score ranging from 0 to 20, 20 to 40 and above 40 were 80%, 58% and 14%, respectively.

**Conclusion:** The MESIF score is associated with long-term survival of CIF patients. The MESIF score might be useful to identify CIF patients who need closer clinical monitoring or early consultation at transplantation centres. Further external validation and confirmation is required.

**Disclosure:** Nothing to disclose.
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