

ABSTRACTS

37th Belgian Week of Gastroenterology 2025

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**BELGIAN ASSOCIATION FOR THE STUDY OF THE LIVER (BASL) /
BELGIAN LIVER INTESTINE COMMITTEE (BLIC)**

- A01 -

DISCORDANCE BETWEEN SKELETAL MUSCLE SIZE AND STRENGTH IN TYPE 2 DIABETIC PATIENTS IN RELATION TO THE SEVERITY OF MASLD. C. Terken (1), S. André-Dumont (1), G. Henin (1), L. Orioli (2), A. Loumaye (2), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépatogastroentérologie, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Endocrinologie, diabétologie et nutrition.

Introduction: Type 2 diabetes (T2D) affects around 9% of the Belgian population. Metabolic dysfunction-associated steatotic liver disease (MASLD) is an under-screened complication for which calculation of non-invasive tests may be imprecise. A link between MASLD, T2D and peripheral tissues such as skeletal muscle is suspected, although no functional data are available.

Aim: First, to assess the prevalence and severity of MASLD in patients with T2D by systematic transient elastography; second, to assess body composition in particular muscle mass and third to assess muscle function and the presence of frailty.

Methods: This mono-centric cross-sectional study includes adult patients with T2D attending the diabetes consultation of the Cliniques universitaires Saint-Luc from April to October 2024. Liver assessment is performed using the controlled attenuation parameter and transient elastography (Fibroscan® mini 430, Echosens, Paris, France). Skeletal muscle is assessed by function tests, frailty scores (liver frailty index, LFI and 5-frailty phenotype, 5FP) and bioimpedance. Sarcopenia is defined (geriatric EWGSOP2 society) by the association of low muscle function (handgrip strength <27kg for men and <16 kg for women or sit to stand >15 sec) and myopenia (appendicular skeletal mass index <7 kg/m² for men and <5.5 kg/m² for women). Sarcopenic obesity (ESPEN society) is the co-existence of obesity or adiposity and sarcopenia defined by low muscle function (handgrip strength <27kg for men and <16 kg for women or sit to stand ≥17 sec) and altered body composition (increased fat mass and SMM/W ≤37% for men and ≤27.6% for women). Physical activity is assessed using the international physical activity questionnaire (IPAQ).

Results: Of the 113 patients screened, 8 were excluded (neuromuscular disorders, treatment with cortisone or methotrexate). The population was 38% female, with an average age of 62 (± 12) and a mean body mass index of 30 kg/m² (± 4.9). Mean CAP was 280.7 dB/m (± 53.6) and median elasticity 6 kPa (3.0-23.1). 91% of patients had steatosis (CAP ≥215 dB/m) linked to MASLD (95%) or MetALD (5%). 20% of patients with steatosis have increased liver elasticity compatible with severe fibrosis (≥7.8 kPa M probe; ≥6.4 kPa XL probe). Compared with patients with steatosis and normal hepatic elasticity, those with steatosis and increased elasticity had significantly higher weight, BMI and skeletal muscle index (86 vs 102 kg, p = 0.0005; 30 vs. 35 kg/m², p = 0.003 and 8.4 vs. 9.7 kg/m², p = 0.01). They also had significantly lower muscle function assessed by the sit-to-stand (11.4 vs. 14.3 sec, p = 0.04) despite similar physical activity (1297 vs. 1640 METs/week, p = 0.49) and the same amount of sitting time (579.4 vs. 507.5 min, p = 0.13). The LFI classified 8.6% and the 5PF 7.6% of patients as fragile. Robust patients had lower hepatic elasticity (5.2 vs. 6.1 kPa, p = 0.02) than others, but were also younger (52.7 vs. 64.0, p = <0.0001). Only 5.5% of patients were sarcopenic following the EWGSOP2 definition. These were older (77 vs. 62 years, p = 0.007) but did not have more severe liver disease (median liver elasticity: 5.8 vs. 5.8 kPa, p = 0.9) or greater weight (74.4 vs. 88.9 kg, p = 0.08). In contrast, 24.5% of patients had sarcopenic obesity following ESPEN guidelines. These were not older and did not have more severe liver disease either (65.6 vs 60.2 years, p = 0.0567; 5.8 vs. 5.9 kPa, p = 0.6192).

Conclusions: Ninety-one percent of T2D patients present with hepatic steatosis, and 20% with fibrosing disease. The severity of liver damage is interestingly associated with lower muscle strength, unrelated to reduced physical activity, and non-intuitively with higher muscle mass. This could be explained by a possible overload of muscle fat in this at-risk group of patients, underlining the muscle-liver axis. The prevalence of sarcopenia is highly dependent on the diagnostic criteria used (geriatric or nutrition societies).

- A02 -

EDUCATIONAL NEEDS IN PATIENTS WITH LIVER CIRRHOSIS. L. Seynhaeve (1), S. De Meulder (2), J. Decaestecker (2), J. Dewyspelaere (2), C. De Vloo (2), L. De Decker (3), J. Lelong (3), L. Kinnaer (4) / [1] AZ Delta, Roeselare, Belgium, Maag-darm-lever, [2] AZ Delta, Belgium, Gastroenterology - hepatology, [3] Ghent University, Ghent, Belgium, Master in Science in Nursing and Midwifery, [4] Ghent University, Ghent, Belgium, Department of Public Health and Primary Care.

Introduction: Liver cirrhosis is a progressive liver condition with various causes, including viral infections, metabolic disorders, and lifestyle factors. The global burden of liver cirrhosis is substantial, contributing to significant morbidity, mortality, and healthcare costs worldwide. Each year, approximately 1 million people die from liver cirrhosis, making

it the 11th most common cause of death globally. (1) Patients and society often link liver cirrhosis primarily to alcohol consumption, which can lead to stigma. This limited understanding of alternative causes not only impacts patients' emotional well-being but may also hinder effective medical management. A deeper understanding of patients' information needs and emotional responses at diagnosis is crucial for enhancing patient education and providing tailored support to improve their overall quality of life.

Aim: The aim of this study was to explore the experiences of patients with liver cirrhosis regarding their emotional and medical management and to identify their information needs at the time of diagnosis.

Methods: A qualitative research method with an exploratory design was employed. Semi-structured interviews were conducted to gain insight into the experiences of liver cirrhosis patients and their information needs. Patients with compensated and decompensated liver cirrhosis were recruited using a convenience sampling strategy in a single centre in Belgium. The interviews aimed to explore how patients managed their condition and what specific information they required at different stages of their disease. All interviews were audio-recorded with the participants' consent to ensure accurate data capture, and verbatim transcription was performed to preserve the authenticity of the participants' responses. This allowed for a more in-depth and nuanced thematic analysis. Methodological rigor was ensured through researcher triangulation, inclusion/exclusion criteria, and data saturation. Peer debriefing also supported the analytical process.

Results: In total, 20 patients were interviewed. Three major themes emerged from the analysis: (1) medical management of liver cirrhosis; (2) emotional management of liver cirrhosis and (3) the need for clear and comprehensive information. Upon receiving their diagnosis, many participants experienced feelings of disbelief and a sense of injustice. This reaction was often rooted in the widespread misconception that liver cirrhosis is exclusively linked to excessive alcohol consumption. As a result, there was a strong desire for a more accessible and detailed explanation of the condition. Participants expressed a need to better understand the diagnosis itself, including the underlying causes, the range of symptoms, potential complications, the likely prognosis, available treatment options and the necessary steps for follow-up care.

Conclusions: This study has contributed to identifying the experiences and educational needs of patients with both compensated and decompensated liver cirrhosis. Findings revealed that, at the time of diagnosis, patients had limited knowledge of their condition, raising questions about the diagnosis, symptoms, complications, prognosis, treatment and necessary follow-up. Additionally, misconceptions about the causes of cirrhosis led to societal stigma and personal prejudice associated with their diagnosis. These results highlight the need for developing targeted educational materials to better inform liver cirrhosis patients and reduce stigma.

- A03 -

MUSCLE FUNCTION IS ALREADY IMPAIRED IN NON-CIRRHOTIC PATIENTS WITH STEATOTIC LIVER DISEASES COMPARED TO HEALTHY CONTROLS. G. Henin (1), A. Goffaux (2), S. Declerck (2), S. André-Dumont (2), E. Pendeville (3), M. Valet (4), T. Lejeune (5), G. Dahlqvist (1), A. Loumaye (6), P. Stärkel (1), N. Ianthier (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'hépto-gastroentérologie, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Laboratoire d'Hépto-Gastroentérologie (GAEN), [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de kinésithérapie et ergothérapie, [4] Grand Hôpital de Charleroi, Charleroi, Belgium, Service de médecine physique et réadaptation, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de médecine physique et réadaptation, [6] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'endocrinologie, diabétologie et nutrition.

Introduction: Muscle function decay and frailty are prevalent in cirrhosis whatever the cause. However, muscle function evaluation in non-cirrhotic patients is lacking, as well as data by etiology, including steatotic liver diseases (SLD). Our aim is to determine if muscle function already decays in non-cirrhotic SLD and if the SLD subtype impacts muscle function.

Aim: Our aim is to determine if muscle function already decays in non-cirrhotic SLD and if the SLD subtype impacts muscle function.

Methods: SLD patients were prospectively recruited and classified according to the recent SLD subtype categories. Liver disease was assessed by transient elastography (Fibroscan®). Cirrhotic patients were excluded. Controls were defined by the absence of liver steatosis on controlled attenuation parameter (< 215 dB/m). Muscle function was assessed by isokinetic dynamometer (Cybex®). All patients and controls also underwent the three tests used to calculate the liver frailty index (LFI): handgrip strength, sit-to-stand test and balance test. SLD patients and controls were classified based on the LFI as robust ($LFI < 3$) or pre-frail/frail ($LFI \geq 3$). Results are expressed as means $\pm$ SD.

Results: One hundred and thirty-seven patients with SLD were included: 69 with alcohol-related liver disease (ALD) and 66 with metabolic dysfunction-associated steatotic liver disease (MASLD). Thirty healthy participants matched for sex and age (controls: 47.8 years ± 14.1 , ALD: 50.2 ± 10.8 , MASLD: 52.5 ± 10.4 ; $p = 0.16$) were used as controls. However, the groups differed for several parameters, such as alanine aminotransferase (controls: 18.4 IU/L ± 10.2 , ALD: 74.8 ± 53.2 , MASLD: 48.3 ± 29.5 ; $p < 0.0001$), liver stiffness (controls: 4.4 kPa ± 1 , ALD: 8.9 ± 3.5 , MASLD: 9 ± 3.9 ; $p < 0.0001$) and body mass index (controls: 22.1 kg/m² ± 2 , ALD: 26.3 ± 5 , MASLD: 33.3 ± 6.4 ; $p < 0.0001$). LFI was higher in all SLD subgroups compared to controls (controls: 2.2 ± 0.8 , ALD: 3.2 ± 0.8 , MASLD 3.1 ± 0.7 ; $p <$

0.0001) without any difference between MASLD and ALD patients ($p = 0.67$). 56.5 % of ALD patients and 58.5 % of MASLD patients were considered pre-frail or frail ($p = 0.81$) compared to only 10 % of control patients ($p < 0.0001$). LFI negatively correlated with right knee extension evaluated by isokinetic dynamometer in all SLD patients ($N = 137$, $r = -0.53$; $p < 0.0001$).

Conclusions: LFI is an accurate method to assess muscle function in non-cirrhotic SLD patients. Muscle function assessed by the LFI decays compared to age-matched non-SLD controls. Frailty is not influenced by the SLD subtype. This reinforces the concept of a muscle-liver axis already in the early stages of SLD.

- A04 -

LIVER TRANSCRIPTOMICS ANALYSIS UNRAVELS THE SEQUENTIALITY OF LIVER STEATOSIS MECHANISMS IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTOHEPATITIS. G. Henin (1), A. Lamotte (2), M. Nachit (2), A. Lorient (3), I. Leclercq (2), N. Lanthier (2) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepato-gastroenterology, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, laboratory of Hepato-gastroenterology (GAEN), [3] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, BIOINFO core Facility, de Duve Institute.

Introduction: Hepatic steatosis is secondary to a complex metabolic dysregulation of lipid homeostasis. Pathophysiological mechanisms are numerous and include dysregulations in lipid uptake, de novo synthesis, oxidation and secretion. Specific drugs targeting lipid metabolism are currently evaluated in clinical trials with inconsistent results. We suggest that the pathophysiology of steatosis may evolve with MASLD progression, and the mixed effects may reveal a mismatch between the deregulated mechanisms and the drug used.

Aim: To analyse the evolution of gene expression of key lipid metabolism genes during MASLD-MASH disease progression in mice.

Methods: Foz/foz mice (FOZ) were fed normal diet (ND)(3.39 kcal/g, 16% of lipids, A03 Research Diets) or high-fat diet (HFD)(5.24 kcal/g, 60% of lipids, D12492 Research Diets). Liver tissue was harvested at baseline (control group, $N=5$) and after 4 (FOZ ND=3, HFD=4), 12 (FOZ ND=6, HFD=8) or 32 (FOZ ND=6, HFD=6) weeks. Formalin-fixed paraffin-embedded liver samples were used for histological scoring (SAF score) using haematoxylin & eosin staining. Total RNA from liver samples was extracted and purified using Qiagen® mini kits prior to bulk RNA sequencing (Macrogen Europe). Sequencing data were normalized according to timepoint and diet and analysed RStudio. Differential gene expression and enrichment analysis (Gene Ontology database, biological process) were performed as follows: FOZ ND week 0 (control group) versus FOZ HFD week 4, FOZ ND week 0 versus FOZ HFD week 12, FOZ ND week 0 versus FOZ HFD week 32. Differentially expressed genes (DEG) were defined by a p adjusted value (padj) < 0.05 and $|\log_2\text{FoldChange}| > 1$. Enrichment results are presented by Normalized Enrichment Score (NES) and p adjusted value.

Results: FOZ mice fed HFD reached maximal liver weight to body weight ratio at 32 weeks ($p < 0.001$). Insulin resistance is present at 4 weeks of HFD as assessed by the HOMA-IR index ($p < 0.01$). FOZ mice fed HFD exhibited the whole MASH spectrum with fluctuating transcriptomics changes over time. At week 4, liver histology highlighted isolated steatosis with 284 DEG involved in 685 enriched pathways including fatty acid biosynthetic process ($\text{NES} = 13.9$, $\text{padj} = 1.2\text{e-}4$)(Ppar γ , Hacd4, Obp2a), lipid transport ($\text{NES} = 9.7$, $\text{padj} = 8.0\text{e-}8$)(Ppar γ , Vldlr, Pltp), lipid storage ($\text{NES} = 21.5$, $\text{padj} = 3.0\text{e-}6$)(Cav1, Clstn3, Mup1) and fatty acid oxidation ($\text{NES} = 9.4$, $\text{padj} = 0.02$)(Ppar γ , Obp2a, Sox9). At week 12, liver histology reported steatohepatitis with 469 DEG involved in 504 enriched pathways including lipid transport ($\text{NES} = 14.7$, $\text{padj} = 3.6\text{e-}15$)(Cd36, Ppar γ , Ppar δ , Pltp), lipid storage ($\text{NES} = 24.2$, $\text{padj} = 1.66\text{e-}7$)(Fitm1, Bltp1, Cidec) and fatty acid oxidation ($\text{NES} = 22.2$, $\text{padj} = 2.7\text{e-}7$)(Acaa1b, Ehhadh, Ppar δ). At week 32, fibrosing steatohepatitis was observed with 750 DEG involved in 1167 enriched pathways including lipid transport ($\text{NES} = 11.3$, $\text{padj} = 6.3\text{e-}21$)(Cd36, Apom, Ppar δ), lipid storage ($\text{NES} = 24$, $\text{padj} = 1.4\text{e-}15$)(Fitm1, Bltp1, Cidec; Ppar γ) and fatty acid oxidation ($\text{NES} = 11$, $\text{padj} = 7.4\text{e-}7$)(Hao2, Ppar γ , Ppar δ). At the gene level, the lipid metabolism key regulator Ppar γ was downregulated in a time-dependent manner ($\text{Log}_2\text{FC} = -1.6$, $\text{padj} = 9\text{e-}5$ at week 4; $\text{Log}_2\text{FC} = -1.8$, $\text{padj} = 9\text{e-}6$ at week 12 and $\text{Log}_2\text{FC} = -2.35$, $\text{padj} = 6.6\text{e-}9$ at week 32). Fatty acid oxidation related genes are all downregulated at week 12, such as Obp2a ($\text{Log}_2\text{FC} = -3.17$, $\text{padj} = 0.003$) and Acaa1b ($\text{Log}_2\text{FC} = -1.64$, $\text{padj} = 9.9\text{e-}9$). Lipid storage genes expression also greatly change over time. Cidec and Fitm1 are involved in lipid droplet homeostasis preventing lipotoxicity of free fatty acids. Both Cidec and Fitm1 are significantly downregulated at week 12 ($\text{Log}_2\text{FC} = -2.13$, $\text{padj} = 3\text{e-}6$; $\text{Log}_2\text{FC} = -1.37$, $\text{padj} = 1.68\text{e-}7$ respectively) and at week 32 ($\text{Log}_2\text{FC} = -2.7$, $\text{padj} = 2\text{e-}5$; $\text{Log}_2\text{FC} = -1.02$, $\text{padj} = 2\text{e-}4$ respectively).

Conclusions: We report the dynamic changes of pathophysiological mechanisms potentially involved in hepatic steatosis occurring in a MASH mouse model over time using bulk RNAseq. These time-dependent shifts in gene expression of potential therapeutic targets may significantly influence the response to MASLD treatments.

- A05 -

EVALUATION OF A MASLD OUTPATIENT CLINIC AND REFERRAL PATHWAY FOR PATIENTS WITH SUSPECTED METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE. C. Vos (1), H. Van

Vlierberghe (2), X. Verhelst (2), L. Devisscher (3), S. Raevens (2), S. Lefere (2), A. Geerts (2) / [1] Ghent University, Ghent, Belgium, Faculty of Medicine and Health Sciences, [2] Ghent University Hospital, Gent, Belgium, Department of Internal Medicine and Paediatrics, Hepatology Research Unit, [3] Ghent University, Ghent, Belgium, Department of Basic and Applied Medical Sciences.

Introduction: One in four adults in Belgium suffers from metabolic dysfunction-associated steatotic liver disease (MASLD). Fibrosis stage is strongly correlated with the clinical outcome. However, only a minority of patients with MASLD has advanced fibrosis. The MASLD clinic in Ghent University Hospital is an accessible referral point for patients with suspected MASLD. Fibrosis stage is measured at the first visit with a FibroScan, creating a non-invasive risk stratification from which a further approach is decided on.

Aim: The aim was to assess the profile and fibrosis stage of the referred patients and to perform an overall assessment of the MASLD clinic.

Methods: All patients seen in the MASLD clinic of Ghent University Hospital between October 2017 and December 2023 were included. FibroScan was performed by trained nurses using the FibroScan® Mini+ 430 device (M- or XL-probe). Liver steatosis was detected either on biopsy, on ultrasound or with a Controlled Attenuation Parameter of ≥ 248 dB. Only FibroScan results with $\text{IQR} \leq 30$ were considered valid and used for analysis. If the FibroScan score was ≥ 8.50 kPa, liver biopsy was indicated. Data from patients' records was collected retrospectively and stored on a REDCap database. All statistical analyses were performed using the IBM SPSS Statistics software.

Results: Between 2017 and 2023, 328 patients were seen at the clinic (51.2% male, 48.8% female). The median age and BMI at the first visit were 55 years (IQR 46 - 62) and 30.9 (IQR 27.0 - 34.7), respectively. The most common metabolic comorbidities were hypertriglyceridemia (56.7%), hypertension (54.6%) and type 2 diabetes (29.9%). In 106 patients (32.3%) a liver biopsy was performed. Steatosis or steatohepatitis was found in 92.5%. 35.8% of biopsies revealed a fibrosis stage F0-1, 34.0% F2, 23.6% F3 and 6.6% F4. 77 patients (23.5%) had concomitant liver disease. Most prevalent was alcohol-associated liver disease affecting 50 patients (15.2%), of whom 48 (96.0%) also had a metabolic profile. Other hepatic comorbidities included hepatitis B virus (2.4%), hepatitis C virus (1.2%) and cholestatic liver disease (1.2%). 317 patients (96.6%) had a metabolic profile, of whom 245 (77.3%) had no concomitant liver disease. In 210 (85.7%) of these patients with metabolic dysfunction and no concomitant liver disease steatosis was present. The median FibroScan value at the first visit measured 6.90 kPa (IQR 4.90 – 10.30). 62.2% had a FibroScan score < 8.50 kPa. This cut-off had a sensitivity of 84.2% and a specificity of 52.4% predicting F2 or more on liver biopsy (AUROC = 0.761). 73.0% had a FibroScan value < 10.00 kPa, with a sensitivity and specificity of 86.4% and 64.9% respectively to detect F3 or more (AUROC = 0.848). The median FIB-4 score at the first visit was 1.14 (IQR 0.87 – 1.66) and was < 1.30 in 59.4%. A score of 1.30 had a sensitivity of 66.7% and a specificity of 65.4% indicating F3 or more (AUROC = 0.733). Using the Agile3+ score with a 0.451 cut-off to predict F3 or more in patients without hepatic comorbidity, a sensitivity of 90.0% and a specificity of 77.3% were reached (AUROC = 0.836). One patient had hepatocellular carcinoma (HCC). There were no new cases of HCC diagnosed during the follow-up period. 14 patients died during this period (4%). The causes of death were liver disease (3), non-HCC malignancy (2), cardiovascular disease (1), infection (1) and unknown or other (7).

Conclusions: Patients with significant fibrosis receive a structured follow-up at the MASLD clinic to detect fibrosis progression timely and avoid complications. However, a significant proportion of patients does not have significant fibrosis and is therefore not at immediate risk for complications. In these cases, discharge to primary care with lifestyle advice and monitoring fibrosis with FIB-4 was recommended. Moreover, a MASLD referral pathway could be implemented in the future where specialized nurses perform FibroScan and only patients exceeding a certain value are seen by a specialist physician, further reducing the number of visits in secondary and tertiary health care.

- A06 -

THE ROLE OF INTERLEUKIN-8 IN PRIMARY SCLEROSING CHOLANGITIS-ASSOCIATED IMMUNE CELL DYSREGULATION. L. Heyerick (1), K. De Muynck (1), Z. De Vos (1), S. Lefere (2), J. Roels (3), N. Vandamme (3), M. Van Der Linden (4), A. Hoorens (4), A. Geerts (2), S. Raevens (2), X. Verhelst (2), H. Van Vlierberghe (2), L. Devisscher (1) / [1] Ghent University, Ghent, Belgium, Department of Basic & Applied Medical Sciences, Gut-Liver Immunopharmacology Unit, [2] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics, Hepatology Research Unit, [3] VIB, Gent, Belgium, VIB Single Cell Core, [4] Ghent University Hospital, Ghent, Belgium, Department of Pathology.

Introduction: Primary sclerosing cholangitis (PSC) is a chronic, progressive, fibroinflammatory liver disease. Dysregulated systemic and hepatic immune cell responses are implicated in the pathogenesis of PSC and could serve as a diagnostic and therapeutic target. However, PSC-associated systemic immune cell profiles remain insufficiently characterised.

Aim: We unravelled peripheral immune cell subsets of PSC patients and healthy controls at the single cell level and further investigated its implications in PSC pathogenesis.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated by density gradient centrifugation from fresh EDTA-anticoagulated peripheral blood from PSC patients and healthy controls (HCs). PBMC cell suspensions were: a) FACS-purified, single cell Gel Bead-in-Emulsions were generated and RNA-sequencing libraries were created and analysed, or b) evaluated for interleukin-8 (IL-8) expression in CD14⁺ cells by flow cytometry. IL-8 concentrations were determined in the sera of PSC-patients, without prior liver transplantation, and of healthy controls. Adult male C57BL/6/J mice were subjected to common bile duct ligation (CBDL) surgery and a) after two weeks, monocyte/macrophage populations were sorted by FACS and processed for bulk sequencing, or b) mice were treated 12 days with reparixin (a potent CXCR1- and weak CXCR2-antagonist), SB225002 (a selective CXCR2-antagonist), navarixin (a dual CXCR1/2 antagonist) or with vehicle.

Results: Based on single cell analyses of PBMCs, we identified a population of CD14-positive monocytes with enriched IL8-expression in PSC patients (n=7) compared to HCs (n=4), which was confirmed on flow cytometry analyses (mean expression 52.9% in PSC and 12.2% in HC, $p < 0.05$). Serum protein analyses showed that PSC patients are also characterised by increased IL-8 levels in the systemic circulation (n=57 for PSC, n=15 for HCs, age- and sex-matched). In addition, PSC patients with advanced fibrosis (Metavir stage F3/F4) had significantly higher serum concentrations of IL-8 compared to patients without advanced fibrosis (F0/F2, $p < 0.05$). AUROC analysis showed good performance of IL-8 to assess risk of liver-transplant free survival at 3 years of follow-up (AUROC 0.78). Bulk sequencing of isolated mouse liver monocyte-derived macrophages in CBDL-induced cholestasis showed significantly upregulated expression of the IL-8 mouse homologs Cxcl1 and Cxcl2 2 weeks after surgery compared to sham-operated mice. Moreover, reparixin-treated mice exhibited no significant upregulation of proinflammatory and fibrotic markers in comparison to sham operated mice, while this was the case for vehicle-, SB225002- and navarixin-treated mice.

Conclusions: PSC patients are characterised by a population of CD14-positive monocytes enriched in IL8-expression and by elevated IL-8 concentrations in the systemic circulation. Serum IL-8 concentrations might serve as prognostic marker for liver-transplant free survival. Reparixin, a dual CXCR1/2-antagonist with increased selectivity for CXCR1 suppresses CBDL-induced liver injury and further research should focus on unravelling its potential as a therapeutic target.

- A07 -

SPLenic ELASTOGRAPHY AND PLATELET COUNT: KEY TOOLS FOR MANAGING PSVD AND PORTAL HYPERTENSION. L. Ponsalet (1), G. Dahlqvist (2), N. Lanthier (2), B. Delire (2), S. André-Dumont (2) / [1] UCL Saint Luc, Brussels, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology.

Introduction: Porto-sinusoidal vascular disorder (PSVD) represents a recently recognized clinical entity. Patients with PSVD commonly present presinusoidal portal hypertension (PH) along with its associated complications (thrombocytopenia, splenomegaly, ascites, varices and/or hepatic encephalopathy). PSVD is observed in several conditions such as haematological disorders, genetic disorders, haemocoagulative disorders, cardiovascular diseases or drug induced injury. In the case of PSVD, spleen stiffness measurement (SSM) could help us in identifying patients with portal hypertension and who are at high risk of developing oesophageal varices and bleedings, which are the primary complications associated with this condition alongside portal vein thrombosis.

Aim: The aim of the SPLENO-HYPE study is to prospectively follow patients with PSVD who have benefited from an assessment, in particular by measuring liver and spleen stiffness measurement, and to study the links between SSM, clinical characteristics and complications.

Methods: Interim (6-month) analysis of our prospective monocentric study of PSVD patients defined following the recent guidelines. Data will include demographic data, past medical history, routine clinical examination, routine blood test including liver function tests and biological markers of portal hypertension, liver biopsies findings and hepatic and SSM with the FibroScan® Expert 630.

Results: During the first 6-month period, 22 patients with PSVD were included, 20 with nodular regenerative hyperplasia (NRH) and 2 with incomplete septal fibrosis on the liver biopsy. Among the 22 patients, the majority (20/22, 90.91%) exhibited clinical and biological markers of significant portal hypertension. Thrombocytopenia (platelet count $< 150,000/\text{mm}^3$) was observed in 77% of patients (17/22) as well as splenomegaly with an average spleen size of 16.5 ± 2.7 cm. Oesophageal varices were present in 85% of the cohort (17/20) including 7 with grade 2 and 5 with grade 3 varices. The mean liver stiffness was 12.6 ± 8.7 kPa. Half of the patients had values below 10 kPa, 27 % had values between 10 and 15 kPa, and 23 % exceeded 15 kPa. Notably, most patients with values below 10 kPa showed signs of significant portal hypertension, including thrombocytopenia, splenomegaly (8/11), and esophagogastric varices (9/11). All patients without significant portal hypertension had values under 15 kPa. The mean SSM was 65.6 ± 25.3 kPa. A weak positive correlation was observed between SSM and the grade of oesophageal varices ($R^2 = 0.178$), while the correlation was stronger between platelet count and oesophageal varices ($R^2 = 0.441$). Only three patients had values below 40 kPa. These patients showed no signs of significant portal hypertension. On all patients with SSM > 40 kPa, only one patient did not have evidence of significant portal hypertension. When comparing patients with SSM < 40 kPa (n=3) to those with increased SSM, there were no significant differences in

terms of platelet count, spleen size, ALBI score, or liver elastography. However, the presence of oesophageal varices differed significantly ($p < 0.001$).

Conclusions: Patients with PSVD commonly present with significant portal hypertension features, including thrombocytopenia, splenomegaly, and oesophageal varices. Elevated SSM, often surpassing the 40 kPa threshold observed in cirrhosis, together with a liver stiffness measurement incompatible with cirrhosis indicates a diagnosis of PSVD and may serve as a useful marker for screening oesophageal varices. Integrating platelet count into the assessment could further enhance screening strategies. Validation in larger cohorts is needed to confirm these findings, as well as the prognostic value of these elements on the development of complications.

- A08 -

DRUG-INDUCED LIVER INJURY IN BIOPSY-SCALED PRECISION-CUT LIVER SLICES. M. Lobo (1), N. Eysackers (1), A. Smout (1), S. Verhulst (1), N. Messaoudi (2), L. Van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Faculty of Medicine and Pharmacy, [2] UZ Brussel, Brussels, Belgium, Gastroenterology.

Introduction: Repeated consumption of certain drugs that can lead to hepatocyte damage, also known as drug-induced liver injury (DILI), is one of the major safety concerns for pharma companies, regulatory agencies and clinicians. An important challenge is the lack of methods to predict adverse effects of drug-drug interactions on the liver. While rodent models are used for pre-clinical tests, these are not up to par in predicting the DILI risk of a drug in humans. Among the many in vitro alternatives for in vivo DILI testing, human precision-cut liver slices (PCLS) have emerged as a promising ex-vivo model with great potential to faithfully replicate liver functionality. PCLS retains the liver's native microarchitecture and cellular diversity while offering a simpler preparation process than other 3D culture models. However, the usual diameter of PCLS cultures is rather large (5-8 mm) and thus large liver resections are needed to culture human PCLS which become scarce with the current evolution of robot-assisted surgery.

Aim: To develop biopsy-scaled (1mm) PCLS cultures for the evaluation of DILI.

Methods: First, healthy male BALB/c mice (Charles River) were used for baseline studies and in-house developed BALB/c-Tg(Pdgfrb-GFP)x strain for live imaging. Median and left lobes of euthanized mice are excised, cut in 250um thick slices using a Leica 1200S vibratome, punched using a 1mm or 3mm biopsy puncher (Kai® Medical) and cultured in 24 or 96-well plates. Samples are snap-frozen at different culture times and conditions. RNA extraction was performed using TRIzol®. qPCR was done using a QuantStudio™ 3 Real-Time PCR System (ThermoFisher). RNA sequencing library was prepared using the QuantSeq 3' mRNA-Seq method (Lexogen) and sequenced on a NovaSeq (Illumina). Whole slice immunostaining was carried out on formalin-fixed samples with fluorescently-labelled antibodies. Imaging was done using a Zeiss LSM® 800 confocal microscope and an EVOS M7000® microscope.

Results: Comparison of hepatocyte marker expression between 1mm and 3mm slices over 5 days suggests that a smaller slice diameter better preserves hepatocyte functionality in mouse PCLS cultures. GSEA analysis of RNAseq data of day 0 and day 5 slices revealed a high enrichment of ECM remodelling pathways and wound healing responses in day 5 slices. Using BALB/c-Tg(Pdgfrb-GFP) mice we could confirm hepatic stellate cell (HSC) activation over time demonstrated by an increase in the GFP signal. Exposure to a pro-inflammatory cocktail and TGFβ further increased the GFP signal showing the responsiveness of the cultures. Furthermore, the 1mm slices allowed paracetamol-driven liver damage observed both on RNA and immunostainings. We optimized the culture of PCLS in 96-well plates which facilitated the determination of IC50 concentrations of APAP and Omeprazole after 2 days of exposure. Part of our findings in mice could be replicated in human 1mm PCLS cultures.

Conclusions: PCLS of 1mm diameter from both human and mouse liver samples demonstrated good preservation of hepatocyte functionality in culture compared to larger slices. The use of BALB/c-Tg(Pdgfrb-GFP) transgenic mice facilitates the evaluation of DILI drugs as well as fibrosis-inducing agents. The 1 mm slices will allow for testing human liver biopsy-derived slice cultures for DILI as well as pro- and anti-fibrotic drugs and thus also hold promise for personalized medicine approaches.

- A09 -

18F-FDG PET/CT AS A RECURRENCE PROGNOSIS TOOL IN LIVER TRANSPLANTATION FOR MILAN OUT HEPATOCELLULAR CARCINOMA. K. Mombaerts (1), A. Lamproye (2), P. Lovinfosse (3), C. Lambrecht (4), C. Amicone (1), M. Vandermeulen (5), N. Meurisse (5), N. Gilbo (5), O. Warling (2), J. Delwaide (1), P. Honore (5), R. Hustinx (3), O. Detry (5) / [1] CHU Liege, Liège, Belgium, Dpt of Hepatogastroenterology, [2] CHU de Liège, Liège, Belgium, Dpt of Hepatogastroenterology, [3] CHU Liege, Liège, Belgium, Dpt of Nuclear Medicine and Oncological Imaging, [4] CHU de Liège, Liège, Belgium, Dpt of Abdominal Surgery and Transplantation, [5] CHU Liege, Liège, Belgium, Dpt of Abdominal Surgery and Transplantation.

Introduction: As there is a lack of deceased liver donors, the liver allocation system of many countries has included a tight selection of the hepatocarcinoma (HCC) patients who may benefit the most from liver transplantation (LT) with the

lowest risk of recurrence. For years, this risk of HCC recurrence was related only to the size and the numbers of the HCC nodules. However, it is clear now that, if size and number matter, the biology of the HCC itself is also of great importance.

Aim: The aim of this study was to evaluate the prognostic value of 18F-fluorodeoxyglucose positron emission tomography coupled with computed tomography (18F-FDG PET/CT) in preLT assessment of patients with chronic liver disease and HCC.

Methods: This is a single-centre retrospective study on 115 HCC patients (mean age: 62 ± 7 y) who benefited from 18F-FDG PET/CT before any bridge therapy and underwent LT between January 2010 and December 2021. Follow-up was ended on December 31, 2023. 18F-FDG PET/CT was considered positive when the ratio between the SUVmax of the tumour and the SUVmax of the liver parenchyma (RSUVmax) was > 1.15 (PET pos). RSUVmax was compared to other preLT prognostic factors, as Milan criteria (in/out), AFP score ($\leq$ or > 2), Up-To-Seven score (in/out), and Metroticket 2.0 score. Overall survival and recurrence-free survivals were evaluated by Kaplan-Meier method. Comparisons of survival between prognostic factors were made using Cox regression.

Results: Among the 115 HCC patients, 32 patients (27.8%) were Milan out, 21 (18.3%) AFP score > 2 , and 11 (9.6%) Up-to-seven out at time of LT listing. RSUV max was > 1.15 in 28 (24.7%) patients. Overall survival was 88.7% and 70.8% at 2 and 5 years, respectively. Recurrence-free survival (RFS) was 91.6% and 80.8% at 2 and 5 years, respectively. In recurrence-free survival analysis in the Milan out group, RSUVmax > 1.15 was the only predictive factor for recurrence in uni- and multivariate analyses. Interestingly, there was no 5-yr RFS difference between Milan in/PET neg, Milan in/PET pos and Milan out/PET neg patients (88%, 83% and 77% respectively), but RFS was significantly worse in Milan out/PET pos patients (20%).

Conclusions: FDG-PET/CT with an RSUVmax cut-off value of 1.15 is a strong prognostic factor for recurrence in Milan out patients. Milan out /PET neg HCC patients might have a good prognosis after LT. Further prospective studies should test whether 18F-FDG PET/CT) should be systematically included in the preLT assessment of Milan outpatients.

- A10 -

SARCOPENIA IN PATIENTS RECEIVING TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IS INDEPENDENTLY ASSOCIATED WITH INCREASED RISK OF COMPLICATIONS AND MORTALITY. E. Vanderschueren (1), P. Meersseman (2), A. Wilmer (2), V. Vandecaveye (3), E. Dubois (1), A. Van Eldere (1), J. Clerick (1), J. Peluso (4), E. Claus (4), L. Bonne (4), C. Verslype (1), G. Maleux (4), W. Laleman (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of General Internal Medicine, Medical Intensive Care Unit, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Radiology, Abdominal Radiology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Radiology, Interventional Radiology.

Introduction: Sarcopenia is an acknowledged risk factor for individuals with chronic liver disease, however, the influence on outcomes in patients receiving transjugular intrahepatic portosystemic shunt (TIPS) remains underexplored.

Aim: This study evaluates the association between sarcopenia and incidence of complications – including hepatic encephalopathy, ischemic hepatitis, cardiac decompensation, recurrence of ascites or variceal bleeding – and mortality post-TIPS. Additionally, it explores the evolution of muscle mass after TIPS placement.

Methods: A retrospective analysis was performed on patients who underwent TIPS for variceal bleeding (VB) or refractory ascites (RA) between 2011-2021 in the University Hospital of Leuven and had available cross-sectional imaging. Sarcopenia was assessed using transverse psoas muscle thickness (TPMT), normalized by patient height, at the level of the umbilicus and the level of vertebra L3. TPMT was measured at baseline, with a subset of 85 patients having a second TPMT after 1-2 years for assessment of evolution.

Results: Of the 175 patients, 57.7% underwent TIPS for RA and 42.3% for VB with a median follow-up of 453 days (IQR 76-1179). TPMT at L3 level could be assessed in all patients, while TPMT at umbilical level could not be measured in 28.6% due to anatomical limitations, therefore TPMT-L3 was used to define sarcopenia. Sarcopenia was present in 30.9% of patients at baseline. Sarcopenic patients exhibiting a higher prevalence of complications (74.1% vs. 57.9%, $p=0.04$) and one-year mortality (53.4% vs. 22.3%, $p<0.001$) post-TIPS, despite similar MELD scores, Child-Pugh scores and portosystemic gradients at baseline. Notably, 58.8% of patients showed an increase of $>10\%$ from baseline TPMT/length post-TIPS, with the greatest improvement observed in severely sarcopenic patients ($+4.00 \pm 4.55$ mm/m vs. -0.82 ± 2.68 mm/m, $p<0.001$) and in those patients free from TIPS-related complications ($+3.18 \pm 4.09$ mm/m vs. $+1.31 \pm 3.21$ mm/m, $p=0.022$).

Conclusions: Sarcopenia increases the risk of complications and mortality following TIPS. Importantly, sarcopenia improves in patients receiving TIPS, with the highest gain in those with the lowest baseline TPMT pre-TIPS, particularly when they remain without complications. TPMT is a valuable tool for pre-TIPS risk assessment and post-procedural monitoring. These findings support the continued use of TIPS in patients with sarcopenia, with close surveillance to optimize outcomes and potentially maximize the benefits of improved muscle mass.

SERUM BIOMOLECULES IMPROVE LIVER ENZYME-BASED PREDICTION SCORES OF SIGNIFICANT FIBROSIS AND FIBROTIC MASH. N. Beyene (1), L. Schoenmakers (2), W. Kwanten (2), E. Dirinck (3), A. Verrijken (3), J. Derdeyn (2), T. Steinhauser (2), T. Vanwolleghem (2), A. Driessen (4), C. De Block (3), S. Francque (2), L. Vonghia (2) / [1] Laboratory of Experimental Medicine and Paediatrics, University of Antwerp, Antwerp, Belgium, Translational Research in Immunology and Inflammation, [2] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [3] Antwerp University Hospital, Edegem, Belgium, Endocrinology, Diabetology and Metabolic Diseases, [4] Antwerp University Hospital, Edegem, Belgium, Department of Pathology.

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common chronic liver disease with growing importance. Isolated steatosis (MASL) can progress to metabolic dysfunction-associated steatohepatitis (MASH) with or without fibrosis. Significant fibrosis ($\geq$ F2 fibrosis) or fibrotic MASH (i.e., MASH with $\geq$ F2) have a higher risk of developing advanced liver disease. The gold standard for identifying MASH and liver fibrosis remains biopsy-based histological evaluation, an invasive and costly procedure. Thus, biopsy-free prediction models are still needed to detect liver fibrosis and fibrotic MASH.

Aim: Establishing a serum-based non-invasive score model to predict significant liver fibrosis and fibrotic MASH.

Methods: Two comparable cohorts, a derivative and validation, comprising respectively 120 and 118 patients, were assessed. These patients underwent liver biopsy for a suspicion of MASLD at the Gastro-enterology and Hepatology Department of the Antwerp University Hospital. The NAFLD activity score (NAS) system was used to determine the histological MASLD features. Beside standard serum biochemistry, serum biomolecules of metabolic, inflammatory, and vascular proteins were measured using an enzyme-linked immunosorbent assay (ELISA). The FIB4 index was computed as $FIB4 = (Age \times AST \text{ (IU/L)}) / (\text{Platelets (109/L)} \times \sqrt{ALT \text{ (IU/L)}})$. Multivariate analysis was performed to identify independent predictors of fibrosis $F \geq 2$ and fibrotic MASH. These variables were combined in logistic regression analysis to generate a unique prediction model. Diagnostic performance was then assessed by the area under the receiver operating characteristic curve (AUROC). The AUROC of the different models and FIB-4 were compared using the DeLong test via R. $P < 0.05$ was considered statistically significant for all the analyses.

Results: The derivation cohort included patients with fibrosis $F \geq 2$ (40%), MASH (40%), and fibrotic MASH (28.3%), while the validation cohort comprised fibrosis $F \geq 2$ (44%), MASH (45.8%), and fibrotic MASH (33.9%). A new model known as Model-2S3 was developed by unweighted integration of two enzymes and three serum biomolecules. In the derivation cohort, Model-2S3 predicted fibrosis $F \geq 2$ with an AUC of 0.96 (95% CI: 0.93–0.99), maintaining 94% sensitivity and 91% specificity. For fibrotic MASH, Model-2S3 achieved an AUC of 0.90 (95% CI: 0.83–0.95), with 85% sensitivity and 86% specificity. Model-2S3 significantly outperformed FIB4 in predicting fibrosis $F \geq 2$ (AUC: 0.83, 95% CI: 0.76–0.90, $P = 0.002$) or fibrotic MASH (AUC: 0.71, 95% CI: 0.61–0.80, $P = 0.001$). An alternative model encompassing three liver enzymes (Model-E, i.e., ALT, AST, and GGT) performed acceptable but also worse than Model-2S3 for prediction of fibrosis $F \geq 2$ (AUC: 0.89, 95% CI: 0.83–0.95, $P = 0.008$) and fibrotic MASH (AUC: 0.78, 95% CI: 0.70–0.87, $P = 0.01$). In the validation cohort, Model-2S3 maintained high accuracy, predicting fibrosis $F \geq 2$ with an AUC of 0.95 (95% CI: 0.92–0.99), 84% sensitivity, and 98% specificity. For fibrotic MASH, it achieved an AUC of 0.89 (95% CI: 0.83–0.96), with 85% sensitivity and 87% specificity. In this cohort, Model-2S3 also significantly outperformed FIB4 and Model-E in predicting fibrosis $F \geq 2$ and fibrotic MASH.

Conclusions: A composite score of serum biomolecules and enzymes yields high accuracy to predict significant fibrosis or fibrotic MASH. This new model outperformed scores based on routinely available parameters and might be considered as a promising non-invasive tool.

FEATURES AND OUTCOMES OF PRIMARY SCLEROSING CHOLANGITIS WITH AND WITHOUT INFLAMMATORY BOWEL DISEASE IN A BELGIAN TERTIARY REFERRAL CENTRE. K. Ahabchane (1), D. Degré (2), A. Cremer (2) / [1] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Internal medicine, [2] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Gastroenterology.

Introduction: Primary sclerosing cholangitis (PSC) is a rare, chronic, and cholestatic liver disease, characterized by progressive intrahepatic and/or extrahepatic bile duct fibrosis and stenosis, predominantly affecting young men. Approximately 70% of PCS patients are also diagnosed with inflammatory bowel disease (IBD).

Aim: This study aims to describe the characteristics and outcomes of patients with PSC in a single tertiary centre, comparing isolated PSC to PSC with coexisting IBD (PSC-IBD) and assessing whether IBD influences PSC progression.

Methods: This retrospective monocentric study included patients diagnosed with PSC between January 1993 and December 2022. Data were collected on demographics, clinical presentations, laboratory findings, imaging, histology, treatments, and complications. Comparisons were made between isolated PSC and PSC-IBD patients.

Results: A total of 97 patients were included, with 56% (54/97) male and a median age at PSC diagnosis of 39 years (interquartile range [IQR]: 25–50 years). 93% (90/97) of patients presented with abnormal liver tests. Pruritus and angiocholitis were present in 17% (16/97) and 8% (7/97) of cases at the time of diagnosis, respectively. The diagnosis of PSC was made based on magnetic resonance imaging (MRI), biopsy, endoscopic retrograde cholangiopancreatography (ERCP), or a combination of MRI and biopsy in 86% (83/97), 7% (7/97), 6% (6/97), and 1% (1/97) of patients, respectively. Small-duct PSC was identified in 7% (7/97) of patients, and 4% (4/97) had an overlap syndrome with autoimmune hepatitis (AIH). 1 patient had small-duct PSC associated with AIH. IBD was present in 54% (52/97) of patients, with ulcerative colitis (UC) in 67% (35/52) and Crohn's disease (CD) in 33% (17/52). IBD preceded, coincided with, or followed PSC diagnosis in 62% (32/52), 21% (11/52), and 17% (9/52) of patients, respectively. PSC-IBD patients were younger at PSC diagnosis ($p=0.004$) and had a lower body mass index (BMI) ($p=0.003$) than those with isolated PSC. Over a median follow-up of 7 years (IQR: 2–13 years), comprising 831 patient-years: Angiocholitis occurred in 23% (22/97) of patients, and secondary biliary cirrhosis in 25% (24/97), with 83% (20/24) of cirrhosis cases leading to portal hypertension. Nine malignancies were observed in 8 patients, including 5 cholangiocarcinomas, 2 gallbladder adenocarcinomas, and 2 colorectal cancers. 13% (13/97) of patients died (1 due to gallbladder adenocarcinoma, 2 due to transplant rejection, 3 due to cholangiocarcinoma, and 7 due to non-hepatic causes). Liver transplantation (LT)-free survival rates were 98% at 1 year and 90% at 5 years. Median LT-free survival was 16 years (95% confidence interval [95% CI]: 12–20 years). Survival comparison showed no significant difference between isolated PSC (13 years, [95% CI]: 2–23 years) and PSC-IBD (16 years, [95% CI]: 13–20 years, $p=0.090$). Multivariate Cox analysis identified age at PSC diagnosis, bilirubin, albumin, creatinine levels at PSC diagnosis, and secondary biliary cirrhosis as independent predictors of mortality and/or liver transplantation.

Conclusions: This study provides a comprehensive overview of PSC characteristics and outcomes in a Belgian tertiary centre. The association with IBD was less frequent than reported elsewhere. Liver complications were more frequent in isolated PSC patients. We did not find a statistically significant difference in median transplant-free survival between isolated PSC patients and PSC-IBD patients. Prognostic factors included age at diagnosis of PSC, albumin, bilirubin, creatinine, and secondary biliary cirrhosis.

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DEVELOPING A DIAGNOSTIC IMMUNOHISTOCHEMISTRY PANEL FOR HEPATOCYTE BALLOONING IN MASLD USING A MULTI-OMICS APPROACH. S. Anak (1), T. Ostyn (1), A. Antoranz Martinez (1), D. El Abyad (1), J. Verbeek (2), S. Van der Merwe (2), S. Pirenne (1), D. Tiniakos (3), Q. Anstee (4), T. Roskams (1), O. Govaere (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Imaging and Pathology, Translational Cell and Tissue Research, [2] KUL - University of Leuven, Leuven, Belgium, Laboratory of Hepatology, CHROMETA / Department of Gastroenterology and Hepatology, University Hospitals Leuven, [3] Newcastle University, Newcastle Upon Tyne, United Kingdom, Translational and Clinical Research Institute, Faculty of Medical Sciences / Dept of Pathology, Aretaieio Hospital, National & Kapodistrian University of Athens, Athens, Greece, [4] Newcastle University, Newcastle Upon Tyne, United Kingdom, Translational and Clinical Research Institute, Faculty of Medical Sciences / Newcastle NIHR Biomedical Research Centre.

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a chronic liver disease driven by the accumulation of triglycerides in hepatocytes, affecting about 38% of the adult population globally. The disease is strongly linked with the metabolic syndrome and is becoming the number one indication for liver transplantation. MASLD covers a spectrum of pathologies, ranging from steatotic liver (MASL) to active inflammatory steatohepatitis (MASH), which is characterised by lobular inflammation and hepatocyte ballooning degeneration. Histologically assessment of hepatocyte ballooning is an essential component for diagnosis and clinical trial enrolment, yet its reliable identification through histology remains a problem (Brunt et al., 2022). The raising concerns in interobserver variability in the assessment of hepatocyte ballooning through H&E staining has been reported by different studies emphasising the urgent need for markers to reliably diagnose MASH.

Aim: This study aims to unravel the complexity of the spectrum of ballooning degeneration in hepatocytes and discover a diagnostic panel to improve the histologic assessment of ballooned hepatocytes in clinics, utilising a spatial multi-omics approach.

Methods: This study applies a variety of state-of-the art techniques such as spatial transcriptomics, bulk RNA transcriptomics, classical immunostaining and immunofluorescence multiplexing on human FFPE liver samples from patients diagnosed with MASLD. GeoMX Human Whole Transcriptome Atlas profiling was performed on 8 biopsies from at-risk MASH fibrosis stage F3 patients. Regions of interest were selected based on the presence of prominent hepatocyte ballooning. Fluorescent PanCK, CD68 and CD45 markers were used to segment epithelial, macrophage and immune cell population, respectively. A total of 80 segments were processed for high throughput RNA sequencing. Genes were considered differentially expressed with absolute log2 Fold Change > 0.5 and FDR < 0.05. The clinical relevance of the identified differentially expressed genes were explored in bulk RNA transcriptomics. Samples for the bulk RNAseq (n=206) have been drawn from the European MAFLD registry and scored by an expert liver pathologist according to

the semi-quantitative NASH-CRN Scoring System. RNA sequencing analysis was carried out as previously described, with graphs generated via respective R packages (Govaere et al., 2020). Key targets were validated on sequential sections from MASH patients by immunohistochemistry. Immunofluorescent multiplexing staining will be performed on 20 liver samples representing a whole spectrum of the disease to resolve the cellular complexity and correlate expression patterns with ballooning severity/type at single cell resolution.

Results: Comparison of the regions with prominent ballooning and no ballooning degeneration identified 194 differentially expressed genes in a total of 19 segments within the epithelial cell population. Epithelial cells displayed an upregulation in stress-response markers (SQSTM1/p62, UBD), cell remodelling marker (Annexin 2), and retinol metabolism marker (AKR1B15). Exploring the clinical relevance of key markers in bulk RNASeq data showed that the expression of AKR1B10, AKR1B15, and UBD linearly correlated with hepatocyte ballooning score (0-2), fibrosis stage (0-4) and lobular inflammation (0-3). Validation of key markers on liver samples from MASH patients showed that classical, non-classical ballooned hepatocytes as well as hepatocytes, which do not contain the features of ballooning, exhibit a different pattern of expression of these markers. Nuclear and cytoplasmic expression of AKR1B10 was seen in classical ballooned hepatocytes and intermediate periportal hepatocytes, representing a spectrum of hepatocytes in the disease condition. UBD and p62 expression was detected in smaller subset of ballooned hepatocytes. While ballooned hepatocytes with fine-threaded Mallory-Denk Bodies showed immunopositivity for UBD, SQSTM1/p62 immunopositivity was observed in a smaller subset of ballooned hepatocytes, displaying coarse-grained Mallory-Denk Bodies. Annexin 2 stained a wide range of cells including the macrophages, bile ducts, cholangiocytes as well as ballooned hepatocytes, suggesting a broad adaptive response in multiple cell types.

Conclusions: This study identified a spectrum of hepatocyte ballooning in patients with MASH, reflecting different stages of stress response and metabolic adaption. Furthermore, we showed the clinical applicability of these markers in the grading and staging of the MASLD spectrum, indicating their diagnostic relevance.

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THE EVOLUTION OF PHYSICAL FITNESS AFTER LIVER TRANSPLANTATION AND ITS ROLE ON LONG-TERM OUTCOMES: A RETROSPECTIVE SINGLE-CENTRE STUDY. E. Desloovere (1), S. Leunis (1), H. Van Criekeing (1), L. Schepers (1), A. Van Craenenbroeck (2), V. Cornelissen (3), S. De Smet (4), S. Bogaerts (5), S. Fieuws (6), D. Monbaliu (1) / [1] KUL - University of Leuven, Leuven, Belgium, Microbiology, Immunology and Transplantation, Abdominal Transplantation, [2] KUL - University of Leuven, Leuven, Belgium, Microbiology, Immunology and Transplantation, Nephrology and Renal Transplantation Research Group, [3] KUL - University of Leuven, Leuven, Belgium, Rehabilitation Sciences, Research Group for Rehabilitation in Internal Disorders, [4] KUL - University of Leuven, Leuven, Belgium, Exercise Physiology Research Group, Department of Movement Sciences, [5] KUL - University of Leuven, Leuven, Belgium, Development and Regeneration, Locomotor and Neurological Disorders, [6] KUL - University of Leuven, Leuven, Belgium, Public health and primary care, I-BioStat.

Introduction: Liver transplantation (LT) is a life-saving treatment for end-stage liver disease (ESLD), yet long-term mortality remains higher than the general population. Cardiovascular diseases rank among the top three leading causes of death in LT recipients with a functioning graft, with low physical fitness as a critical but modifiable risk factor. Patients with ESLD typically exhibit low physical fitness, however, there is limited longitudinal long-term data on how physical fitness evolves post-transplantation and on its potential impact on survival.

Aim: This study aimed to analyse changes in peak oxygen uptake (VO_{2peak}), 6-minute walk distance (6MWD), and hand grip strength from pre-transplant listing up to one-year post-transplantation. Additionally, this study aimed to assess the association between aforementioned physical fitness parameters and survival rates at 1-, 5-, and 10-years post-transplantation.

Methods: This single-centre retrospective cohort study included 81 adult ESLD patients who underwent transplantation between September 2009 and January 2015. Physical fitness parameters were measured pre-transplant and immediately, at 3 months, and at 1-year post-transplantation. Longitudinal changes were analysed using a multivariate linear model with weighted generalised estimating equations (GEE) to handle the correlation over time. Pairwise comparisons were conducted for each time point versus the pre-transplant baseline, applying a Dunnett-Hsu correction for multiple comparisons. Results are reported as means, 95% confidence intervals (CI), and percentage of the normative value for each time point, with p-values of the pairwise comparisons. Associations between pre- and post-transplant physical fitness parameters and 1-, 5-, and 10-year patient survival were evaluated using multiple logistic regression, correcting for age.

Results: Mean age at transplantation was 55 ± 12 y, with 53% male patients. Pre-transplant VO_{2peak} was 20.5 mL/kg/min (95% CI: 18.4-22.7; 66% of the normative value), declining to 18.0 mL/kg/min (16.1-19.9; 59%; p=0.055) immediately post-transplant before recovering to 20.2 mL/kg/min (18.2-22.2; 66%; p=0.991) at 3 months and 22.5 mL/kg/min (19.3-25.7; 75%; p=0.545) at 1 year. Similarly, 6MWD declined from 458 m (424-492; 61%) pre-transplant to 399 m (364-433; 53%; p=0.001) post-transplant, before improving to 502 m (468-536; 70%; p=0.016) at 3 months and 534 m (505-563; 77%; p<0.0001) at 1 year. Handgrip strength followed a similar trajectory, decreasing from 28.9

kg (26.5-31.4; 74%) pre-transplant to 23.4 kg (20.9-25.9; 58%; $p<0.0001$) post-transplantation, recovering to 26.4 kg (23.8-29.1; 68%; $p=0.011$) at 3 months and 29 kg (26.1-31.8; 76%; $p=0.999$) at 1 year. Pre- and post-transplant physical fitness parameters, measured immediately and at 3 months post-transplantation, were not significantly associated with survival at any time point. However, the 6MWD at 1-year post-transplantation was significantly associated with 10-year survival (odds ratio: 1.035, 95% CI: 1.002–1.069, $p=0.036$). In contrast, handgrip strength and VO_{2peak} at 1-year post-transplantation were not significantly associated with 10-year survival.

Conclusions: Physical fitness is severely impaired before transplantation and deteriorates immediately afterward. While partial recovery occurs within the first-year post-transplantation, physical fitness levels remain below normative values, reaching approximately 75% of the predicted benchmarks. Importantly, the significant association between 6MWD 1-year post-transplantation and 10-year survival highlights its value as a predictor of long-term survival. While the effect per meter may seem small, even modest improvements in walking distance could have meaningful implications for long-term survival. These findings suggest that LT alone does not fully restore physical fitness, highlighting the need for targeted rehabilitation programs to optimize recovery and improve overall outcomes.

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HARNESSING HUMAN IMMUNE SYSTEM MOUSE MODELS TO VALIDATE NADPH OXIDASE 1 INHIBITION AS A TREATMENT FOR HEPATOCELLULAR CARCINOMA. Z. De Vos (1), L. Heyerick (1), H. Stocks (2), A. Wullaert (3), A. Hoorens (4), S. Lefere (5), S. Raevens (5), A. Geerts (5), X. Verhelst (5), H. Van Vlierberghe (5), L. Devisscher (1) / [1] Ghent University, Ghent, Belgium, Department of Basic & Applied Medical Sciences, Gut-Liver Immunopharmacology Unit, Ghent University, Ghent, Belgium, [2] VIB, Gent, Belgium, VIB-UGent Centre for Inflammation Research, VIB, Ghent, Belgium, [3] University of Antwerp, Antwerp, Belgium, Cell Death Signalling Lab, Department of Biomedical Sciences, University of Antwerp, Antwerp, Belgium, [4] Ghent University Hospital, Ghent, Belgium, Department of Pathology, Ghent University Hospital, Ghent, Belgium, [5] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics, Hepatology Research Unit, Ghent University, Ghent, Belgium.

Introduction: NADPH oxidases (NOX) are reactive oxygen-producing enzymes of which the isoform NOX1 is present in the tumour microenvironment (TME) of hepatocellular carcinoma (HCC) and promotes HCC development and metastasis. NOX1 inhibition (NOX1i) has been shown to alter the TME in classical experimental HCC models and might serve as a therapeutic target. However, implementation in the clinic is hampered by low translatability of these classical HCC models.

Aim: Here, we employed next-generation human immune system (HIS)-HCC models that enable investigation of treatments in the context of human immune responses and provide evidence for NOX1i as strategy to target the TME in HCC.

Methods: Two HIS-HCC models were set up to investigate NOX1i in the context of human innate or adaptive immune responses, with a focus on the monocyte/macrophage or T cell compartment, respectively. For the myeloid model (My-HIS), irradiated NSG-QUAD mice were reconstituted with human cord blood-derived CD34+ cells, and human orthotopic HCC tumours were induced 4 weeks post engraftment. For the T cell-HIS model, orthotopic HCC tumours were induced in NSG mice, and mice were reconstituted with human T cells using healthy peripheral blood mononuclear cells. Mice received NOX1i (ML171) or vehicle twice per week for 3 weeks. Immune cell populations were analysed by flow cytometry. Liver disease and tumour burden were analysed by macroscopy and expression of inflammatory, fibrosis, HCC and proliferation markers.

Results: In the My-HIS-HCC model, humanization in livers and tumours reached 30-50% and consisted of monocytes, macrophages, dendritic cells, NK cells and B cells. Significantly lower human CD45+ cells were observed in tumour and surrounding tissue of NOX1i-treated My-HIS-HCC mice, which was mainly attributed to reduced numbers of monocytes and macrophages in tumour and surrounding tissue. NOX1i did not affect macroscopic tumour development in My-HIS-HCC mice. However, the expression of HCC and proliferation markers, including Glypican-3 and Ki67, was significantly lower in tumours of NOX1i-treated My-HIS-HCC mice. This was accompanied with lower expression of cytokines, chemokines and growth factors involved in cancer progression upon NOX1i. PD-L1 and PD-1 expression was also significantly lower in HCC tumour and surrounding tissue, respectively, in NOX1i-treated, compared to control-treated My-HIS-HCC mice. Humanization in the T cell-HIS-HCC model reached up to 70% and primarily consisted of T cells, with a tendency towards reduced percentages in livers of NOX1i-treated mice. The CD4+/CD8+ T cell ratio did not differ between treatment groups. Within the population of CD4+ T cells, mainly T helper 2 cells were encountered in blood, liver, and tumour tissue without differences between groups. NOX1i did not significantly affect tumour size nor the expression of HCC and proliferation markers in the T cell-HIS-HCC model. However, as in the My-HIS-HCC model, the expression of cytokines and markers involved in cancer progression, including PD-1 and PD-L1, was significantly lower in tumour tissue of NOX1i-treated, compared to untreated, T cell-HIS-HCC mice.

Conclusions: Our data show that NOX1i effectively alters the TME in humanized HCC models, with the most pronounced effects observed in mice harbouring human monocytes and macrophages, the My-HIS-HCC model. This

aligns with previous reports on the therapeutic potential of NOX1i in classical HCC models by affecting monocyte/macrophage function and favours translation to the clinic.

- A16 -

IN THE REFHEPS HEPATOTOXICITY NETWORK, ANTICANCER DRUGS ARE MORE FREQUENTLY INVOLVED IN HEPATITIS CASES AND ANTINEOPLASTIC-INDUCED LIVER INJURY HAVE SPECIFIC CHARACTERISTICS. B. Delire (1), L. Meunier (2), D. Larrey (2), E. De Martin (3), Y. Horsmans (4) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepatology, [2] CHU Montpellier, France, Hepatology, [3] AP-HP Hôpital Paul Brousse, Centre Hépatobiliaire, Inserm UMR-S 1193, Université Paris-Saclay, Villejuif, France, Hepatology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepatology.

Introduction: Drug-induced liver injury (DILI) is a major cause of drug withdrawal and discontinuation of new drug development. Anticancer drugs are frequently implicated in DILI. A new Belgian-French DILI network called REFHEPS (Réseau pour l'étude de l'Hépatotoxicité des Produits de Santé) was created in January 2022.

Aim: The aim of this study is to analyse cases of hepatotoxicity reported to the REFHEPS network and to compare cases involving anticancer therapies with conventional drugs-induced hepatotoxicity cases.

Methods: All cases reported to REFHEPS since January 2022 were retrospectively analysed. The type of hepatitis (cytolytic, cholestatic or mixed), the severity and the drug were assessed according to international criteria (RUCAM and DILIN methods).

Results: Since 2022, 393 cases have been submitted to REFHEPS. Thirty-six cases were excluded due to differential diagnosis or insufficient data, and 92 are currently being analysed. A total of 265 cases were included. The mean age of the patients was 53 years (± 18.8) and the majority were women ($n=163$; 61,5%). The mean RUCAM score was 6.8 (± 2). The type of liver injury was predominantly cytolytic ($n=164$; 62%), followed by cholestatic ($n=69$; 26%) and mixed ($n=28$; 11%). The distribution of disease severity was: mild ($n=90$; 33,9%), moderate ($n=75$; 28,3%), moderate-severe ($n=57$; 21,5%), severe ($n=29$; 10,9%) and fatal or requiring transplantation ($n=12$; 4,5%). Patients were treated with corticosteroids in 93 cases (35%), with ursodeoxycholic acid in 41 cases (15%) and with N-acetylcysteine in 45 cases (17%). Hepatitis resolved in 79% of the cases and 7% of the patients developed chronic liver damage. Anticancer drugs were the most common cause of hepatotoxicity (56%), especially immune checkpoint inhibitors. The most important other drug classes involved in DILI cases were analgesics (39%), especially NSAIDs, antibiotics (12%) and medicinal herbs and plants (8%). Comparison between anticancer and other drugs showed that anticancer hepatotoxicity cases involved older patients (60.6 vs 43.5 years, $p<0,001$), were more cholestatic (38.1% vs 11.4%, $p<0,001$) and generally less severe (6.8% vs 26.7%, $p<0,001$), were more frequently biopsied (51.4% vs 33.3%, $p=0,005$) and were more frequently treated with corticosteroids (50.7% vs 15.4%, $p<0,001$).

Conclusions: Since its creation, REFHEPS has collected more than 300 cases of drug-induced hepatotoxicity, with cancer drugs being more frequently involved. There are significant differences between the hepatotoxicity of cancer therapies and conventional treatments.

- A17 -

ADIPOSE TISSUE RADIODENSITY: A PROGNOSTIC MARKER FOR LIVER TRANSPLANT PRIORITIZATION. G. Dahlqvist (1), M. Lepour (2), S. Declerck (3), N. Lanthier (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepatogastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepatogastroenterology, [3] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, GAEN/IREC.

Introduction: Body composition has emerged as a critical factor in chronic diseases, particularly cirrhosis. Sarcopenia and myosteatosis are well documented in cirrhosis, while adipose tissue parameters such as expansion or radiodensity have been less studied. Their prognostic value has, however, been established respectively in metabolic syndrome and cancer.

Aim: This study aimed to evaluate the impact of body composition on morbidity and mortality in patients listed for liver transplantation (LT) before and after LT and explore its potential integration into LT priority scoring.

Methods: In this prospective observational study, 158 adult LT candidates (June 2021–October 2023) underwent baseline and 6-month post-LT assessments, including nutritional status, functional parameters, and CT-based evaluation of muscle and subcutaneous adipose tissue (SAT) at the third lumbar level (L3). Low SAT radiodensity thresholds were set at -83 HU for women and -74 HU for men. The cut-off for low muscle radiodensity (compatible with myosteatosis) was SM-RA < 41 HU for patients with a BMI < 25 kg/m² and < 33 HU for patients with a BMI $\geq$ 25 kg/m². Outcomes included mortality and emergency hospitalizations, analysed using Kaplan-Meier survival curves.

Results: Of 158 candidates, 125 had cirrhosis (81.6% male, mean age 56.5 ± 10.47 , MELD 15.9 ± 7.26). 104 cirrhotic patients underwent liver transplantation during the study period. Patients with high SAT density ($n=50$) had more severe disease compared to patients with low SAT density ($n=75$) as evidenced by higher prevalence of ascites (79.2% vs.

47.2%, $p=0.0003$), higher Child-Pugh score (9.5 ± 2.43 vs. 7.1 ± 2.34 , $p<0.0001$) and MELD score (19.1 ± 7.46 vs. 13.5 ± 6.15 , $p<0.0001$). Frailty indicators with higher liver frailty index (LFI 4.1 ± 0.86 vs 3.6 ± 0.58 ; $p=0.014$), and lower skeletal mass index (SMI $51 \text{ cm}^2/\text{m}^2 \pm 13.99$ vs $56.0 \text{ cm}^2/\text{m}^2 \pm 9.88$; $p=0.0132$), were worse in high-density SAT patients, though muscle density did not differ significantly ($40.3 \pm 11.75 \text{ HU}$ vs $44.7 \pm 11.04 \text{ HU}$ $p=0.052$). High-density SAT was linked to increased mortality throughout the study period (HR 7.46 (95%CI 2.12-26.21), $p=0.0002$) and morbidity/mortality (HR 2.96 (95%CI 1.63-5.37, $p=0.002$), and in the pre-transplant period mortality (HR 11.32, 95% CI:2.53-50.65, $p<0.0001$) and morbi/mortality (3.55, 95% CI: 1.75-7.19, $p=0.0002$). Stratification revealed the worst outcome in patients with both high-density SAT and presence of myosteatosi (n=19; HR 4.61, 95% CI: 2.05-10.40, $p=0.0005$).

Conclusions: Elevated SAT radiodensity together with low muscle radiodensity concern 15.2% of the cirrhotic patients awaiting LT and predict poorer outcomes. This can be interpreted as the deleterious coexistence of both adipose tissue inflammation and myosteatosi. These findings support defining a particular “at risk” patient phenotype to improve prognostic accuracy and prioritize candidates on the LT waiting list.

- A18 -

RETROSPECTIVE STUDY ON SIMULTANEOUS LIVER KIDNEY TRANSPLANTATION: RENAL OUTCOME AND PREVALENCE OF ACUTE CELLULAR REJECTION. D. Pint (1), S. Abid (2), S. Sapna (3) / [1] University of Antwerp, Antwerp, Belgium, Gastroenterology/Hepatology, [2] King's College Hospital London, London, United Kingdom, Hepatology, [3] King's College Hospital London, London, United Kingdom, Nephrology.

Introduction: There has been a long-standing hypothesis that simultaneous liver-kidney transplantation (SLK) has an immune protective effect for the transplanted kidney from the hepatic allograft. This hypothesis was challenged when recent data showed increased rejection rates for both liver and kidney grafts in patients with pre-existing DSA, particularly against class II HLA with mean fluorescence intensity (MFI) of >10000 . In 2014, the immunosuppression protocol in our unit was changed following a case of antibody-mediated rejection (ABMR) and renal graft loss after SLK related to DSA to class II HLA. In the new protocol, enhanced immunosuppression is given to patients who are deemed high risk for ABMR based on their flow crossmatch results. The enhanced immunosuppression protocol consists of induction with basiliximab and further maintenance with tacrolimus, prednisolone, and mycophenolic mofetil and anti-HLA antibody profiles twice weekly.

Aim: This study aims to evaluate liver, kidney, and overall survival outcomes in SLK recipients over a 5-year follow-up period following the protocol change. Additionally, the study assesses the incidence of acute and chronic rejection episodes in kidney grafts within the first 5 years post-SLK.

Methods: The study is a descriptive retrospective observational cohort study analysing all SLK from 2014 to 2019 in King's College Hospital London. Renal function with creatinine levels and eGFR using the Modification of Diet in Renal Disease (MDRD) formula was assessed at 1 month, 1 year, and 5 years post-transplantation. Additionally, the study investigated the incidence of acute and chronic rejection episodes in the transplanted kidney within the first 5 years following SLK. Data regarding pre-existing DSA to HLA class I and II was collected.

Results: Out of the 1161 liver transplants performed between 2014 and 2019, 36 (3.1%) were SLK. Indications for SLK were diverse, with polycystic kidney and liver disease being the most prevalent indication in 25 patients (69.4%). After a follow-up of 5 years, 18 patients (50%) achieved an estimated glomerular filtration rate (eGFR) greater than $45 \text{ mL/min/1.73 m}^2$. One patient (2.9%) needed renal replacement therapy (RRT) after 5 years, and two patients (5.3%) were deceased. Additionally, renal allograft outcomes were analysed based on the presence or absence of acute rejection within the first year. The mean eGFR was compared between the two patient groups. At 1-month post-transplant, eGFR was significantly higher in the non-AR group ($52 \text{ mL/min/1.73 m}^2$) compared to the AR group ($33 \text{ mL/min/1.73 m}^2$, $p=0.022$). However, the mean eGFR at the 5-year benchmark in the non-AR group was $50 \text{ mL/min/1.73 m}^2$ compared to $40 \text{ mL/min/1.73 m}^2$ in the AR group and was not statistically significant anymore ($p=0.081$) and one patient in the non-AR group required RRT. AR of the kidney transplant was observed in 9 patients (22%), while no episodes of chronic rejection were recorded during the 5-year follow-up period. Both acute TCMR and ABMR occurred in 5 out of 36 patients (13.9%), with one patient with both TCMR and ABMR. The length of stay was longer in the AR group, with a mean of 36 days compared to 26 days in the non-AR group ($p=0.027$). The presence of pre-transplant anti-HLA antibodies was analysed. Of the nine patients with an AR episode, two patients (22%) had class I anti-HLA antibodies, four patients (44%) had both class I and II anti-HLA antibodies, and three patients had no preformed DSA. Only one patient with ABMR was class I and II anti-HLA antibodies negative pre-transplant.

Conclusions: Our findings show that SLK is a viable and effective treatment option for patients with concurrent liver and kidney diseases. Patients who are deemed high risk for ABMR due to the presence of preformed DSA class II HLA antibodies should receive the enhanced immunosuppression protocol and close monitoring of their DSAs after transplant. This could help to diagnose ABMR and start treatment early on. Our study showed that despite the occurrence of an AR episode, renal outcome does not differ significantly after a 5-year follow-up period when AR is managed properly.

RESULTS OF THE « HEP C NAMUR PROJECT »: RETRIEVAL OF LOST TO FOLLOW-UP AND BARRIERS TO LINKAGE TO CARE FOR HEPATITIS C SCREENING IN THE PROVINCE OF NAMUR (BELGIUM). A. Marot (1), K. de Fays (2), M. Van Hoof (3), J. Martinet (4), F. De Leuze (5), O. Borgniet (6), A. Putignano (2), M. Geheot (2), B. Van Houte (7), C. Dumont (7), P. Deltenre (8) / [1] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Gastroenterology and Hepatology, [2] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [3] Clinique Saint-luc Bouge, Namur, Belgium, Department of Gastroenterology and Hepatology, [4] Vivalia Libramont, Libramont, Belgium, Department of Gastroenterology and Hepatology, [5] CHU UCL Namur site Sainte Elisabeth, Brussels, Belgium, Department of Gastroenterology and Hepatology, [6] CHU Dinant Godinne, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [7] CHR Namur, Namur, Belgium, Department of Gastroenterology and Hepatology, [8] Clinique Saint-Luc Bouge; CHU UCL Namur; CUB Hôpital Erasme, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Chronic hepatitis C virus (HCV) infection is a medical and public health concern. Although screening for HCV is easy, barriers exist which prevent assessment and treatment of individuals potentially infected with HCV infection. Loss to follow-up (LTFU) is one of these barriers that prevents HCV elimination.

Aim: Retrieving HCV LTFU patients to re-engage them with care in the Province of Namur and better understanding the reasons why they were LTFU.

Methods: This is a retrospective study of individuals screened for HCV within the 6 hospitals labs in the Province of Namur between January 1, 2012 and December 31, 2018. We defined HCV patients LTFU as: 1) patients with detectable HCV antibodies and confirmed detectable HCV RNA evaluated by a specialist in the past but not treated; 2) HCV patients without detectable HCV RNA but with cirrhosis and no regular follow-up; and 3) patients with detectable HCV RNA never evaluated by a specialist. Linkage to care was defined as: 1) asking confirmatory HCV RNA testing with positive results after screening HCV antibody; and 2) follow-up appointment for assessment and/or treatment established with a specialist. General Practitioners (GPs) were contacted by mail and/or by phone to find missing information and to contact unknown HCV patients. Demographic and baseline laboratory values were collected. Factors potentially associated with absence of linkage to care were evaluated.

Results: During the study period, a total of 1383 individuals were found to have detectable HCV antibodies. After exclusion of those who were not eligible to therapy (N=969), 414 HCV LTFU patients were identified: 161 patients had already been evaluated by a specialist in the past (135 patients with detectable HCV RNA and 26 cirrhotic patients with undetectable HCV RNA and without surveillance), and 253 individuals were not aware of their HCV status. In the first group, 71 patients were eligible for antiviral treatment. In the second group, 90 individuals were contacted by their GP with no further follow-up. Positive HCV RNA testing was carried out in 14 patients (10%), meaning that HCV RNA testing was already available for the majority of them. Overall, 85% (138/163) of the second group were viraemic and 75 of them were eligible for antiviral treatment. In the whole study population, 172 patients LTFU were not linked to a specialist for further care. Currently, 110 patients with detectable HCV RNA and with a highly probable indication for antiviral treatment were contacted but did not get yet an appointment with a specialist, and 36 patients were assessed for therapy.

Conclusions: Retrieving LTFU HCV patients and re-engaging them with care is feasible but difficult to implement due to lack of resources for contacting patients and/or GPs. A confirmatory HCV RNA test was available in most of the HCV LTFU patients but a follow-up appointment for assessing indication of treatment was often not established with a specialist. Several barriers exist concerning GPs who play a major role to link HCV patients LTFU to care. At a patient level, lack of awareness about consequences of untreated chronic HCV infection also hinders access to therapy.

SYSTEMATIC SCREENING FOR HBV, HCV AND HIV IN HOSPITALISED PSYCHIATRIC PATIENTS: A FEASIBLE APPROACH ON THE ROAD TOWARDS ELIMINATION OF VIRAL HEPATITIS. M. Coessens (1), H. Ruymbeke (2), J. Schouten (1), I. Velghe (3), J. Kleinen (4), L. De Weirde (5), A. Berens (6), M. Destoop (7), J. Decoster (8), W. Verlinden (2) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and Hepatology, [2] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and hepatology, [3] Psychiatrisch Ziekenhuis Sint-Lucia, Sint-Niklaas, Belgium, Psychiatrie, [4] Psychiatrisch Ziekenhuis Sint-Hiëronymus, Belgium, Psychiatrie, [5] Vitaz, Sint-Niklaas, Belgium, Psychiatrie, [6] Universitair Psychiatrisch Centrum Duffel, Duffel, Belgium, Psychiatrie, [7] Zorggroep Multiversum Campus Alexianen, Belgium, Psychiatrie, [8] Zorggroep Sint-Kamillus, Belgium, Psychiatrie.

Introduction: Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections are a major global health problem. Human immunodeficiency virus (HIV) has similar routes of transmission. The World Health Organization has set targets to eliminate viral hepatitis by 2030. People with serious mental illnesses are at increased risk of infection with these blood-borne viral (BBV) infections. HCV prevalence in people with severe mental illness is often overestimated in studies

based on risk-based screening approaches. We aim to assess the prevalence of these BBV by means of a generalized screening approach.

Aim: The primary objective is to assess the prevalence of HBV, HCV and HIV in hospitalised psychiatric patients. Prevalence data will be compared to the general Belgian population (GBP). The secondary objective is to identify associations between BBV infection and psychiatric diagnosis.

Methods: This multi-centre prospective prevalence study was conducted between 2017 and 2024 in 5 psychiatric hospitals (PH) and in a psychiatric ward of a regular hospital in the region of East-Flanders, Antwerp, and Flemish Brabant. All newly admitted adult patients in these PH were offered to participate voluntarily in this study. For all patients who signed the informed consent form, the patient's age, gender and psychiatric diagnosis according to DSM-IV criteria, were documented and serum testing was performed [Hepatitis B surface antigen (HBsAg) and antibody (HBsAb), Hepatitis B core antibody (HBcAb), HCV antibody (HCVAb) and HIV antibody (HIVAb)]. Patients with positive serology were referred to a hepatologist or infectious disease specialist. In addition, serological data of 2 forensic psychiatric centres (FPC Antwerp and FPC Ghent) were collected. According to current national and international guidelines, patients residing in a FPC should be routinely screened for BBVs. Therefore, serological data were readily available and collected retrospectively, in addition to demographic data.

Results: A total of 2213 patients with a mean age of 42 years old were included in the study [PH: 1634 (73,84%); FPC 579 (26,16%)]. Significantly more male patients were residing in a FPC. HBsAg, HCVAb, HIVAb test results were obtained in 93,13%, 97,11% and 89,74% of included patients. Psychiatric diagnoses were obtained in 4 out of 6 psychiatric hospitals for 1061 patients. In total, 20.55% suffered from a psychotic disorder, 12.82% from intranasal or intravenous drug dependency, and 12.91% from a personality disorder. In total, 14 patients were HBsAg+ [PH: 5/1503 (0.33%); FPC: 9/558 (1.61%); TP: 14/2061 (0.68%)]. HBsAg seroprevalence was significantly higher in the FPC group ($p<0.0001$) and in the total study population ($p=0.0003$) than in the general Belgian population [0.27% (0.13% - 0.49%)]. In addition, 99 out of 2108 patients (4,70%) tested positive for HBcAb, significantly more in FPC than in PH [PH: 48/1554 (3.09%); FPC: 51/554 (9.21%); $p<0.0001$]. A total of 32.22% patients has serologically proven immunity to HBV, similar between the PH and FPC group. HCV antibodies were found in 74/2149 (3.44%) of patients. HCV antibodies were significantly more prevalent in patients residing in a FPC (38/561, 6.77%) compared to the PH group (36/1588, 2.27%) ($p<0.0001$). Compared to the prevalence in the Belgian population (0.22%), a significantly higher prevalence was found in our total study population ($p<0.0001$), in the PH ($p<0.0001$) and FPC ($p<0.0001$) group. 22 patients tested HCV PCR+. HCV antibodies were more prevalent in patients with IV/IN drug dependency ($p<0.0001$); there was no significant association with other psychiatric diagnoses. No associations between HBV and HIV and any psychiatric diagnoses were identified. HIV antibodies were found in 9/1986 (0.45%) of patients [PH: 7/1436 (0.49%); FPC: 2/550 (0.36%)]. Prevalence of HIV was significantly higher in the PH group ($p=0.003$) and the total study population ($p=0.002$) compared to the general Belgian population (0.17%). Linkage to care is still ongoing.

Conclusions: Given that HBV, HCV and HIV seroprevalence is significantly higher in the study population than in the general Belgian population, we advocate for a generalised HBV, HCV and HIV screening in all hospitalised psychiatric patients. Implementing this screening in the standard admission procedure of all psychiatric hospitals, is a highly feasible strategy on the road towards elimination of viral hepatitis.

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INSUFFICIENT IMPLEMENTATION OF PRETHERAPEUTIC HEPATITIS B AND C SCREENING GUIDELINES IN ACADEMIC AND GENERAL. BELGIAN HOSPITALS. M. Coessens (1), J. De Graeve (2), A. Geerts (2), W. Verlinden (1), J. Schouten (1) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and Hepatology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and Hepatology.

Introduction: Hepatitis B virus reactivation (HBVr) still occurs in clinical practice, suggesting poor implementation of preventive screening guidelines. Data on this topic are urgently needed to refocus where necessary.

Aim: This study aims to assess implementation of pretherapeutic HBV and HCV screening guidelines in haematologists (H) and pretherapeutic HBV screening guidelines in oncologists (O).

Methods: A retrospective patient file analysis was done in the haematology and oncology department in two academic and two general hospitals in Belgium [GH1, GH2, AC1, AC2]. All patients that had at least two documented administrations of any systemic chemotherapy or immunosuppressive therapy regimen were included. Presence of appropriate HBV/HCV screening was documented, in addition to demographics and the class of drugs with the highest risk of reactivation. At the haemato-oncology department in one general hospital, screening rates were re-evaluated after an awareness session.

Results: In total, pretherapeutic HBV screening rates were assessed in 1589 patients (GH1 n=459; GH2=407; AC1 n=383; AC2 n=340). Correct pretherapeutic HBV screening rates in haemato-oncological patients are low overall (GH1: 31.58%; GH2: 9.34%; AC1: 37.60%; AC2: 52.94%). Correct pretherapeutic HCV screening rates were also suboptimal in haematological patients (GH1: 48.44%; GH2: 27.27%; AC1: 81.20%; AC2: 87.50%). High-risk therapy regimes (B-cell depleting agents and anthracyclines) were administered in 49.47% of haematological and 20.62% of oncological patients. Correct HBV screening rates were significantly higher in academic versus general hospitals and in

three centres when only HBsAg is assessed, instead of the combination of HBsAg and HBcAb, as recommended by the guidelines (GH2: 20.39% vs 9.34%; AC1: 53.79% vs 37.60%; AC2: 55.29% vs 52.94%). Correct pretherapeutic HBV screening rates are higher in haematological versus oncological patients ($p < 0.0001$). As much as 31.02% and 48.54% of haematological and oncological patients on molecules with a high risk of reactivation (B-cell depleting agents and anthracyclines), respectively, were not screened at all. HBV and HCV screening rates in haemato-oncologists improved after the awareness session [HBV, HCV: H 49.23% up to 58.06% $p < 0.001$, HBV: O 25.7% up to 59.12% $p < 0.001$]. One patient with isolated anti-HBc antibodies on rituximab seroconverted (HBsAg+) and was, thanks to our intervention, successfully treated for hepatitis B reactivation with tenofovir.

Conclusions: Pretherapeutic hepatitis B and C screening is performed suboptimal prior to initiation of chemotherapy therapy regimens in both an academic and general hospital setting. Suboptimal HBV screening prior to administration of frequent and high-risk therapy regimens (B-cell depleting agents and anthracyclines) is worrisome. However, we showed that one single awareness session already significantly improved screening adherence.

- A22 -

CHRONIC LIVER DISEASE AND AUTOIMMUNE HAEMOLYTIC ANAEMIA: A CASE SERIES. D. Pint (1), A. Suddle (2), M. Ceesay (3) / [1] University of Antwerp, Antwerp, Belgium, Gastroenterology/Hepatology, [2] King's College Hospital London, London, United Kingdom, Hepatology, [3] King's College Hospital London, London, United Kingdom, Haematology.

Introduction: Chronic anaemia is common in patients with chronic liver disease (CLD), often due to multifactorial causes and causes increased morbidity and mortality rates. Autoimmune haemolytic anaemia (AIHA) is a rare autoimmune disorder that can complicate CLD. AIHA is characterised by autoantibody-mediated red blood cell destruction, and its coexistence with CLD, presents diagnostic and management challenges.

Aim: This study aims to explore the clinical characteristics, management, and outcomes of patients with AIHA and CLD at King's College Hospital over a 21-year period.

Methods: This retrospective case series involved adult patients (≥ 18 years) with a diagnosis of both CLD and AIHA at King's College Hospital from 2002 to 2022. Data on demographics, liver disease aetiology, AIHA treatment, and outcomes were collected from electronic health records. The patients were identified using search criteria for various CLD combined with AIHA diagnosis. AIHA diagnosis was based on laboratory parameters, including a positive direct anti-globulin.

Results: Ten patients (70% female) with concurrent AIHA and CLD were identified. The median age at time of diagnosis for CLD and AIHA was 34 years and 43 years, respectively. The most common liver disease was autoimmune hepatitis (40%), followed by alcohol-related liver disease (30%). 80% of the patients presented with chronic liver disease before the onset of AIHA. Seven patients (70%) had cirrhosis, and five (50%) received liver transplantation. In three cases, AIHA occurred post-liver transplantation. Treatments included corticosteroids (90%), IVIG (40%), and rituximab (40%). Rituximab was particularly used in treatment-refractory cases or post-liver transplant patients. Treatment-refractory AIHA occurred in four patients (40%), 2 of which developed treatment-refractory AIHA after their liver transplantation. Possible cofactors that were identified that might influence the development of AIHA in patients with CLD were COVID-19 infection in 3 patients (30%), cytomegalovirus (CMV) infection in 1 patient (10%), and Crohn's disease in 1 patient (10%).

Conclusions: This study highlights the complex pathophysiology and treatment landscape for AIHA in patients with chronic liver disease, particularly those who have undergone liver transplantation. Our findings underscore the necessity for further research to better understand the role of chronic liver disease as an immunological trigger for AIHA. Investigating the pathways linking liver inflammation and immune dysregulation could provide valuable insights into the pathogenesis of AIHA in patients with CLD as well as patients developing AIHA post-liver transplantation.

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INTESTINAL TRANSPLANTATION: AN UNDERUTILIZED PROCEDURE WITH OUTCOMES COMPARABLE TO OTHER SOLID ORGAN TRANSPLANTS: A SINGLE-CENTRE RETROSPECTIVE ANALYSIS. A. Dubois (1), T. Vanuytsel (2), D. Monbaliu (3), L. Ceulemans (4), J. Pirenne (3) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology, immunology and transplantation, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology/Hepatology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal transplantation, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Thoracic Surgery.

Introduction: Intestinal failure (IF) is a complex condition, affecting 5 to 80 individuals/M inhabitant in Europe. Although total parenteral nutrition (TPN) is the first line treatment, intestinal transplantation (ITx) remains the only life-saving option for patients with severe HPN/IF complications. However, ITx presents significant surgical and immunological challenges, with outcomes historically falling short compared to other solid organ transplants.

Aim: This study aims to report the results of a single-centre ITx cohort of patients transplanted between October 2000 and October 2024.

Methods: The study cohort includes 32 patients, with a median (min-max) follow-up of 5.03 (0.09-21.73) years. Data were retrospectively analysed for descriptive variables (age, sex ratio, ITx indication, graft type) and outcome (hospital stay, acute rejection (AR) rate, patient and graft survival). A comparison was also conducted between liver-inclusive (LI) and non-LI grafts. Continuous variables are reported with median (min-max). Categorical variables are reported in proportions (%) and compared with Fisher/Chi-square test. Kaplan-Meier curves are used for survival rates and compared by Log-rank test.

Results: Of the 32 ITx, median age was 42 (2-62) yr (5 children, 16%), and sex ratio 1/1. Causes of IF were short bowel syndrome (SBS) (44%), dysmotility (22%), splanchnic thrombosis (16%), reTx (9%), microvillus inclusion (3%), tumour (3%), and liver Tx/frozen abdomen (3%). Graft types repartition was 12 (38%) isolated intestine, 9 (28%) liver/intestine, 10 (31%) multivisceral (MvTx, liver/stomach/pancreas/bowel), and 1 (3%) modified MvTx (stomach/pancreas/bowel). Postoperative results were: median ICU/hospital stay: 14 (2-70)/105 (55-680) days; AR: 47% (15/32); 1-/5-/10-yr patient and graft survival: 81%/74%/57% and 71%/67%/56%, respectively. In the last 10 yrs, 65% of ITx included liver (13/20 vs. 6/12 before, $p=0.474$). Liver-inclusive (LI) grafts (vs. non LI) had less AR (42% vs. 54%, $p=0.720$), no graft loss due to rejection (acute or chronic) (0% vs. 31%, $p=0.02$), and a 1-/5-/10-yr patient and graft survival of 73%/73%/64% (vs 92%/75%/45%, $p=0.948$) and 73%/73%/64% (vs 69%/61%/45%, $p=0.525$), respectively (Fig.1). The current waiting list counts 5 MvTx (no isolated intestine).

Conclusions: Outcomes after ITx, contrary to common belief, are comparable to other life-saving organ transplants. Over time, we observed an increase in liver-inclusive grafts, which, despite being surgically more challenging, offer improved long-term outcomes.

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THE IMPACT OF CARDIOPULMONARY FITNESS ON STEATOTIC LIVER DISEASE IN A COMBINED LIFESTYLE INTERVENTION FOR ADOLESCENTS WITH OBESITY. M. Buytaert (1), I. Coomans (2), E. Dupont (3), K. Vandekerckhove (4), S. Lefere (1), R. De Bruyne (5) / [1] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics, [2] University Hospital Ghent (UZ Gent), Ghent, Belgium, Paediatric cardiology, [3] Zeepreventorium, De Haan, Belgium, Medical staff, [4] University Hospital Ghent (UZ Gent), Ghent, Belgium, Department of Internal Medicine and Paediatrics; Paediatric cardiology, [5] University Hospital Ghent (UZ Gent), Ghent, Belgium, Department of Internal Medicine and Paediatrics; Paediatric hepatology.

Introduction: The interplay between liver and muscle health is incompletely understood, especially in adolescents. Cardiopulmonary exercise testing (CPET) evaluates cardiopulmonary fitness. Its association with metabolic dysfunction-associated steatotic liver disease (MASLD) and MASLD evolution during a lifestyle intervention is poorly characterized.

Aim: Assessment of the association between cardiopulmonary fitness at the start and liver health at the start and after 6 months in the context of a combined lifestyle intervention for adolescents with (severe) obesity.

Methods: Adolescents aged 12 – 18 years old living with (severe) obesity who received a structured, combined lifestyle intervention in a residential setting were prospectively followed for 6 months. CPET was performed at the start using a stepwise load increasing protocol. Raw data were analysed, and the maximal parameters were obtained. Lean mass was obtained by DEXA scanning. MASLD was defined as a CAP value ≥ 248 dB/m, and resolution as a CAP < 248 dB/m at 6 months when baseline CAP values were ≥ 248 dB/m.

Results: 119 adolescents (60 boys) with obesity were included, with a median (interquartile range) age of 16 (15 – 17) years. The median (IQR) BMI z-score was 2.87 (2.51 – 3.17). 85 adolescents (71.4 %) had MASLD, of which 58.8% were boys. Maximal cardiopulmonary fitness (expressed as the percentage of the predicted VO₂max; VO₂max%) was significantly lower in patients with MASLD, with a median (IQR) of respectively 53.5 (46.1 – 58.5) vs. 42.8 (35.7 – 52.1) % ($p < 0.001$). Strikingly, VO₂max/kg did not differ between groups, whereas VO₂max on lean mass was significantly lower in patients with MASLD: 39.5 (33.9 – 44.8) vs. 35.5 (30.3 – 40.3) ml/kg/min ($p = 0.036$). This highlights the importance of fat-free mass on cardiopulmonary fitness and MASLD. Next, data on resolution of baseline MASLD after 6 months intervention were available for 66 patients, of whom 33 (50.0 %) had resolution. Interestingly, a higher VO₂max/kg and VO₂max% at baseline were associated with steatosis resolution, respectively 19.7 (16.6 – 22.1) vs. 16.1 (13.9 – 19.2) ml/kg/min ($p < 0.001$) and 45 (41 – 54) vs. 36 (29 – 52) % ($p = 0.006$). Moreover, this was also observed for VO₂max on lean mass: 37.7 (33.8 – 43.6) vs. 32.9 (27.8 – 37.2) ml/kg/min ($p = 0.003$). These results remained significant when including weight z-scores at 6 months and gender in a binary logistic regression model. As a sensitivity analysis, the analyses were repeated with MASLD defined by the presence of liver steatosis on ultrasound, and the results remained as well significant.

Conclusions: Cardiopulmonary fitness is associated with liver health. Baseline cardiopulmonary fitness, independent from (fat) mass, in adolescents with obesity is associated with MASLD and could be an important contributor to MASLD resolution during a combined lifestyle intervention.

MODELLING ISCHEMIC CHOLANGIOPATHY: EXPLORING PRIMARY HUMAN CHOLANGIOCYTE ORGANOIDS AS A TRANSLATIONAL RESEARCH TOOL. E. Dos Santos (1), M. Meuwis (2), A. De Roover (3), O. Detry (3), N. Gilbo (3) / [1] Université de Liège, Liège, Belgium, CREDEC, [2] ULiège, Belgium, Hepato-Gastroenterology and Digestive Oncology Department, [3] ULg and CHU de Liège, Liège, Belgium, sciences cliniques.

Introduction: Liver transplantation is the best treatment for end-stage liver failure and primary liver cancer. Although long-term results are excellent, one-third of the recipients will develop ischemic cholangiopathy (IC) within the 1st year post-transplant. IC causes diffuse biliary strictures resulting in sepsis, secondary biliary cirrhosis, and graft failure, with 50% of IC patients requiring re-transplantation. Ischemic injuries occurring at the time of organ procurement and preservation are the main risk factors for IC. However, the limited understanding of cholangiocyte ischemia-reperfusion injury is a significant barrier to preventing and treating IC. Deceased organ donation occurs through two main pathways: donation after brain death (DBD) and donation after circulatory death (DCD). In both donor types, the liver graft is preserved with static cold storage in hypothermic, ischemic conditions. DCD donors don't meet the criteria for brain death but have no viable treatment options. In such cases, life-supporting can be withdrawn for the purpose of organ donation, resulting in circulatory arrest and ensuing brain death. Therefore, DCD livers suffer more severe injuries due to the additional normothermic ischemia during circulatory arrest. Consequently, DCD liver recipients face 11 times higher risk of developing IC.

Aim: The main objective of this work was to establish human cholangiocyte organoids (CO) as a preclinical model to investigate the pathophysiology of cholangiocyte injury during liver preservation and transplantation. Additionally, we pilot the comparison of CO generated from DBD and DCD donors to investigate if donation-induced injury traits are retained in this model. Organoid development and characterisation are detailed using RT-PCR and imaging techniques.

Methods: The generation of human CO started with the procurement of gallbladders from both DBD (n=2) and DCD (n=2) donor livers accepted for transplantation. The gallbladder mucosa was then subjected to mechanical dissociation. Cholangiocytes were isolated and cultured in matrigel with R-spondin, Epithelial Growth Factor, Dickkopf-related protein 1, and Rho kinase inhibitor Y-27632. The generation of CO from primary human cholangiocytes was confirmed via RT-qPCR through the expression of the specific cholangiocellular markers: cytokeratin 7 (KRT7) and 19 (KRT19) and gamma-glutamyl transferase 1 (GGT1), and the stemness marker SRY-Box Transcription Factor 9 (SOX9). CO development was monitored daily for a month at passages 0, 1, and 3 using optical and live cell imaging (Incucyte). We manually counted organoid numbers and measured their diameter using the Incucyte, comparing CO derived from DBD and DCD samples with 2-way ANOVA. A p-value<0.05 was considered significant.

Results: CO were visible in bright field optical imaging starting from the first culturing day as small hollow spheres lined with cells surrounding a clear lumen. In the following days, all CO progressively increased their size and showed signs of division and propagation, reaching confluence within an average of 6 (+1) days. Successful generation of CO was confirmed by the positive expression of the mature cholangiocyte-specific marker genes KRT7, KRT19, GGT1, and SOX9 by RT-qPCR, regardless of the type of donation. Additionally, live cell imaging showed that primary cholangiocytes procured from DCD donors generated significantly fewer CO than cholangiocytes derived from DBD donors (p=0.001) at passage 0. Although, in both donation groups the number of organoids increased significantly over time (p<0.0001), the CO generated from DCD samples grew at a significantly slower rate compared to CO generated from DBD donors (p<0.0001). This difference was not visible at passage 1 and 3. There was no difference in CO size between donor groups at any of the considered culture passages. Further phenotypic and functional characterization is ongoing.

Conclusions: Our results indicated that human gallbladders procured from liver grafts accepted for transplantation are an adequate source of primary cholangiocyte for the successful generation of CO retaining both stemness and mature cholangiocyte profiles. Furthermore, our preliminary results suggest that this CO model can retain donation-induced injury traits, such as lower cholangiocyte viability and defective regeneration typically observed in DCD livers, at least at passage 0. Nevertheless, further expansion of the sample size and thorough characterization and functional testing are necessary to validate this model and will be the object of further experimentations.

DRAGON PLC: AN INTERNATIONAL MULTICENTRE RANDOMIZED CONTROLLED TRIAL TO COMPARE COMBINED PORTAL AND HEPATIC VEIN EMBOLIZATION WITH PORTAL VEIN EMBOLIZATION ALONE IN PATIENTS WITH PRIMARY LIVER CANCERS. S. James (1), J. Smits (1), R. Korenblik (1), M. Dewulf (1), C. van der Leij (2), O. Detry (3), R. van Dam (1), *. The DRAGON Trials Collaborative (4) / [1] Maastricht University Medical Centre, Maastricht, The Netherlands, Surgery, [2] Maastricht University Medical Centre, Maastricht, The Netherlands, Radiology and Nuclear Medicine, [3] CHU de Liège, Liège, Belgium, Abdominal Surgery and Transplantation, [4]

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Introduction: Patients with primary liver cancers (PLC) are often ineligible for liver resection because an inadequate future liver remnant (FLR) poses too high a risk of post-hepatectomy liver failure. FLR growth can be induced by portal vein embolization (PVE), the current standard. PVE combined with embolization of the hepatic veins (PVE/HVE) is expected to increase resectability, degree of hypertrophy and kinetic growth rate of the FLR.

Aim: The aim of the DRAGON PLC RCT is to evaluate the superiority of PVE/HVE over PVE regarding overall survival and resectability in patients with PLC.

Methods: During 2.5 years, 358 patients with perihilar cholangiocarcinoma (pCCC), intrahepatic cholangiocarcinoma (iCCC) or hepatocellular carcinoma (HCC) requiring preoperative FLR regeneration will be randomized to PVE/HVE or PVE (1:1, stratified by tumour type). Work instructions standardize the interventions. Clinical and imaging data are collected 1, 3 and 6 weeks after PVE(HVE), concerning resection, and during 5 years of follow-up. Split primary endpoints are defined as: FLR considered sufficient for resection 3 weeks after embolization and 5-year overall survival. FLR volume and function increase, quality of life and costs, among other secondary endpoints, are also assessed.

Results: The DRAGON PLC RCT has been granted funding by the Dutch Cancer Society, ZonMw and KCE, and is due to start accrual at the beginning of 2025. Nine Belgian centres will participate in the trial, with the CHU de Liège as the Belgian coordinating centre.

Conclusions: The effect of PVE/HVE on resectability and survival is expected to illuminate new treatment pathways, ensuring rapid, safe and cost-effective extended liver resections.

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CHARACTERIZATION OF IMMUNE CELL POPULATIONS IN THE MICROENVIRONMENT OF MICE LIVER DURING THE PROGRESSION OF LIVER FIBROSIS TO HEPATOCELLULAR CARCINOMA. A. Ajith (1), J. Evrats (1), C. Bouzin (2), F. Smets (1), E. Sokal (1), M. Najimi (1) / [1] Université catholique de Louvain (UCLouvain), Belgium, Laboratory of Paediatric Hepatology and Cell Therapy (PEDI), [2] Université catholique de Louvain (UCLouvain), Belgium, Plateforme d'imagerie (2IP).

Introduction: Hepatocellular carcinoma (HCC) is a classic inflammation-driven cancer, with the majority of cases arising in the setting of chronic liver disease (CLD), especially cirrhosis. Profiling the dynamic changes in immune cell populations during the progression of CLD from fibrosis to HCC is critical for enhancing prognostic accuracy and improving therapeutic strategies.

Aim: This study aims to characterize the dysregulated immune microenvironment and spatial distribution of immune cells as CLD progresses from fibrosis to HCC using diethylnitrosamine (DEN) and carbon tetrachloride (CCl₄) induced mouse model.

Methods: A single injection of DEN at 4 weeks of age, followed by continuous injections of CCl₄ for 6 and 21 weeks were administered respectively, to induce liver fibrosis and HCC in mice. Immune cell profiling was performed using multiplex immunofluorescence on formalin-fixed paraffin-embedded (FFPE) liver sections from control, fibrosis, and HCC groups. The HCC group was further subdivided into tumour, invasive margin (IM), and non-tumour tissue (NTT) regions, to study in detail the tumour microenvironment and its interaction with the surrounding tissues.

Results: Immune profiling revealed significant changes in hepatic immune cell populations across the disease stages. Total leukocyte and myeloid cell densities (cells/mm²) remained largely consistent across groups. However, macrophage populations exhibited significant variation. Kupffer cell (KC) levels were stable, while infiltrating macrophages (Inf mph) increased markedly, rising approximately 5-fold in tumour regions and 10-fold in the IM and NTT regions of HCC livers and 3-fold in fibrosis livers, compared to controls. T lymphocyte (CD3⁺) populations showed a progressive increase, particularly CD4⁺ T cells, which exhibited a 5-fold increase in fibrosis and a 10-fold increase in the IM and NTT regions of HCC livers compared to controls. Among the different immune cell populations analysed, regulatory T cells (Tregs) demonstrated the most substantial rise, increasing 125-fold in the IM region and 80-fold in the NTT regions of HCC livers. In the HCC liver microenvironment, Spearman's correlation analysis revealed complex interactions between various immune cell populations. Notable correlations in the tumour region included those between proliferating cells and proliferating KCs ($r = 0.59$, $p = 0.035$), proliferating hepatocytes and proliferating infiltrating macrophages ($r = 0.67$, $p = 0.012$), tumour CD8⁺ T cells and proliferating infiltrating macrophages ($r = 0.60$, $p = 0.032$), and KCs and Tregs ($r = -0.56$, $p = 0.048$). Similarly, in the IM region, significant correlations were observed between KCs and proliferating hepatocytes ($r = 0.72$, $p = 0.0096$), CD8⁺ T cells and proliferating infiltrating macrophages ($r = 0.73$, $p = 0.009$), tumour CD4⁺ T cells and IM CD4⁺ T cells ($r = 0.60$, $p = 0.030$), and tumour CD8⁺ T cells and IM Tregs ($r = -0.63$, $p = 0.023$).

Conclusions: This study provides a comprehensive analysis of immune cell dynamics during CLD progression, highlighting significant immune cell infiltration and redistribution, particularly in IM region of the HCC liver. The marked increase in Inf mph and Tregs suggests a skewed immunosuppressive phenotype and evolving immune microenvironment as fibrosis progresses towards HCC.

EVALUATION OF BELGIUM'S PROGRESS TOWARDS HBV ELIMINATION: RESULTS FROM A NATIONAL SEROSURVEY. A. Furquim d'Almeida (1), E. Ho (2), P. Beutels (3), K. Maertens (4), N. Hens (3), P. Van Damme (4), H. Theeten (4), T. Vanwolleghem (5) / [1] University of Antwerp, Antwerp, Belgium, Viral Hepatitis Research group, Laboratory of Experimental Medicine and Paediatrics, [2] University of Antwerp, Antwerp, Belgium, Viral Hepatitis Research Group, Laboratory of Experimental Medicine and Paediatrics, [3] University of Antwerp, Antwerp, Belgium, Centre for Health Economics Research and Modelling of Infectious Diseases (CHERMID), Vaccine & Infectious Disease Institute (VAXINFECTIO), [4] University of Antwerp, Antwerp, Belgium, Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute (VAXINFECTIO), [5] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology.

Introduction: The WHO strives to eliminate HBV by 2030 by reducing the hepatitis B surface antigen (HBsAg) prevalence to $\leq 0.1\%$ in ≤ 5 -year-olds and achieving at least 90% coverage of 3 doses of HBV vaccine (HepB3). In addition, universal infant HBV vaccination is recommended. This has been implemented in Belgium since 1999, with a catch-up at 12-years of age. In 2021, the vaccine coverage in Belgium was estimated to be 97.1% in 18–24-month-old children. We previously showed that HBsAg positivity alone overestimates the HBV prevalence and hepatitis B core antibody (anti-HBc) confirmatory testing should be performed in low-endemic countries.

Aim: In this nationwide serosurvey, we evaluated Belgium's progress to reach the WHO elimination targets and assessed the impact of the national vaccination strategy by systematically analysing HBsAg, anti-HBc and hepatitis B surface antibodies (anti-HBs).

Methods: A total of 4968 individual residual serum samples were collected from ambulatory patients at 10 private diagnostic laboratories in Belgium – geographically representing the whole country – during Q2/Q3 2020 (outside COVID-19 lockdown). The number of samples in each laboratory was stratified per region, age group (10-year age bands) and sex. HBsAg, anti-HBs and anti-HBc were analysed on the Abbott Alinity I. The samples were weighted by comparing sample and population frequencies by sex, 10-year age band and province. Quantifiable anti-HBs titers (limit of quantification (LOQ) = 2 IU/L) were evaluated as a proxy for HBV vaccine uptake, therefore not taking into account natural waning of vaccine-induced antibodies and residual HBV immune memory.

Results: HBsAg was detected in 2/89 (2.2%) samples from children aged ≤ 5 years. Both samples were anti-HBc negative (< 1 S/CO), corresponding to the absence of chronic HBV infection. In our study, 2336 of the 4968 (47.0%) samples were HBsAg and anti-HBc double negative and had a quantifiable anti-HBs titer, indicative of prior HBV vaccination. Weighted analysis estimated a vaccination degree, based on anti-HBs $> \text{LOQ}$, of minimum 47.2% (95% CI 45.5% – 48.8%) for the Belgian population. This was significantly higher in the younger age groups. More specifically, the weighted proportion with anti-HBs titers > 2 IU/L was significantly higher ($p < 0.001$) in the ≤ 33 -year-olds (71.5%, 95% CI 69.1% – 73.7%) compared to the > 33 - year-olds (31.2%, 95% CI 29.2% – 33.2%), which is in line with the Belgian vaccination policy implemented in 1999.

Conclusions: In this population-based nationwide serosurvey, none of the samples of ≤ 5 -year-olds were HBsAg and anti-HBc double positive. At least 71.5% (95% CI 69.1% - 73.7%) of the age cohort subject to the universal vaccine program had quantifiable anti-HBs titers. These results reinforce that Belgium is on track to reach the 2030 WHO HBV elimination targets.

PHYSICAL FITNESS METRICS IN LIVER TRANSPLANT RECIPIENTS EARLY POST-TRANSPLANTATION: OUTCOMES AND EXPLORATORY COMPARISON OF CORRELATIONS WITH OXYGEN UPTAKE. H. Van Crielinge (1), S. Leunis (1), L. Vrancken (2), A. Van Craenenbroeck (3), V. Cornelissen (4), S. De Smet (5), D. Monbaliu (6) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation, Abdominal Transplantation, KU Leuven, Leuven, Belgium, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Microbiology, Immunology and Transplantation, Abdominal Transplantation, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation, Nephrology and Renal Transplantation Research Group, KU Leuven, Leuven, Belgium, [4] KUL - University of Leuven, Leuven, Belgium, Department of Rehabilitation Sciences, Research Group for Rehabilitation in Internal Disorders, KU Leuven, Leuven, Belgium, [5] KUL - University of Leuven, Leuven, Belgium, Exercise Physiology Research Group, Department of Movement Sciences, KU Leuven, Leuven, Belgium, [6] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation, Abdominal Transplantation, KU Leuven, Leuven, Belgium.

Introduction: Peak oxygen uptake ($\text{VO}_{2\text{peak}}$) is an objective measure of cardiorespiratory fitness and an independent predictor of mortality before and after liver transplantation. Post-transplant $\text{VO}_{2\text{peak}}$ assessments are not routinely implemented due to equipment cost, the need for qualified personnel, reimbursement issues, time investment, and clinical

contra-indications such as graft and anastomosis complications, and cardiovascular instability. Other components of health-related physical fitness and frailty have previously been shown to be more feasible to implement whilst also predicting outcomes in liver transplant recipients.

Aim: This study aimed to quantify health-related physical fitness and physical frailty in de novo liver transplant recipients whilst exploring correlations between VO₂peak and other commonly used health-related physical fitness metrics, including the Liver Frailty Index (LFI), Short Physical Performance Battery (SPPB), 4-meter gait speed, 6-Minute Walking Distance (6MWD), Hand Grip Strength (HGS) and five times Sit-To-Stand (STS) time.

Methods: Baseline data from the PHOENIX-Liver trial (NCT06302205), an ongoing RCT investigating the role of post-transplant aerobic training intensity, were analysed. In 46 de novo liver transplant recipients (58 ± 12 years, 67% men, three to five months post-transplantation) the following physical fitness variables were evaluated: relative and percentage-predicted VO₂peak, LFI, SPPB, 4-meter gait speed, percentage-predicted 6MWD, percentage-predicted HGS, and five times STS. Correlations between relative VO₂peak ($\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), as well as percentage-predicted VO₂peak, and other aforementioned variables of physical fitness and frailty, were analysed using Pearson or Kendall's Tau correlation coefficients.

Results: Participants exhibited a relative VO₂peak of $17.9 \pm 5.9 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, corresponding to $66 \pm 20\%$ of the percentage-predicted value. The average LFI was 3.96 ± 0.73 , with 20% of participants being categorized as frail, 66% as pre-frail, and 14% as robust. The average SPPB score was 10 ± 2 , and the 4-meter gait speed averaged 3.9 ± 2.6 seconds. Participants scored $59 \pm 36\%$ and $66 \pm 17\%$ of the percentage-predicted values for 6MWD and HGS, respectively. The STS test was completed in an average time of 13.2 ± 9.3 seconds. Among the tested indices, LFI showed the strongest correlation with VO₂peak: $r = -0.58$ ($P < 0.001$) with relative VO₂peak and $r = -0.724$ ($P < 0.001$) with percentage-predicted VO₂peak. The correlation coefficients of the other indices with relative VO₂peak, ranked in descending order, were 0.49 ($P < 0.001$) for SPPB, -0.458 ($P = 0.002$) for gait speed, 0.35 ($P = 0.019$) for percentage-predicted 6MWD, -0.246 ($P = 0.125$) for STS, and 0.243 ($P = 0.108$) for percentage-predicted HGS. The correlation coefficients with percentage-predicted VO₂peak, ranked in descending order, were 0.53 ($P < 0.001$) for SPPB, 0.46 ($P = 0.002$) for percentage-predicted HGS, -0.41 ($P = 0.006$) for gait speed, 0.36 ($P = 0.018$) for percentage-predicted 6MWD, and -0.296 ($P = 0.064$) for STS.

Conclusions: Three to five months after transplantation, liver transplant recipients exhibit cardiorespiratory fitness levels that remain suboptimal and near the threshold for full independent living. LFI strongly and SPPB moderately correlated with VO₂peak. The LFI incorporates hand grip strength, chair stands, and balance testing, requiring only basic equipment (handheld dynamometer, chair, and stopwatch) and minimal time. These advantages support its potential as a cost-effective, scalable tool for routine follow-up after liver transplantation aiding in monitoring recovery, risk prediction, and tailoring interventions. Rehabilitation promoting post-transplant physical fitness could enhance well-being after transplantation.

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NON-INVASIVE ASSESSMENT OF HEMODYNAMIC IMPACTS OF CIRRHOSIS: PREDICTIVE FACTORS OF POST-TIPS CARDIAC DECOMPENSATION. C. Delaere (1), J. Vachiery (2), A. Lemmers (3), C. Moreno (3) / [1] ULB, Brussels, Belgium, Internal Medicine, [2] Erasme Hospital, Brussels, Belgium, Cardiology, [3] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Introduction: Cirrhosis is a major cause of morbidity and mortality, with portal hypertension as a primary driver of complications. Cardiovascular complications, especially heart failure, are frequently observed in cirrhosis and play a substantial role in morbidity and mortality. Acute global heart failure occurs in 10-20% of patients following transjugular intrahepatic portosystemic shunt (TIPS) placement. Despite the high prevalence of cardiovascular complications, they are insufficiently studied prior to intervention, particularly before TIPS.

Aim: Identify risk factors for cardiovascular events, particularly acute heart failure, within two years after TIPS placement in patients with cirrhosis.

Methods: This retrospective single-centre study included patients with hepatic cirrhosis who underwent TIPS for refractory ascites at Erasme Hospital between January 2010 and December 2022. Clinical, biological, and pre-TIPS cardiac ultrasound data were collected, focusing on right ventricular function and its coupling with the pulmonary artery using TAPSE (tricuspid annular plane systolic excursion), TRV (tricuspid regurgitation velocity), TAPSE/sPAP (tricuspid annular plane systolic excursion/systolic pulmonary artery pressure) and TAPSE/TRV ratios. Patients who did not undergo a pre-TIPS cardiac ultrasound at Erasme Hospital were excluded. Univariate logistic regressions were performed to evaluate risk factors for clinically significant heart failure (right, left, or global) occurring within two years following the intervention.

Results: Of 131 patients in the database, 67 were included. Alcohol-related cirrhosis was the most common aetiology (84%). The median MELD score was 11. 81% of the patients received a TIPS with a final diameter of 8 mm. The median gradient measured at the end of the procedure was 9 mmHg. A favourable response to the procedure was observed in 52% of patients, signifying that the need for repeated paracentesis was effectively eliminated. Echocardiographic analysis revealed preserved right ventricular function, with a median TAPSE of 24 mm and a median TRV of 2.43 m/s. Heart failure occurred in 12% of patients following TIPS placement. Higher TAPSE (OR = 0.86; $p = 0.045$), TAPSE/PAPs (OR = 0.03; $p = 0.041$), and TAPSE/TRV ratios (OR = 0.69; $p = 0.033$) were associated with a reduced risk of post-intervention heart

failure. Additionally, a higher residual porto-systemic gradient was significantly linked to a lower risk of heart failure (OR = 0.6; p = 0.001).

Conclusions: This study underscores the importance of evaluating the coupling between the right ventricle and pulmonary artery as a predictor for acute heart failure post-TIPS. These findings highlight the need for careful patient selection to optimize clinical outcomes following TIPS placement.

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IMPLEMENTATION OF A HEPATOLOGY CLINICAL NURSE SPECIALIST IN BELGIUM: CHALLENGES AND FACILITATORS. L. Seynhaeve (1), C. De Vloo (1), S. De Meulder (1), J. Dewyspelaere (1), L. Harlet (1), J. Decaestecker (1) / [1] AZ Delta, Belgium, Gastroenterology – hepatology.

Introduction: The decision to recruit a Hepatology Clinical Nurse Specialist (CNS) at AZ Delta Hospital was inspired by a study by Morando et. al showing that specialized care providers could reduce mortality and hospital readmissions in patients with cirrhosis and ascites (1). Furthermore, the gastroenterology team had already witnessed the successful implementation of a CNS for Inflammatory Bowel Diseases (IBD) and a CNS for digestive oncology. Both factors led to the decision to recruit a Hepatology CNS, addressing the increasing need for specialized care in hepatology, where complex patient needs require enhanced coordination and expertise.

Establishing the Role: While the role of a CNS in hepatology was already well established in countries like the Netherlands and the UK, Belgium had no such precedent. A primary challenge was defining the scope of practice for the CNS. Furthermore, integrating a CNS into a multidisciplinary care team required adjustments in workflow, particularly in delineating responsibilities between the CNS and other healthcare providers such as physicians, social workers and dietitians. **Facilitators and Successes** The key to the successful implementation of the CNS role was a strong support from the hospital's gastroenterology department. The department's physicians also played a crucial role by directly funding the CNS position, ensuring its sustainability. Support from a care manager further facilitated the CNS's integration and development. The first phase of implementation, launched in January 2018, focused on extensive training for the CNS. This included observing hepatologist consultations, mastering liver elastography techniques such as FibroScan and shear wave and expanding knowledge in the field of liver diseases. This foundational period ensured that the CNS was well-prepared to assume an independent role within the hepatology team. As the role evolved, a nurse-led consultation model was introduced. In this model, patients with liver disease are first seen by the CNS, who conducts comprehensive assessments including medication reviews, lab result evaluations and liver stiffness measurements. The CNS also plays a pivotal role in patient education, referring patients to other disciplines as needed (e.g., social workers, dietitians, and psychiatric liaisons). This integrated approach not only improved the patient's experience but also optimized the hepatologist's time, allowing for a more efficient consultation process.

Role Expansion: As the CNS role matured, collaborative projects emerged, including a partnership with a psychiatric centre to assess the prevalence of Hepatitis C, B and HIV. This initiative demonstrated the CNS's leadership in clinical practice and research. The CNS's responsibilities expanded to managing pre-transplant assessments, coordinating with transplant centres and leading hepatology meetings. These monthly meetings helped improve patient care and contributed to ongoing service enhancements. The CNS also played a key role in the creation of a multicentre hepatology forum to discuss complex cases. A summary of the different roles at different levels that a CNS hepatology can take (non-restrictive list) are listed in Figure 1.

Challenges: Despite successes, challenges remain. The development of a liver cirrhosis care pathway is ongoing, aiming to track key performance indicators like readmissions and patient survival. While the CNS has improved care coordination, robust data demonstrating its direct impact on these metrics is still lacking. Collecting this data will be critical to fully validate the role's effectiveness. Additionally, integrating e-health solutions to monitor patients in real time and better track symptoms remains an area of improvement. However, integrating these technologies into current workflows and ensuring they are tailored to the patients' needs remain ongoing challenges.

Legal Regulation of the CNS: In Belgium, the CNS role currently lacks formal legal recognition. However, this will change with the new Royal Decrees which are expected in January 2025. The Decrees will define the criteria for the CNS title and outline the medical activities and conditions under which a CNS can practice. This legal framework will further strengthen the role and provide clarity on responsibilities.

Conclusion: The introduction of a Hepatology CNS at AZ Delta Hospital has demonstrated clear benefits in improving care coordination, enhancing patient outcomes and addressing the needs of patients with liver disease. While challenges persist, particularly in data collection and the implementation of e-health solutions, the role continues to play a vital part in optimizing patient care.

- A32 -

THE CHALLENGE OF TREATING HEPATITIS C PATIENTS IN A PSYCHIATRIC CENTRE. L. Yengue (1), X. Saloppé (2), B. Delaunoy (3), S. Chabert (4) / [1] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium,

Gastroenterology Department, [2] Centre de Recherche en Défense Sociale, Tournai, Belgium, Psychologie, [3] Centre Régional Psychiatrique Les Marronniers, Tournai, Belgium, General medicine, [4] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Hepatogastroenterology.

Introduction: Hepatitis C is a viral infection of the liver caused by the hepatitis C virus (HCV). It is a life-threatening disease that is spread through contact with infected blood. There are approximately 71 million chronically infected people worldwide. Despite the lack of an effective vaccine, treatment of infected patients has improved over the years thanks to early detection. It prevents serious liver damage and improves long-term health.

Aim: Try to highlight the challenges of treating Psychiatric and forensic groups compare to the general population.

Methods: A cross-sectional, monocentric study involving 79 patients between 2012 and 2022. Inclusion criteria were patients over 18 years of age with active HCV viral infection. Infection was diagnosed by HCV serology in all patients admitted to the regional psychiatric centre "Les Marronniers", involving two services: "Hôpital Psychiatrique Sécurisé" (HPS) and "Hôpital Psychiatrique Générale" (CHS). A positive serological result was confirmed by polymerase chain reaction (PCR), which determined the viral load and genotype of the virus. Patients' livers were assessed for underlying liver disease using Fibroscan® and liver ultrasound. Patients were offered treatment according to the recommendations of the European Association for the Study of Liver (EASL). Three months later, at the end of treatment, PCR was performed to measure sustained virologic response (SVR). The Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-V) is used to diagnose the various psychiatric disorders. The patient's pathology and symptoms were taken into account in the psychiatric treatment.

Results: 40.5% of patients were in the HPS and 59.5% in the CHS. 79 patients in both units had positive serology and 62% were confirmed by PCR. 49 patients fulfilled the treatment criteria, 62.5% were in the HPS and 22.6% in the CHS. The predominant genotype among those with active infection was 1a (49%, n=24). 82.4% of the treated patients had an undetectable viral load after 3 months, 90% in the HPS and 71.4% in the CHS. However, of all patients with a positive viral load prior to treatment, only 22.6% received treatment in the CHS (7 patients). In the HPS, patients were more likely to receive treatment with 62.5% (10 patients). 50% of the patients in the HPS were on the schizophrenic spectrum, 19.1% in the CHS. 9.4% had an alcohol-related disorder in the HPS compared to 42.6% in the CHS. 21.9% in the HPS and 4.3% in the CHS had an intellectual Handicap. Zero percent of patients had a depressive disorder in the HPS and 19.1% in the CHS.

Conclusions: Three main points can be drawn from our study. First, HPS has a higher rate of effective treatment than CHS, which can be explained by the specialised team working around the patients and the strategy put in place. Secondly, depression and alcohol or drug abuse are barriers to treatment adherence. Finally, we can say that an HCV-infected psychiatric patient with psychiatric co-morbidity can be treated and cured. However, to achieve the same results as the general population, they must be placed in a specialised and close structure with an explicit strategy to deal with the pathology.

- A33 -

FACTORS AFFECTING HIGH-SENSITIVITY C-REACTIVE PROTEIN LEVEL IN PATIENTS WITH HEPATIC STEATOSIS. I. Paliy (1), S. Zaika (2), D. Pali (3) / [1] National Pirogov memorial medical university, Vinnytsya, Ukraine, Vinnytsya, Ukraine, Internal and Family Medicine, [2] National Pirogov memorial medical university, Vinnytsya, Ukraine, Vinnytsya, Ukraine, Internal and Family medicine, [3] National Pirogov memorial medical university, Vinnytsya, Ukraine, Vinnytsya, Ukraine, Epidemiology.

Introduction: Recently, highly sensitive C-reactive protein (hsCRP), as a marker of inflammation in the liver, has received much attention in the study of MASLD, a metabolically associated fatty liver disease. However, the factors influencing increased synthesis of hsCRP have not been studied.

Aim: To explore the possibility of using lipid and uric acid indicators as factors reflecting the level of hsCRP in patients with hepatic steatosis.

Methods: We examined 48 patients with liver steatosis diagnosed based on ultrasound. hsCRP, as well as total cholesterol, triglycerides, HDL, LDL, VLDL, and uric acid, were determined in all patients. Patients were divided into two groups depending on the level of hsCRP. The first group included patients with a level of hsCRP ≤ 1.0 mg/l; the second group - > 1.0 mg/l. The first group consisted of 19 patients (12 men and 7 women), with an average age of 54.2 ± 3.1 years, and the second group – 29 patients (13 men and 16 women), average age of 55.8 ± 2.6 years. The groups did not differ in age, BMI, or presence of concomitant diseases. The difference between the studied indicators was studied by average arithmetic mean and standard error of the arithmetic mean, the correlation analysis was carried out by studied with the determination of the correlation coefficient (r).

Results: We found that the level of uric acid, triglycerides and VLDL in patients of the II group was significantly ($p < 0.01$) higher compared to the patients of the I group and was for uric acid ($378,7 \pm 14,2$ $\mu\text{Mol/l}$ vs. $295,8 \pm 17,9$ $\mu\text{Mol/L}$), triglycerides ($2,8 \pm 0,69$ mMol/L vs. $1,32 \pm 0,19$ mMol/L) and VLDL ($0,94 \pm 0,19$ mMol/L vs. $0,51 \pm 0,09$ mMol/L) respectively. No differences were found between other investigated indicators ($p > 0.05$). We established a

correlation between hsCRP and the level of uric acid ($r = 0.34$), between hsCRP and the level of triglycerides ($r = 0.51$) and between hsCRP and the level of VLDL ($r = 0.47$). For the rest of the indicators, no correlations were established ($p > 0.05$).

Conclusions: According to the study results, it was established that in patients with liver steatosis, the increased level of hsCRP depends on the triglycerides, VLDL and uric acid levels in the blood plasma.

- A34 -

A LOW LEVEL OF CERULOPLASMIN IS ASSOCIATED WITH AN ATHEROGENIC PROFILE AND THE PRESENCE OF MASLD AT A YOUNGER AGE. R. Gason (1), S. André-Dumont (2), E. Wain (1), F. Ausloos (1), N. Lanthier (2) / [1] Centre hospitalier régional de Verviers, Verviers, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology.

Introduction: Ceruloplasmin (Cp) is a copper metabolism protein produced by the liver. It is known for its role as a copper transporter in the body and is notably used as a marker for the diagnosis of Wilson disease. It also has an antioxidant effect, involved in iron metabolism. Several studies have established a link between low ceruloplasminemia and the presence of metabolic dysfunction-associated steatotic liver disease (MASLD), but its significance within this hepatopathy is poorly understood.

Aim: To record Cp values in a population of MASLD patients < 50 years of age and to study patient characteristics according to this level (anthropometric data, severity of liver disease, diabetic status, insulin resistance, dyslipidaemia).

Methods: Prospective bi-centric study in patients < 50 years of age with MASLD defined by the presence of steatosis and at least one cardiometabolic criterion, in whom a Cp value was requested as part of the liver disease work-up. Patients with Wilson disease proven by abnormal cupruria and alcohol-related liver disease (ALD) were excluded.

Results: Fifty-five patients were recruited (63% women). Median age was 40 years (20-50 years) and mean BMI 33 kg/m² (± 5.5 kg/m²), with a mean abdominal circumference of 111 cm (± 11 cm). 43% of patients had a known diagnosis of treated dyslipidaemia, 44% had treated hypertension and 34% had treated type 2 diabetes. In non-diabetics, the mean HOMA-IR score was 4.4 (± 3.0). Mean blood Cp level was 0.25 g/L (± 0.05 g/L). Mean ferritin was 201 μ g/L (± 61 μ g/L). The lipid profile showed mean total cholesterol at 191 mg/dL (± 42 mg/dL) with median HDL-c at 42 mg/dL (14-111 mg/dL). Patients showed moderate transaminase disturbances (mean ASAT 46 IU/L ± 25 and mean ALAT 68 IU/L ± 34) with median elasticity at 6.3 kPa (2.2 - 25.1 kPa) for a mean controlled attenuation parameter (CAP) at 312 dB/m (± 58 dB/m) (Fibroscan®). No correlation was found between ceruloplasmin levels and elasticity, CAP, transaminases or other biological values such as ferritin or HOMA-IR. However, by distinguishing two groups of patients on the basis of ceruloplasmin blood assay, with Cp ≤ 0.2 g/L ($n=8$) and with ceruloplasmin > 0.2 g/L ($n=47$), we highlighted that patients with Cp ≤ 0.2 g/L are significantly younger than patients with normal Cp: 28 years vs. 42 years, $p < 0.0001$. On the other hand, their metabolic profile was similar, including BMI (31.6 kg/m² vs. 33.3 kg/m², $p = 0.41$), abdominal perimeter (110 cm vs. 111 cm, $p = 0.8$), HOMA-IR (4.9 vs. 4.3, $p = 0.69$) and ferritin level (262 μ g/L vs. 191 μ g/L, $p = 0.26$), with the exception of HLD-c, which was significantly lower in the population with lowered Cp compared with patients with normal levels (34 mg/dL vs. 43 mg/dL, $p = 0.03$). Despite the younger age, elasticity (6.6 kPa vs. 6.1 kPa, $p = 0.5$) and CAP (293 dB/m vs. 314 dB/m, $p = 0.40$) data were similar in both groups.

Conclusions: In a MASLD population, a lower Cp level is significantly associated with younger age and a riskier atherogenic profile (lower HDL-c) and may be explained by the protein's antioxidant properties. This justifies not using Cp levels solely to exclude Wilson disease, since its low level probably confers an increased cardiovascular and liver risk in these patients. This needs to be assessed in prospective follow-up studies.

- A35 -

PREVALENCE OF HEPATITIS B AND C IN PATIENTS WITH DIABETES MELLITUS. M. Coessens (1), J. Schouten (1), P. Coremans (2), N. Van Doninck (2), V. Saegeman (3), E. Willems (3), W. Verlinden (1) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and Hepatology, [2] Vitaz, Sint-Niklaas, Belgium, Endocrinology, [3] Vitaz, Sint-Niklaas, Belgium, Laboratory Medicine.

Introduction: Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections represent significant global health challenges, with chronic infection leading to liver cirrhosis, hepatocellular carcinoma, and increased mortality. Diabetes mellitus (DM), particularly type 2 diabetes, has emerged as a comorbidity associated with higher risk for viral hepatitis, but the prevalence of HBV and HCV infections in diabetic populations remains underexplored in many regions.

Aim: This study aims to evaluate the prevalence of HBV and HCV infections among patients with diabetes.

Methods: A prospective study was conducted in a large non-university hospital (Vitaz, Sint-Niklaas) from January 2024 to October 2024. Patients in the diabetes convention and patients with a HbA1c above 6.5% were included. Patients underwent serological testing for HBV (hepatitis B surface antigen [HBsAg], anti-HBc) and HCV (anti-HCV antibodies).

Results: We included 1310 patients from the diabetes type 1 convention; 180 from the type 2 convention and 103 patients with a HbA1c above 6.5% in neither convention. Of the 1593 diabetic patients, 0.69% tested positive for HBVsAg which is significantly higher compared to the general Belgian population (GBP 0.27%) ($p=0.001$). HBVsAg positive patients were born outside of Western Europe in 93% of cases. Of all positive HBsAg patients, 36% were new diagnoses and 36% were lost-to-follow-up after a former diagnosis. Of all diabetic patients, 0.5% tested positive for HCVAb, which is significantly higher compared to the GBP (0.22%) ($p=0.016$). HCV positive patients were born outside of Western Europe in 60% of cases.

Conclusions: This study provides valuable insights into the higher prevalence of HBV and HCV infections in patients with diabetes in Belgium compared to the general population, emphasizing the need for enhanced screening, vaccination, and management strategies in this high-risk population. Early detection and treatment of viral hepatitis in diabetic patients can improve long-term health outcomes and reduce the risk of liver-related morbidity and mortality.

BELGIAN NETWORK ON GASTROINTESTINAL REGULATORY MECHANISMS (GIREM)

- B01 -

DEMONSTRATING THE NEUROGENIC CAPACITY OF ADULT ENTERIC GLIA CELLS AND ASSESSING THEIR POST-TRANSPLANTATIONAL FUNCTIONALITY USING CALCIUM IMAGING AND ELECTROPHYSIOLOGY IN EDNRB-/- MICE IN THE CONTEXT OF HIRSCHSPRUNG DISEASE. K. Van Mechelen (1), J. Zhao (1), H. Yu (1), M. Di Natale (1), M. Oviedo Querejazu (1), J. Furness (1), M. Hao (1), L. Stamp (1) / [1] University of Melbourne, Parkville, Australia, Anatomy and Physiology.

Introduction: Gastrointestinal functions are largely regulated by the enteric nervous system. While enteric neurons serve as the main messengers of the ENS, enteric glial cells were traditionally viewed as support cells. However, recent research has revealed a much wider array of glial functions, including gut motility, interactions of the ENS with the epithelium and immune system, and acting as neural stem cells within the ENS. This latter role highlights the plasticity of EGCs, enabling the ENS to restore gut function in response to homeostatic imbalances, such as inflammation or disease. Although glial proliferation and differentiation into enteric neurons is limited under normal conditions, their neurogenic potential holds promise for applications like cell therapy to treat enteric neuropathies, such as Hirschsprung Disease (HSCR). HSCR is a neurodevelopmental disorder where, a variable section of the distal colon is aganglionic, leading to a complete disruption of gut motility and is fatal if left untreated. Currently, treatment involves surgical removal of the aganglionic section of the colon via pull-through surgery. While this is lifesaving, over 50% of children continue to experience ongoing symptoms after surgery, including constipation, incontinence, and enterocolitis. Recently, stem cell transplantation has emerged as a promising alternative for treating HSCR, addressing the underlying problem by regenerating the missing ENS and restoring normal gut function.

Aim: In this study, we aimed to investigate the neurogenic potential of EGC both in vitro and following transplantation in vivo, while also identifying the optimal culturing conditions to maximize EGC proliferation.

Methods: EGCs were isolated from the small intestines of adult tamoxifen-induced Sox10|Chr2 or Sox10|GCaMP3 mice, expressing either the blue light-gated ion channel channelrhodopsin-2, or the calcium indicator GCaMP3, respectively. After tissue dissociation, fluorescent cells were FACS sorted and cultured into gliospheres for two weeks in the presence of two growth factors, GDNF and/or NRG. Surface area was monitored at different timepoints. To investigate neurogenic potential in vitro, EdU was added during the last 6 hr of culture, and gliospheres were subsequently processed for immunolabeling. For in vivo analysis, two gliospheres were transplanted into the aganglionic colon of Ednrb-KO mice, a pre-clinical model of HSCR. Post-surgery, 50% of recipient mice received daily EdU injections. After one week, these grafted colon tissues were harvested for immunolabeling. In parallel, calcium imaging and electrophysiological measurements were performed on KO and control mice, both with and without gliosphere transplantation.

Results: GDNF significantly increased sphere size, while NRG had no significant additional effect on gliosphere proliferation, regardless of GDNF's presence. A similar pattern was observed when examining the percentage of EdU+ nuclei, with GDNF alone yielding the highest proportion and NRG showing an insignificant impact on proliferation. Based on these results, GDNF was added to the culturing medium in the remaining follow-up experiments to maximize proliferation. On average, 20% of the DAPI+ nuclei in cultured gliospheres were positive for the enteric neuronal marker HuCD, indicating that EGCs differentiated – directly or indirectly – into enteric neurons in vitro. To assess in vivo differentiation, graft-derived neurons were counted, and the area of the transplant sites was quantified. On average, we observed 20 ± 3 neurons per $10,000 \mu\text{m}^2$ of graft-derived area, with a total graft core area of $700,000 \pm 110,000 \mu\text{m}^2$. In 4 out of 7 tissues, the presence of at least one EdU+ nucleus in a graft-derived neuron suggests that neuronal differentiation also occurs in vivo. One week after transplantation, graft-derived GCaMP3-expressing cells exhibited fluctuations in intracellular calcium concentrations in response to high K^+ and DMPP. Using electrophysiology, Chr2-expressing gliospheres were selectively stimulated with blue light. Membrane potentials were recorded from smooth muscle cells in the transplant region using a sharp electrode, and responses were induced in 2 out of 10 tissues.

Conclusions: Enteric glial cells show neurogenic differentiation in vitro and in vivo and have the potential to give rise to functional neurons. This characteristic can be exploited in cell therapy for HSCR.

- B02 -

EXPLORING MOLECULAR DRIVERS OF AGING IN ENTERIC NEURONS: DNA DAMAGE, TRANSCRIPTIONAL SILENCING, AND MITOCHONDRIAL CHANGES. L. Mombeek (1), A. Brosens (1), R. Jehoul (1), M. Thijssen (2), W. Boesmans (1), D. Wilson (1) / [1] Hasselt University, Hasselt, Belgium, Neurosciences, [2] Maastricht University Medical Centre, Maastricht, The Netherlands, Department of Pathology.

Introduction: Aging is characterized by the progressive loss of molecular, cellular, and physiological integrity, leading to functional decline and increased disease and mortality risks. Both stochastic and deterministic genomic changes, such as genomic instability and shifts in the epigenetic landscape, along with changes in the transcriptome, proteome, and

secretome, contribute to the weakening of resilience mechanisms that maintain cellular, tissue, and organismal health. A core aspect of aging is genomic instability, where DNA damage leads to permanent genome disruptions. The enteric nervous system (ENS) regulates gastrointestinal (GI) function through its intricate networks of neurons and glia. Age-related changes in the ENS are associated with functional disruptions in gut innervation, leading to altered motility, secretion, and sensation, which may cause conditions such as chronic constipation and faecal incontinence. Thus, it seems likely that ENS aging and the gradual accumulation of DNA damage and associated genomic instability is a key driver of neurodegenerative GI disorders. The role and consequences of DNA damage during ENS aging remain poorly understood, yet is essential to understand how aging compromises ENS function and contributes to age-related GI dysfunction.

Aim: Characterize the molecular hallmarks of enteric neuronal aging related to DNA damage accumulation, epigenetic changes, mitochondrial dysfunction, and cellular senescence.

Methods: Molecular and structural changes in the ENS were studied in young (2 months), middle-aged (15 months), and old (24 months) C57BL/6 mice. DNA damage, heterochromatin, and senescence markers were assessed using immunofluorescence for gamma histone 2AX (gamma H2AX), tri-methylation at the 9th lysine residue of the histone H3 (H3K9me3), and cyclin-dependent kinase inhibitor 1 (p21), respectively. Transcriptional changes were analysed using a publicly available single-cell RNA sequencing (scRNA-seq) dataset (Drokhlyansky, 2020). Mitochondrial morphology was evaluated via transmission electron microscopy (TEM).

Results: Our data suggest a series of molecular changes in aging enteric neurons in mice that may help uncover the mechanisms underlying the functional GI defects observed in aging individuals. Aging enteric neurons show a progressive increase in DNA damage, marked by elevated gamma H2AX levels, alongside the accumulation of inactive heterochromatin as indicated by H3K9me3 and 4',6-diamidino-2-phenylindole (DAPI) colocalization. This heterochromatin formation correlated with age-dependent global transcriptional silencing, as revealed by scRNA-seq analysis, where essential DNA repair genes were significantly downregulated. Elevated p21 expression, which was specific to old neurons, also suggested senescence activation. These observations hint that DNA damage accumulation may trigger both heterochromatin formation and senescence-like pathways in the ENS. TEM analysis of aged neurons revealed enlarged, irregularly shaped mitochondria, indicative of compensatory swelling in response to mitochondrial loss or dysfunction. The transcriptomic data further supported mitochondrial dysfunction, with pronounced downregulation of mitochondrial-associated genes. Increased oxidative stress by radicals was implicated by reduced expression of Sod1, a key antioxidant enzyme, observed in both mouse and human scRNA-seq datasets. Together, these findings support a model in which cumulative DNA damage, impaired DNA repair, general transcriptional silencing, and mitochondrial dysfunction drive cellular fates, such as senescence, that contribute to a functional and structural decline in the aging ENS.

Conclusions: Our results suggest a possible sequence of events linking DNA damage to neurodegeneration in aging enteric neurons. Accumulated DNA damage may contribute to heterochromatin formation, potentially leading to transcriptional silencing and reduced DNA repair and mitochondrial gene expression. Impaired DNA repair could exacerbate DNA damage accumulation, while mitochondrial gene downregulation may result in mitochondrial loss. The remaining mitochondria appear to compensate by swelling, which might lead to inefficient energy production and increased reactive oxygen species levels, potentially amplifying DNA damage further. This damage may also promote cell cycle re-entry, with neurons responding by activating cell cycle arrest mechanisms to avoid apoptosis and adopting a senescence-like phenotype. These findings highlight potential therapeutic targets, such as DNA repair pathways and oxidative stress, to mitigate ENS aging and its associated GI dysfunction.

- B03 -

FUNCTIONAL CONNECTIVITY BETWEEN NEURONS IN THE MESENTERY AND MYENTERIC NEURONS IN THE MOUSE ILEUM. C. Fung (1), F. Guo (2), Z. Li (1), P. Vanden Berghe (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] Qingdao University, China, Physiology & Pathophysiology Department.

Introduction: Recent work suggests that a subset of vagal neural crest cells migrates via the intestinal mesentery to contribute to enteric nervous system (ENS) formation, and that some of these cells remain in the mesentery to give rise to neurons which persist postnatally. The function of mesenteric neurons is unknown.

Aim: The aim of this study was to investigate whether neurons serve to locally monitor and regulate activity confined within the mesentery, and if they communicate with the ENS to influence gut motility given their proximity to the gut wall.

Methods: Immunohistochemical stainings were performed on ileal mesenteric preparations to characterise the neurochemistry of mesenteric neurons. Ca²⁺ imaging was performed on ileum-mesentery preparations from adult Wnt1-cre;R26R-GCaMP3 (Wnt1xGCaMP3) mice. The neuronal tracer DiI was applied to ileum-mesentery preparations to examine the projections of mesenteric neurons. To investigate whether communication between mesenteric neurons and the ENS contribute to regulating intestinal motility, motor patterns in ileal segments with and without the mesenteric nerve connections intact were examined. To examine whether neurons in the mesentery may also locally interact with

neighbouring cells such as adipocytes, we imaged Wnt1xGCaMP3 mesenteric preparations loaded with a red Ca²⁺ indicator Cal590.

Results: Mesenteric neurons displayed immunoreactivity for typical enteric markers such as nitric oxide synthase (NOS) and calretinin. Cholinergic varicosities were found closely apposed to mesenteric neurons. Using Ca²⁺ imaging, mesenteric neurons were seen to respond to electrical and chemical (high K⁺ (75 mM), 5-HT, ATP, and nicotinic agonist DMPP) stimulation. Mesenteric neurons responded to myenteric plexus depolarization using high K⁺ and this was inhibited by hexamethonium (nicotinic antagonist). With DiI tracing, some mesenteric neurons were found to project into the gut wall. Furthermore, local activation of mesenteric neurons using DMPP in turn elicited responses in myenteric neurons.

Conclusions: Taken together, we found that mesenteric neurons express similar neurochemical markers as in the ENS, and that there is bidirectional signalling specifically between mesenteric and myenteric neurons. The extent to which mesenteric neurons interact with surrounding adipose, and their contribution to the control of intestinal function remain to be further explored.

- B04 -

ROLE OF DOPAMINE RECEPTOR D1 IN REGULATING INTESTINAL STEM CELL LINEAGE SPECIFICATION IN HUMAN INTESTINAL ORGANOID. S. Boel (1), M. Farhadipour (1), A. Dubois (2), T. Thijs (1), L. Ceulemans (2), I. Depoortere (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Chronic Diseases and Metabolism (CHROMETA), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Leuven Intestinal Failure and Transplantation (LIFT) Centre.

Introduction: The small intestinal epithelium exhibits a high turnover rate, driven by intestinal stem cells (ISC) located at the base of the crypt. These ISCs integrate various signals from their microenvironment to regulate the balance between self-renewal and differentiation into specialized mature epithelial cells, such as absorptive enterocytes and secretory cells (goblet cells, Paneth cells, and enteroendocrine cells (EECs)). Signals from the enteral or serosal supply system can influence stemness through G protein-coupled receptors. Our preliminary transcriptomic data revealed the expression of dopamine receptor D1 (DRD1) in human intestinal organoids (enteroids) enriched in ISCs and transit-amplifying cells. This receptor can be targeted by dopamine delivered via the apical (L-Phe/L-Tyr in the diet, synthesized by gut microbiota) or basolateral (neurotransmitter from the enteric nervous system) supply system.

Aim: This study aimed to investigate whether targeting DRD1 with a synthetic agonist changes the composition of the gut epithelium by regulating stem cell lineage commitment in human enteroids.

Methods: Undifferentiated jejunal enteroids from normal-weight multi-organ donors (n=5), consisting of ISCs and transit-amplifying cells, were exposed to a DRD1 agonist (SKF38393, 5 μ M), or vehicle for two days, followed by an additional two days of differentiation to ensure full maturation mimicking the epithelial turnover time. The effect on proliferation was assessed via an EdU Cell Proliferation Kit on day two and day four of differentiation. Additionally, epithelial composition was analysed through RT-qPCR and whole-mount immunofluorescence staining for chromogranin A (CHGA) at day four of differentiation.

Results: The number of proliferative EdU+ crypt-based cells decreased with 48 $\pm$ 11% and 46 $\pm$ 7% from day two till four of differentiation in vehicle and SKF38393-treated enteroids, respectively, indicating that lineage commitment was promoted after switching to differentiation medium in both groups. Treatment with SKF38393 did not affect the number of EdU+ cells in enteroids from normal-weight individuals compared to vehicle-treated enteroids, indicating no imbalance in the number of ISCs committing toward differentiation. At day four of differentiation, SKF38393 treatment significantly decreased the relative mRNA expression of the secretory Paneth cell marker REG3A by 32 $\pm$ 11% (p=0.05) and EEC marker CHGA by 42 $\pm$ 7% (p=0.01), which was accompanied by a decrease (43%) in the number of CHGA+ cells. No effect was found on the relative mRNA expression of the goblet cell marker MUC2 and enterocyte marker ALPI.

Conclusions: This study is the first to demonstrate that pharmacological activation of DRD1 in human ISCs directs lineage commitment toward fewer secretory enteroendocrine and Paneth cells, potentially influencing appetite regulation and antimicrobial peptide release.

- B05 -

INTESTINAL ORGANOID AS A MODEL FOR SMALL INTESTINAL EPITHELIUM ALTERATIONS IN ALCOHOL USE DISORDER (AUD). A. Toulehoun (1), P. Stärkel (2) / [1] Institut de Recherche Expérimentale et Clinique (IREC), Catholic University of Louvain (UCL), Belgium, GAEN, [2] UCL Saint Luc, Brussels, Belgium, Gastroenterology.

Introduction: Excessive alcohol intake is a public health burden with more than 3 million related deaths worldwide. Evidence indicates that alcohol abuse associated gut barrier dysfunction contributes to alcohol-associated liver disease.

Although some aspects of this process have been elucidated, the role of intestinal epithelium, a major component of the gut barrier, and its alterations in subjects with an Alcohol Use Disorder (AUD) are poorly studied.

Aim: Our preliminary data in humans indicate a profoundly disturbed proliferation-differentiation program in AUD patients. In this context, we first designed an Intestinal Organoid (Enteroid) model susceptible to reproduce partially the alterations found in AUD. We plan to investigate morphological changes as well as signalling pathways alterations observed in vivo. Finally, the model will be used to establish a cause-effect relationship between alcohol and the epithelium modifications in AUD.

Methods: To generate Enteroids, crypts were isolated from control and AUD patients' duodenum biopsies by enzymatic digestion and grown on matrigel. Then, they were submitted to ethanol treatment. After the treatment, Cytotoxicity and viability were assessed using Propidium Iodide and ATP respectively. Gene expression was determined by qPCR.

Results: These 3D models grow, differentiate and later develop a crypt and villi architecture mimicking in vivo condition. Compared to control, AUD Enteroids displayed morphological alterations including the absence of well-defined crypt and villi architecture. Using Propidium Iodide staining assay to assess membrane integrity and cell death, we found increased cell death with rising ethanol concentrations. In addition, the gene expression profile of epithelial cells assessed by qPCR was modified in AUD compared to controls. LGR5, a marker of stem cells, was downregulated whereas Muc2, representing Goblet cells, was upregulated.

Conclusions: These results are in accordance with the observations made in human duodenal biopsies. Therefore, duodenal biopsy derived Enteroids seem to be a valuable model to investigate alcohol-induced epithelial changes ex vivo.

- B06 -

THE ORGANOID TOOLBOX; LEVERAGING A CHEMICALLY DEFINED MEDIUM TO ADVANCE THE STANDARD OF PRACTICE IN INTESTINAL ORGANOID RESEARCH. M. van Sligtenhorst (1), C. Akkaya (1), A. Denadai Souza (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, Laboratory of Mucosal Biology.

Introduction: The intestinal organoid model has allowed for unprecedented insights in development and disease since its establishment. However, close recapitulation of the intestinal landscape is only possible through precise control of cell type differentiation through the medium composition. Current intestinal organoid models often rely on a medium composition that is highly variable due to the use of conditioned media, and generally only give rise to organoids that resemble the fetal intestinal tissue, thus limiting reproducibility and translation of the results.

Aim: Through a chemically defined medium backbone, we aim to create a reference guide for the establishment, expansion, and diverse experimental setups of intestinal organoids that closely recapitulate the native adult intestinal epithelial cellular diversity, while minimizing variability and increasing the translational power.

Methods: Mucosal biopsies underwent crypt isolation alongside RNA single cell sequencing to create a reference landscape of the native adult epithelial cellular diversity. Organoid growth and differentiation, as well as intestinal stem cell growth were quantified by automated high content imaging. Additionally, organoids and intestinal stem cell cultures were characterized using single molecule RNA FISH of LGR5 to assess stem cell content. Polarity of apical-out organoids was confirmed using F-actin staining using phalloidin. Additional characterization of the cellular landscape of organoids will be performed initially through RT-qPCR, and ultimately through single cell RNA sequencing integrated with the native tissue.

Results: The organoid toolbox workflow is anchored in the establishment-expansion-biobanking cycle of organoids. During establishment, crypt isolation of mucosal biopsies was performed alongside single cell RNA sequencing. This has resulted in a fully annotated single cell reference map across different regions of the gut from healthy volunteers, which will be used to integrate single cell RNA sequencing data from matched organoid cultures. Expansion of the organoid culture took place using our fully chemically defined organoid expansion medium, which allowed for the rapid expansion of long living cystic organoids with minimal cell death and differentiation. Three modalities were further explored: a specific expansion of the intestinal stem cell (ISC) pool for more efficient gene editing strategies, differentiation of organoids to promote a cellular diversity corresponding to the native tissue, and apical-out organoids for bacterial invasion and nutrient uptake assays. Through minimal adaptation of the culturing medium, a specific expansion of the ISC pool was achieved in a 2D monolayer (5.34% LGR5+ cells in organoids during expansion vs. 39.50% LGR5+ cells in ISC culture, $p < 0.05$). Dose-dependent growth as a result of different EP4 agonists confirmed the dependency of EP4 activation for ISC growth. Differentiation of organoids was also achieved through minimal adaptation of the backbone medium (25.33% $\pm$ 10.86 of organoids budding during expansion at day 14 vs. 58.17% $\pm$ 15.04 of organoids budding after induction of differentiation at day 14, $p < 0.05$). Lastly, apical-out organoids were generated. These exhibited an inverted polarity, shown through visualization of F-actin with phalloidin. Astonishingly, these organoids have an extremely long lifespan of over six months without the need for subculturing.

Conclusions: With our research we showcase the power of a fully chemically defined medium. Through minimal adaptations to the medium composition, it allows to seamlessly move between different in vitro modalities, such as a specific expansion of the ISC pool, differentiated organoids, and apical-out organoids.

CHARACTERIZATION OF THE ROLE OF NKCC1 IN COLORECTAL CARCINOGENESIS. P. Adam (1), C. Salée (2), M. Stepniak (2), C. Massot (2), J. Loly (3), S. Vieujean (3), C. Reenaers (3), C. Coimbra (4), E. Decker (4), P. Delvenne (5), E. Louis (3), M. Meuwis (6) / [1] GIGA Institute, University of Liège, Liège, Belgium, Translational Gastroenterology Laboratory, [2] GIGA Institute, University of Liège, Liège, Belgium, Laboratory of Translational Gastroenterology, [3] University Hospital CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [4] University Hospital CHU of Liège, Belgium, Abdominal, endocrine and transplantation, [5] University Hospital CHU of Liège, Belgium, Pathological Anatomy and Cytology, [6] University Hospital CHU of Liège, Belgium, Laboratory of Translational Gastroenterology.

Introduction: NKCC1 is a Na-K-Cl cotransporter localized at the cell membrane and in the cytoplasm, predominantly expressed in cells involved in fluid secretion. NKCC1 is overexpressed in pre-tumoural and tumoural lesions of colitis-associated cancer and colorectal cancer (CRC) (Merli et al., 2021). Moreover, NKCC1 expression has been associated with survival outcomes of CRC patients. However, its function in colorectal carcinogenesis remains underexplored. NKCC1 has been recently identified in a colorectal cancer stem cell signature (Lin et al., 2024). These colorectal cancer stem cells are specifically associated with poor cancer prognosis, treatment resistance, and deregulated pathways, including altered ROS levels and oxidative stress responses.

Aim: The aim of this study is to characterize the expression profile of NKCC1 in colorectal cancer cells and to investigate its role in carcinogenesis, with a specific focus on its involvement in the regulation of oxidative stress.

Methods: Oxidative stress was induced in 3 CRC cell lines using H₂O₂ concomitantly with bumetanide (BMT), the catalytic inhibitor of NKCC1. Chemical inhibition or NKCC1 silencing via shRNA were applied to assess cell viability and activation of the mTORC1 pathway, stem cell markers and proliferation/differentiation markers by WB and qPCR. Bulk RNA-sequencing was performed on HT29 knockdown for NKCC1 expression by shRNA. Human intestinal organoids deriving from patient tumours and normal surgical margins, grown under proliferative or differentiated states, were used to characterize NKCC1 at the transcriptional and protein levels. Finally, NKCC1 expression in CRC was investigated using public single-cell datasets (GEO: GSE178341) to determine its specific expression within epithelial and tumoural cell-clusters (Pelka et al., 2021).

Results: Exposure of Caco-2 cells to 1 mM H₂O₂ for 24 hours resulted in 68% cell viability. However, co-treatment with 200 µM bumetanide reduced cell viability to 18%. Similarly, HT-29 cells viability decreased from 62% to 36%, while HCT116 cells showed a reduction from 12% to 5%, with a BMT concentration-dependent effect. Organoids and tumouroids treated with BMT demonstrated activation of the mTORC1 pathway. Bulk RNA-sequencing of HT-29 cells with NKCC1 knockdown revealed enrichment of mTORC1 signalling. Silencing NKCC1 expression via shRNA in CRC cell lines significantly increased cancer stem cell markers (LGR5, CD44, ALDH1A1). During differentiation, human intestinal organoids exhibited a marked decrease in NKCC1 expression, corresponding to a reduction in stem cell marker levels. Single-cell data analysis confirmed that NKCC1 is highly expressed in both normal intestinal stem cells and cancer stem cells.

Conclusions: We confirmed that NKCC1 is expressed in both normal intestinal and cancer stem cells of colorectal tumours. Inhibition of NKCC1 transporter activity reduces cell viability in CRC cell lines, but only under oxidative stress conditions. NKCC1 silencing enhances the expression of cancer stem cell markers, while its chemical inhibition specifically activates the mTORC1 pathway. These findings suggest that NKCC1 plays a critical role in carcinogenesis, especially in cancer stem cells, likely through its ability to regulate oxidative stress. Bulk RNA-sequencing of tumouroids and organoids knockdown for NKCC1 is ongoing and is expected to provide new evidences on the impact of NKCC1 in colorectal carcinogenesis.

SERUM AMYLOID A3 AS A KEY DRIVER OF INFLAMMATORY SIGNALLING ALONG THE MICROBIOME-GUT-BRAIN AXIS. P. Verstraelen (1), N. De Loose (1), R. Verboven (1), K. Grando (2), S. Olubajo (2), S. Van Remoortel (1), C. Tukel (2), J. Timmermans (1), W. De Vos (1) / [1] University of Antwerp, Antwerp, Belgium, Lab of Cell Biology and Histology, [2] Temple University, Philadelphia, United States, Centre for Microbiology and Immunology.

Introduction: Emerging evidence supports a critical role for gut-brain communication in inflammation and neurodegeneration and shows that the enteric microbiome is capable of influencing this axis via secretion of the bacterial amyloid curli.

Aim: We aimed to identify the inflammatory pathways which become activated in the ENS by curli exposure and study their relevance in pathogenic gut-brain communication.

Results: Through curli exposure and subsequent transcriptomic analyses, our study revealed a marked upregulation of Serum Amyloid A3 (Saa3) and other pro-inflammatory factors in enteric glial cells. The inflammatory state was accompanied by increased DNA damage and replication and triggered the influx of T lymphocytes. Notably, recombinant

SAA3 addition was sufficient to recapitulate this phenotype, while Saa3 knock-out attenuated curli-induced DNA damage and replication. Intraperitoneal curli injection, colonization with curli-producing *Salmonella*, as well as DSS-induced colitis, potentially triggered Saa3 transcription in the colon, highlighting the diverse range of pathological conditions in which SAA3 plays a role. Intriguingly, recombinant SAA3 also triggered Saa3 upregulation in vitro, and elevated colonic Saa3 as well as circulating SAA1 levels persisted for up to three months following DSS exposure. These findings suggest that serum amyloids participate in a self-sustaining feedforward loop and remain systemically available for extended periods. Systemic curli exposure also lead to local Saa3 transcription in the meninges and choroid plexus, and in a chronic DSS paradigm applied to APPnl-g-f/MAPT mice, we found that IBA1 immunoreactivity near hippocampal amyloid deposits was modulated in a sex-dependent manner, highlighting the need for further in depth characterization of the neuroinflammatory state.

Conclusions: Together, our results show that serum amyloids represent potential mediators of pathogenic gut-brain communication. Further dissection of the signalling pathways involved in the SAA3-driven feedforward loop may yield novel treatment options targeting SAA-mediated inflammation.

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IDENTIFICATION OF THE MECHANISMS UNDERLYING RESIDENT MACROPHAGE ACTIVATION IN POST-OPERATIVE ILEUS. Z. Wang (1), N. Stakenborg (2), I. Appeltans (1), G. Boeckxstaens (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, TARGID.

Introduction: Postoperative ileus (POI) is an iatrogenic disorder characterized by a transient episode of impaired gastrointestinal (GI) motility following abdominal surgery. Previous studies identified that the activation of tissue resident macrophages orchestrates the inflammatory cascade causing the impairment of GI peristalsis. Yet, the mechanisms leading to the activation of the muscularis macrophages remain unclear.

Aim: To identify the initial trigger causing the activation of muscularis macrophages in the early phase of POI.

Methods: C57Bl/6 mice underwent laparotomy with or without intestinal manipulation (IM) and were sacrificed after 15, 30, 60, and 120 minutes. The muscularis externa was collected, DAPI⁺ nuclei were isolated, and samples from the 30 minutes group underwent FACS sorting followed by single-nuclei RNA sequencing. Raw sequencing reads were demultiplexed, mapped to the mouse reference genome and gene-expression matrices were calculated. After normalization, these cells were clustered using the Seurat workflow. To investigate the role of mechanoreceptor Piezo2, C57Bl/6 mice were treated with the Piezo2 antagonist D-GsMTx4 prior to the manipulation, while the control group received an equivalent volume of saline. The mice were sacrificed after 30 and 60 minutes. RT-qPCR, flow cytometry and histology were used to validate the single nuclei RNA-seq dataset. Cell proliferation was assessed with the Ki67 proliferation marker using both FACS and immunofluorescent staining.

Results: Time-course studies revealed an increase in macrophages, monocytes, and neutrophils starting at 30 minutes post-IM, followed by further rises at 60 and 120 minutes, as assessed by flow cytometry. Meanwhile, immunofluorescence analysis showed that proliferating macrophages (Ki67⁺Iba1⁺) peaked after 60 minutes of IM. To identify the initial trigger responsible for activating muscularis macrophages, we selected the 30 minutes timepoint and performed single-nuclei RNA sequencing on 22,260 nuclei from sham and IM groups. Unsupervised clustering followed by annotation of the integrated gene expression data identified 19 distinct clusters. In line with flow cytometric data, we observed the increase of macrophages and neutrophils in the IM group compared to the sham group. Using the ligand-receptor pair prediction tool (NicheNet) and Gene Ontology (GO) analyses we found that enteric neurons were potential macrophages activators. Transcriptomic analysis and immunofluorescence staining showed the presence of Piezo2 in enteric neurons. Flow cytometry revealed that neutralized Piezo2 by D-GsMTx4 significantly reduced both macrophage and neutrophil at 30- and 60-minutes post-IM. Additionally, qPCR analysis showed a marked reduction in the expression of pro-inflammatory genes Cxcl10 and Ccl4 at both time points following D-GsMTx4 treatment. Notably, the inhibition of Piezo2 suppressed macrophage proliferation, as demonstrated by a significant reduction in Ki67⁺ macrophages through flow cytometry ($P < 0.0001$) and immunofluorescence staining ($P = 0.0324$) after 60 minutes of IM.

Conclusions: We demonstrated that early inflammation in the muscularis externa begins within 30 minutes post-surgery, with Piezo2—a mechanosensor expressed by enteric neurons—serving a pivotal role in activating muscularis macrophages. Chemical inhibition of Piezo2 significantly reduced macrophage proliferation and attenuated pro-inflammatory responses during the early phase of POI. These findings highlight the role of enteric neurons in triggering macrophage activation in POI and suggest that targeting Piezo2 may serve as a novel therapeutic approach to mitigating early inflammation in POI.

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DUODENAL ION FLUXES MAY CONTRIBUTE TO INTESTINAL FLUID LOSSES IN PATIENTS WITH SHORT BOWEL SYNDROME. L. De Meyere (1), A. Verbiest (1), A. Viaene (1), J. Tóth (1), L. Timmermans (1), K. Geboers

Introduction: Short bowel syndrome (SBS) is by far the most common cause of chronic intestinal failure (CIF) and is defined by a small bowel length of less than 200 cm as a result of extensive surgical resections (e.g. due to intestinal infarction or inflammatory bowel disease). Intestinal adaptation is a poorly understood compensatory mechanism of the shortened small intestine to improve intestinal absorption, occurring mainly in the first two years after surgical resection. However, we hypothesize that not only favourable changes enhance intestinal absorption, but also negative alterations of the gut physiology are involved in this natural intestinal adaptation. For example, numerous GI and non-GI conditions have been linked to increased intestinal permeability. However, it is unclear to what extent alterations in barrier function are present in patients with SBS. We used Ussing chambers to assess mucosal integrity (pore + leak pathway) and transepithelial ion secretion, ex vivo. We hypothesize that patients with SBS-CIF have an altered barrier function, with increased secretion and loss of fluids and electrolytes leading a negative fluid balance.

Aim: To investigate alterations in intestinal barrier function in patients with SBS compared to controls.

Methods: We included patients with stable SBS treated at our centre in UZ Leuven. Patients were considered stable if there were no changes in weight ($\leq 5\%$), PS volume ($\leq 25\%$) and PS energy content ($\leq 25\%$) during the last 3 months. Controls were recruited and included in case of no previous GI surgery (except for appendectomy), active GI disease or burdensome symptoms. Duodenal biopsies were collected during gastroduodenoscopy. Three biopsies per individual were mounted in Ussing chambers with an exposed tissue area of 0.017 area/cm². Transepithelial electrical resistance (TEER) was calculated using Ohm's law based on the generated potential difference (PD) when applying a constant current. The paracellular passage was assessed by adding a 4 kDa fluorescein isothiocyanate-labelled dextran (FITC-dx4) at the mucosal side, followed by sampling the serosal side at 30 min intervals and measuring the FITC-dx4 concentration. The average TEER and FITC-dx4 flux at time points 60, 90 and 120 minutes of the 3 biopsies was calculated. Thereafter, the short-circuit current (Isc) that was needed to keep the potential difference (PD) clamped at 0 mV, was measured for 10 minutes to assess ion secretion. Finally, the Isc was measured during 10 minutes after adding luminal amiloride (100 μ M, a blocker of the Na⁺/H⁺ exchanger) and during 10 minutes after adding luminal glucose (15mM, to stimulate the Na⁺/glucose cotransporter 1, SGLT1). The average response of the 3 biopsies was calculated. Data are shown as median (IQR).

Results: Seven patients with SBS, of which 5 patients with a colon-in-continuity, with a median preserved small intestinal length of 100 (30-130) cm and 3.5 (3-7) days of PS per week, and 8 controls were included. Intestinal permeability – measured by TEER and FITC-dx4 flux – was similar between patients with SBS and controls. However, a significantly reduced baseline Isc was observed in patients with SBS (-21.27 (-50.67, 38.71) μ A/cm² vs. controls (34.18 (-19.83, 118.4) μ A/cm², p=0.04). Moreover, the glucose-induced Isc increase was more pronounced in patients with SBS (62.87 (31.93, 87.83) μ A/cm²) vs. controls 31.30 (16.33, 77.67) μ A/cm², p=0.03). No difference in Isc was seen after adding luminal amiloride (patients with SBS -1.83 (-5.45, 6.60) μ A/cm², HV -2.32 (-3.63, 14.87) μ A/cm², p=0.78).

Conclusions: Our preliminary data suggest that patients with SBS do not have an altered duodenal permeability. However, the difference in the basal Isc indicates a more positive potential in the lumen, suggesting a decreased secretion of anions (HCO₃⁻, Cl⁻) to the lumen and/or reduced absorption of cations (Na⁺) by the Na⁺/H⁺ exchangers. The latter seems less likely, since the response to amiloride was not altered. These alterations potentially contribute to fluid losses in patients with SBS. Moreover, the higher glucose-induced Isc, indicates an increased glucose uptake through SGLT1 in patients with SBS, which may contribute to the natural intestinal adaptation process after resection in these patients. However, further research is needed to confirm and explore the possible causes and consequences of ionic imbalances in these patients.

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REPURPOSED DRUG CLIOQUINOL AS A NOVEL TREATMENT FOR TREATING BARRIER DISRUPTION IN INFLAMMATORY BOWEL DISEASES (IBD). A. Zouzaf (1), F. Biscu (1), D. Cicia (1), N. Kadavath (1), V. De Simone (1), J. Duarte Da Rocha Pereira (2), B. Verstockt (3), S. Vermeire (3), K. Thevissen (4), G. Matteoli (1) / [1] KUL - University of Leuven, Leuven, Belgium, CHROMETA - TARGID, [2] Rega Institute- KU Leuven, Leuven, Belgium, Microbiology, Immunology and Transplantation, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] KUL - University of Leuven, Leuven, Belgium, Microbiology, Immunology and Transplantation.

Introduction: Inflammatory bowel disease (IBD) primarily affects the gastrointestinal (GI) tract, a critical barrier organ, often resulting in debilitating symptoms and progressive tissue damage. Approximately 4.9 million people globally suffer from IBD. Current therapies primarily focus on suppressing inflammation rather than directly promoting the healing of the damaged intestinal barrier. This leaves a critical gap in the therapeutic landscape, as inadequate barrier repair perpetuates chronic inflammation and increases the risk of disease progression, complications, and relapses. Effective therapies aiming for mucosal healing are urgently needed to break the cycle of inflammation and restore the integrity of

the gut lining, a key step toward long-term remission in IBD patients. Recent evidence highlights the crucial role of pro-resolving macrophages (M ϕ s) in mitigating chronic intestinal inflammation and promoting tissue repair.

Aim: This study investigates a novel therapeutic approach targeting M ϕ s to induce a pro-resolving phenotype and promote healing. Specifically, we explore the enzyme phosphoglycerate dehydrogenase (PHGDH) as a metabolic checkpoint for M ϕ reprogramming. PHGDH activity is linked to the expression of anti-inflammatory molecules like Arg1 and Retnla. We demonstrate that clioquinol (CQ), a repurposed drug, activates PHGDH and drives anti-inflammatory responses.

Methods: Phgdh expression was assessed in inflamed and non-inflamed mucosal biopsies from patients. A yeast-based screening identified PHGDH activators, including novel and repurposed compounds. Wound-healing assays using human and murine intestinal epithelial cells (CaCo2 and ModeK) were performed to evaluate CQ's effects, both directly and via M ϕ -conditioned medium. Bone marrow-derived macrophages (BMDMs) from WT mice were polarized and treated with CQ, and expression of PHGDH and inflammatory genes was analysed by qPCR. In vivo, zebrafish larval colitis (DSS/TNBS) and acute murine DSS colitis models were employed to assess CQ's therapeutic potential. Outcomes included survival, (hind)gut length, mucosal integrity, and clinical disease activity (diarrhea, stool blood, weight loss). Colonic tissue was analysed by histology, flow cytometry, and qPCR. To delineate M ϕ -specific PHGDH function, CSF1R-driven inducible PHGDH knockout and WT mice were evaluated in a chronic DSS colitis model.

Results: PHGDH expression was significantly reduced in inflamed mucosal biopsies from IBD patients. In vitro, CQ enhanced wound healing in intestinal epithelial cells, mediated by both macrophage-dependent and independent mechanisms. CQ increased PHGDH expression in M2-like macrophages and mitigated M1-like pro-inflammatory responses (reduced il6, ccl5, and nos2 expression). In M1-like macrophages, CQ suppressed inflammatory genes (il1b, ccl5, and nos2) while boosting arg1 expression, a marker of M2-like macrophages. In vivo, oral CQ administration (62.5 mg/kg/day) significantly reduced disease severity in murine DSS colitis compared to vehicle ($p < 0.0001$) and prednisolone ($p = 0.0003$). Zebrafish models corroborated these findings, with improved colitis outcomes under CQ treatment. In chronic DSS colitis, M ϕ -specific PHGDH knockout mice exhibited worse disease outcomes compared to WT controls, underscoring PHGDH's role in inflammation resolution.

Conclusions: CQ promotes wound healing and mitigates inflammation by modulating macrophage polarization, making it a promising therapeutic candidate for repairing the damaged gut barrier and breaking the cycle of chronic inflammation in IBD. These findings position CQ as a safe and effective potential treatment option, albeit more research on the underlying molecular mechanisms is needed.

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THE DIETARY EMULSIFIER K-CARRAGEENAN ALTERS THE INFLAMMATORY STATE, BUT NOT PERMEABILITY, OF INTESTINAL EPITHELIAL CELLS FROM PATIENTS WITH CROHN'S DISEASE. E. Vissers (1), J. Wellens (2), L. Giorio (2), W. Zadora (3), B. Verstockt (4), M. Ferrante (4), S. Vermeire (4), C. Matthys (5), K. Arnauts (2), J. Sabino (4) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, Translational Research in Gastrointestinal Disorders (TARGID), [2] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA), Translational Research Centre for Gastrointestinal Disorders (TARGID), [3] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation, Nephrology and Renal Transplantation Research Group, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Endocrinology.

Introduction: The consumption of ultra-processed foods has increased significantly worldwide and is associated with the rise in inflammatory bowel disease (IBD). However, any causative factors and their underlying mechanisms are yet to be identified. Interestingly, our group found a higher consumption of the dietary emulsifier carrageenan (CGN) in Belgian IBD patients, compared to healthy controls (Wellens et al. ECCO 2025). In addition, studies with animal models and cell lines suggest the involvement of dietary CGN in intestinal inflammation, but its exact role remains unclear.

Aim: This study aimed to elucidate further whether different types of CGN can alter the permeability and inflammatory state of the intestinal epithelium in patients with Crohn's disease (CD).

Methods: Confluent Caco-2/HT29-MTX cocultures ($n=4$) were exposed to either κ -, ι -, or λ -CGN (100 $\mu\text{g/ml}$) for 24 hours. Confluent epithelial monolayers derived from colonic organoids of 5 CD patients were exposed to κ -CGN (100 $\mu\text{g/ml}$), the most abundant subtype in foods, for 48 hours. Two independent experiments were performed per patient ($n = 10$). In both models, inflammation was established by adding an inflammatory mix (100 ng/mL TNF- α , 20 ng/mL IL-1 β , and 1 $\mu\text{g/ml}$ flagellin) to the basolateral side, 24 hours prior to CGN exposure. Changes in permeability were measured by transepithelial electrical resistance (TEER) at predetermined timepoints (0, 12, 24, 48 hours). In organoid-derived monolayers, cytokines were quantified in the apical and basolateral supernatant using the V-PLEX Proinflammatory Panel 1 kit (Meso Scale Diagnostics) and gene expression was analysed with RT-qPCR (Taqman probes, run on Viiia7) ($n = 8$; 2 samples excluded due to low RNA concentrations).

Results: In non-inflamed organoid-derived monolayers, κ -CGN exposure increased the expression of CXCL8 ($p = 0.026$, RM one-way ANOVA) and TNF ($p = 0.001$; RM one-way ANOVA). Interestingly, this pro-inflammatory effect

of κ -CGN was more pronounced when inflammation was already present, with increased expression levels of pro-inflammatory markers upon κ -CGN stimulation (CXCL8: $p = 0.010$; IL-1b: $p = 0.009$; TNF: $p = 0.001$; RM one-way ANOVA), compared to the inflamed control. Release of the cytokines IL-2 ($p = 0.017$), IL-10 ($p = 0.049$), and IL-4 ($p = 0.042$) in the apical supernatant of non-inflamed monolayers was increased ($n = 8$; RM one-way ANOVA) upon κ -CGN exposure. In inflamed monolayers, κ -CGN caused an increase in IL-6 ($p = 0.006$), IL-13 ($p = 0.003$), IL-2 ($p < 0.001$), IL-10 ($p = 0.007$) and IL-4 ($p = 0.001$) in the apical media, compared to the inflamed control ($n = 8$; RM one-way ANOVA). κ -CGN exposure did not affect TEER of non-inflamed ($p = 0.896$) and inflamed ($p = 0.795$) organoid-derived monolayers ($n=10$; RM one-way ANOVA), but induced small alterations in the RNA expression of barrier-related genes. The expression of TJP1, also known as ZO1, ($p = 0.036$; Friedman test) and OCLN ($p = 0.037$; RM one-way ANOVA) increased significantly after stimulation with κ -CGN in a non-inflamed condition, compared to the control. Also in the inflamed condition, the expression of OCLN increased upon κ -CGN stimulation ($p = 0.001$; RM one-way ANOVA). Moreover, exposure to κ -CGN resulted in a decrease of MUC5AC in inflamed monolayers ($p = 0.031$; RM one-way ANOVA) and an increase of MUC5B in non-inflamed monolayers ($p = 0.049$; RM one-way ANOVA). In addition, none of the CGN subtypes altered permeability of non-inflamed or inflamed Caco-2/HT29-MTX cocultures ($n=4$; Kruskal-Wallis test), compared to the unexposed control.

Conclusions: Dietary κ -CGN caused upregulation of inflammatory markers and affected cytokine release of intestinal epithelial cells from CD patients, while permeability remained unaltered. When inflammation was already present, this pro-inflammatory effect was more pronounced, suggesting a role for dietary CGN in perpetuating inflammation during active CD.

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DIETARY MODULATION OF TRPM8: A NOVEL APPROACH TO IMMUNE REGULATION IN IBD. D. Cicia (1), F. Biscu (1), F. Iannotti (2), M. Miraglia (3), C. Ferrante (4), N. Iaccarino (3), S. Cadenas de Miguel (5), B. Ke (6), M. Nani (3), K. Talavera Perez (7), I. Elia (5), R. Capasso (8), A. Izzo (3), E. Pagano (3), G. Matteoli (1) / [1] KUL - University of Leuven, Leuven, Belgium, CHROMETA, [2] Istituto di Chimica Biomolecolare, Consiglio Nazionale delle ricerche, Pozzuoli, Jamaica, Institute of Biomolecular Chemistry ICB, [3] University of Naples Federico II, Naples, Italy, Department of Pharmacy, [4] Gabriele d'Annunzio University, Chieti, Italy, Department of Pharmacy, [5] KUL - University of Leuven, Leuven, Belgium, KU Leuven Cancer Institute, [6] KUL - University of Leuven, Leuven, Belgium, CHROMETA, [7] KUL - University of Leuven, Leuven, Belgium, Department of Cellular and Molecular Medicine LICR, [8] University of Naples Federico II, Naples, Italy, Department of Agricultural sciences.

Introduction: The interaction between diet, genetics, microbiota, and the immune system is central to the pathogenesis of inflammatory bowel disease (IBD). While mechanisms remain unclear, many nutrients influence gut mucosal immune function, influencing both innate and adaptive immunity.

Aim: In this study, we aimed to investigate the role of transient receptor potential melastatin 8 (TRPM8), a non-selective cation channel, in macrophage activation and its modulation by dietary interventions, with the goal of identifying novel therapeutic strategies for inflammatory bowel disease.

Methods: Experiments were conducted on bone marrow-derived macrophages (BMDMs) isolated from the femurs and tibias of C57BL/6J wild-type (WT) and *Trpm8*^{-/-} (B6.129P2-*Trpm8*^{tm1Jul/J}) mice. BMDMs were polarized toward a pro-inflammatory phenotype using IFN- γ (50 ng/mL) and LPS (20 ng/mL) for 18 hours. Pro-inflammatory cytokine levels, including interleukin (IL)-6, IL-1 β , and tumour necrosis factor- α (TNF- α), were quantified in the supernatant collected from WT and *Trpm8*^{-/-} naïve and pro-inflammatory BMDM cultures using commercial ELISA kits, following the manufacturer's instructions. To analyse metabolic reprogramming in pro-inflammatory macrophages, Seahorse extracellular flux assays and cell metabolome quenching were performed. Extracellular acidification rate (ECAR), basal glycolysis, and compensatory glycolysis were measured using an XF24 Seahorse Extracellular Flux Analyzer according to the manufacturer's protocol. Luteolin, a selective TRPM8 antagonist (unpublished data), was used for pharmacological targeting. WT and *Trpm8*^{-/-} BMDMs were pre-treated with luteolin (10 μ M) for one hour before polarization to the pro-inflammatory phenotype. Cytokine quantification and extracellular flux analysis were performed as described above. Additionally, we utilized a DSS-induced colitis model in wild-type and bone marrow chimera *Trpm8*^{-/-} mice, integrating flow cytometry (FACS) analysis to investigate immune responses and inflammatory pathways.

Results: We identified TRPM8 as a mediator of LPS-induced Ca²⁺ influx in macrophages, driving their activation. Notably, TRPM8 is inhibited by luteolin, a dietary flavonoid, which reprograms macrophages toward a pro-tolerogenic phenotype. Both genetic deletion and pharmacological modulation of *Trpm8* in macrophages resulted in impaired activation of pro-inflammatory metabolic and transcriptional pathways, leading to decreased production of key cytokines, including interleukin (IL)-1 β , IL-6, and tumour necrosis factor (TNF)- α . Our findings further revealed that the anti-inflammatory effects of TRPM8 modulation are mediated by lactate, which drives IL-10 release, a hallmark of immune tolerance. In vivo, oral administration of luteolin significantly ameliorated intestinal inflammation in a murine colitis model by dampening the innate immune response. Accordingly, chimera *Trpm8*^{-/-} mice had a better outcome compared to WT mice, and luteolin had no effect on them.

Conclusions: Our findings position TRPM8 as a dietary target to modulate immune function and offer a promising therapeutic avenue for IBD and other chronic inflammatory diseases.

CASE REPORTS

- C01 -

ACTINOMYCOSIS OF THE AMPULLA OF VATER: A CASE REPORT AND LITERATURE REVIEW. J. Bousson (1), C. Van Steenkiste (2), C. Gabriel (3), D. Hoton (4), V. Bouderez (2), P. Deprez (5), S. Van Langendonck (2) / [1] Maria Middelaers Ziekenhuis, Gent, Belgium, Gastroenterology, [2] Maria Middelaers Ziekenhuis, Gent, Belgium, Gastroenterology, [3] Maria Middelaers Ziekenhuis, Gent, Belgium, Pathology, [4] UCLouvain, Cliniques Universitaires St Luc, Belgium, Pathology, [5] UCLouvain, Cliniques universitaires St Luc, Belgium, Gastroenterology.

We present the case of a 76-year-old female referred to our department after the detection of a large tumoural mass in the major papilla of Vater. The lesion, thought to be an ampullary adenoma, was identified during routine upper endoscopy performed to further investigate fatigue and iron-deficiency anaemia. Initial biopsies, however, revealed only chronic active inflammation without evidence of adenoma, dysplasia or malignancy. The patient had a significant medical history, including breast cancer successfully treated 21 years prior and a partial distal pancreatectomy performed 7 years earlier for an intraductal papillary mucinous neoplasm (IPMN) with focal high-grade dysplasia. At our centre, repeat upper endoscopy and endoscopic ultrasound (EUS) revealed a 5 cm hypoechoic mass originating at the major papilla with intraductal extensions into both the common bile duct (CBD) and pancreatic duct (PD). No deep invasion, vascular involvement, or lymphadenopathy was observed. Additional biopsies, both conventional and fine-needle biopsy (FNB), ruled out malignancy, though no definitive diagnosis of adenoma could be established. Due to the patient's medical history, further investigations, including tumour markers (CA 19-9, CA 15-3, CEA) and an FDG PET-CT, were conducted, all yielding normal results. Initially, the patient declined further work up and treatment. Later, she consented to referral for expert re-evaluation, considering an endoscopic ampullectomy. Repeat EUS at the time of referral demonstrated stable findings, but histopathological analysis suggested actinomycosis, despite negative microbiological cultures. The patient commenced a 12-month course of amoxicillin. Follow-up EUS at four months revealed slow but ongoing expansion of the lesion. After 12 months, EUS showed a stable mass with a slightly more pronounced dilatation of both the CBD and PD. Histological evaluation confirmed persistent *Actinomyces* colonies without evidence of dysplasia. Due to prior negative experiences with invasive treatments, the patient preferred continued conservative management. Actinomycosis is known to be a rare, chronic, suppurative, and granulomatous infection caused by *Actinomyces* spp., anaerobic Gram-positive bacteria that normally colonize the human mouth, gastrointestinal tract, and genital tract. Infections are predominantly attributed to *Actinomyces israelii*. The condition is characterized by granulomatous inflammation with fibrosis and has several typical clinical presentations, including cervicofacial actinomycosis following dental infection, pelvic actinomycosis in women with intrauterine devices, pulmonary actinomycosis in smokers with poor dental hygiene, and actinomycosis mimicking malignancies at various anatomical sites, often post-surgery. In all cases, disruption of the normal mucosal barrier facilitates the pathogen's invasion into deeper tissues. Differential diagnoses include malignancy, tuberculosis, and nocardiosis, as actinomycosis spreads progressively and often forms cold abscesses. Treatment typically involves long-term antibiotic therapy, such as penicillin or amoxicillin monotherapy for 6–12 months. In some cases, surgical resection of the tumoural mass may be necessary. Abdominal actinomycosis presents considerable diagnostic challenges due to its rarity, insidious progression, low diagnostic yield from microbiological cultures and biopsies, and nonspecific clinical manifestations. Actinomycosis involving the ampulla of Vater and pancreas is exceptionally rare, with only two cases of ampullary involvement and 13 pancreatic cases identified in our literature review. Notably, both ampullary cases reported in the literature followed pancreaticoduodenectomy, whereas the current case occurred after a distal partial pancreatectomy. These findings highlight the necessity of considering actinomycosis in the differential diagnosis of ampullary masses, particularly in post-surgical patients presenting with histopathological evidence of granulation tissue.

- C02 -

MALIGNANT TRITON TUMOUR OF THE BILE DUCT: A RARE YET RELENTLESS MANIFESTATION OF MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR. A. Dumarey (1), C. Bertels (2), A. Reekmans (3), R. Sciot (4), I. Vanden Bempt (5), V. Van Der Kelen (6), S. van der Merwe (7) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory of Hepatology, [2] UZ Brussel, Brussels, Belgium, Oncology, [3] ASZ, Aalst, Belgium, Gastroenterology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Centrum Menselijke Erfelijkheid (CME), [6] ASZ, Aalst, Belgium, Geriatrics, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology.

An 80-year-old Caucasian woman presented to the emergency department with acute complaints of nausea and decreased appetite, along with progressive lethargy persisting for four weeks. She denied fever or abdominal pain, and vital signs

were within normal range. Physical examination revealed prominent icterus and tenderness in the right upper quadrant of the abdomen. No apparent masses were palpable. Laboratory results included leucocytosis (15,700/ μ L; normal < 10,000/ μ L) with neutrophilia (14,800/ μ L; normal < 6,400/ μ L), elevated CRP (138 mg/L; normal < 5 mg/L), cholestasis (direct bilirubin 10.8 mg/dL; normal < 0.3 mg/dL, alkaline phosphatase 805 U/L; normal < 104 U/L), elevated transaminases (1.5-2 x ULN), and microcytic anaemia of inflammation (haemoglobin 10.6 g/dl; normal > 11.7 g/dl). Cholangitis was suspected, possibly due to an obstructive choledochal mass, and empirical treatment with amoxicillin-clavulanic acid was initiated. Abdominal computed tomography (CT) scan displayed marked dilatation of the intra- and extrahepatic bile ducts, together with inward densities in the common bile duct (CBD) and irregular enhancement of the gallbladder wall. Endoscopic ultrasound revealed a heterogeneous and hypoechogenic mass in the centre of the CBD. It appeared to be well demarcated and did not invade surrounding tissue. Contrast enhancement with SonoVue® exhibited a rapid wash in and a slow wash out with hypo-enhancements over 50 seconds. A small and rounded adenopathy adjacent to the CBD was noted. Endoscopic retrograde cholangiopancreatography was performed for biliary drainage, and discharge consisted of an unusual amount of viscous, mucoid-like liquid. Intraductal visualization was achieved using the SpyScope DS II® catheter, which demonstrated both the intramural origin and the clear delineation of the suspected neoplasm. More proximally, the subhilar mucosa was found to have villous aspects. Targeted biopsies were performed, and a covered stent was placed to maintain duct patency. Due to the observed tumoural phenotype, the differential diagnosis of intraductal papillary mucinous neoplasm of the bile ducts was considered. Unexpectedly, histological examination revealed a different orphan disease named 'malignant triton tumour' (MTT), which was confirmed by additional genetical testing. MTTs concern a rare subset (5%) of malignant peripheral nerve sheath tumours (MPNSTs), classified by the WHO as soft-tissue sarcomas. MPNSTs occur in one in 100,000 individuals, and 50% of cases are associated with neurofibromatosis type 1, of which our patient showed no signs or symptoms. MTTs are characterized by their rhabdomyoblastic differentiation, aggressive behaviour, and resistance to chemotherapy and radiotherapy, resulting in a five-year overall survival of only 10-20%. The patient was well informed but chose supportive care over further imaging and radical treatment options. Her symptoms and laboratory tests gradually improved over the course of two weeks, after which she was discharged. Palliative care options were discussed with the patient and her general practitioner. One month later, she represented to the emergency department due to melena and recurring general discomfort. Urgent gastroscopy revealed a deep bulbous crater with yellow mucus production and active bleeding. Unfortunately, the aggressive biological behaviour described in literature translated into clinical practice, and CT demonstrated infiltration in the bulb, ascending colon, and mesenteric fat, as well as prominent ascites. Major surgery and chemotherapy were offered but refused. The patients' condition deteriorated within days, and upon repeated request, euthanasia was carried out. This case presentation illustrates the key role of an efficient multidisciplinary approach, without which the correct diagnosis would have likely been missed. Most MTTs arise from the trunk, extremities, or head and neck area. Other locations are highly unusual, and to our knowledge, this is the first report of malignant triton tumour in the bile ducts. Large clinical studies are lacking, and the roles of radiotherapy and chemotherapy remain controversial, as neither has demonstrated survival benefit. Better awareness and detailed case reports can contribute to larger oncological trials. This case highlights the practicality of Spyglass™ guided biopsies, as well as the importance of informed decision making and respecting the patient's autonomy in a terminal care setting.

- C03 -

BYPASS ASSOCIATED LATE DUMPING SYNDROME LAMS REVERSION (BALR). V. VandenDriessche (1), E. Kaya (2), P. Yengue (2), J. Desmet (3), M. Lefebvre (2) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Gastroenterology, [2] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastroenterology, [3] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Digestive surgery.

Dumping syndrome (DS) is a common complication of Roux-en-Y gastric bypass (RYGB), occurring in 19–26% of cases (1,2). Symptoms can range from gastrointestinal complaints, such as borborygmi, abdominal pain and nausea, to autonomic symptoms, including perspiration, palpitations, and syncope. These symptoms are often debilitating, significantly reducing quality of life and lead to substantial weight loss and malnutrition (3). Current management for DS includes dietary interventions as first-line treatments. For early DS, viscosity-enhancing agents are typically employed, while acarbose is used for late DS. Third-line therapies include somatostatin analogues. However, when these treatments are ineffective, surgical re-intervention or experimental endoscopic approaches, such as transoral outlet reduction (TORe), may be considered (4). We report a case of refractory late DS in a 44-year-old woman who underwent RYGB eight months prior. Her symptoms included severe postprandial abdominal cramps, diarrhoea, and frequent episodes of lipothymic malaise, leading to extreme malnutrition. Her weight dropped from 103 to 38 kg, and her Sigstad score was 9, strongly indicative of DS (5). Modified oral glucose tolerance testing was inconclusive due to excessive vomiting. The patient did not respond to first-, second- and third-line treatments. Surgical RYGB reversal was suggested, however, due to the patient's fragility and malnourishment was considered too risky, note the overall 30-day complication rate of 29% including anastomotic leaks, sepsis and haemorrhage (6,7). Given her severe malnutrition and excessive symptoms, we opted for a minimally invasive endoscopic solution: Bypass-Associated late dumping syndrome LAMS Reversion

(BALR). Using a lumen-apposing metal stent (LAMS), we restored communication between the remnant stomach and the bypassed gastric cavity, effectively re-establishing normal food bolus flow. Two weeks after the procedure, the patient reported significant improvement in her symptoms. She no longer experienced postprandial cramps, diarrhoea, or lipothymic episodes. Her weight increased from 38 to 41 kg, and her Sigstad score dropped to 0, indicating a complete resolution of DS. At a 16-month follow-up, her weight had further increased to 47 kg, with her Sigstad score remaining at 0. Currently, few reports describe endoscopic reversal (ER) for DS management. One case involved DS resolution as an indirect outcome of EUS-Directed transGastric ERCP (EDGE) in a malnourished patient (8). Another study reported ERs in 17 patients suffering from severe malnutrition after RYGB (9). While data on ER by LAMS for DS remains scarce, EDGE has demonstrated a 99% technical success rate in certain cohorts (10). This case confirms the safe and effective endoscopic management by LAMS placement for managing refractory DS associated with RYGB. ER using LAMS offers a minimally invasive solution for patients with severe symptoms unresponsive to conventional therapies.

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- C04 -

A FIVE-YEAR-OLD BOY WITH A STOMACH IN ALL ITS STATES. E. Lambot (1), P. Eisendrath (2), E. Levy (3) / [1] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Paediatrics, [2] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology and hepatology, [3] CHU Saint-Pierre, Brussels, Belgium, Paediatric Gastroenterology and nutrition.

A five-year-old boy presented with crampy epigastric abdominal pain, soft non-bloody stools and vomiting with view spots of red blood, without fever for five days. Palpebral oedema had also been appearing for a few hours. According to his parents, he has lost 1.2 kg, or 7% of his body weight due to anorexia. He has no past history; no tropical travels and vaccinations were giving accordingly to the Belgium vaccination program. On clinical examination, his blood pressure was high (120/81 mmHg). Skin recoloration time of less than three seconds. The abdomen felt tender at the epigastric area, and there was bilateral palpebral oedema. Blood tests showed no inflammatory syndrome, hypoalbuminemia at 24 g/L (35-45 g/L), normal transaminases and coagulopathy, hyponatremia at 129 mmol/L (136-145 mmol/L), hypocalcaemia at 1.92 mmol/L (2,2-2,6 mmol/L), normal kidney function and no thyroid insufficiency. Urine examination showed no proteinuria or haematuria. No enteropathogenic germs were found on stool culture, but occult blood in stool was positive. Radioallergosorbent test and IgE were normal, making a food allergy less likely. Total IgA and anti-transglutaminase IgA were normal, ruling out coeliac disease. However, Cytomegalovirus (CMV) IgM was positive. The work-up continued with an abdominal ultrasound scan showing thickening of the gastric walls, raising the suspicion of gastroenteropathy. Gastroscopy with biopsy was conducted and it reveals hypertrophy of the gastric folds in the body and fundus of the stomach, a relatively unaffected antrum, erosions of the mucosa and mucus in the lumen. The duodenum was normal. Biopsies of the fundus and corpus of the stomach showed infiltration of neutrophils and eosinophils. Further CMV PCR was positive also in the biopsies taken from the stomach.

Gastroenteropathies cause an abnormal loss of plasma proteins from the digestive tract. They can mimic several pathologies, making diagnosis difficult. The most probable diagnosis was Ménétrier's disease caused by CMV infection. Ménétrier's disease is a type of hyperplastic hypertrophic gastroenteropathy with normal or reduced acid secretion. The main differential diagnosis is Zollinger-Ellison syndrome, which has a similar endoscopic presentation but a different clinical history (peptic ulcers) and increased acid secretion.

Intra-hospital management of the patient was supportive because the disease is often self-limiting. Intravenous albumin was administered three times at 0.5 g/kg and twice at 1 g/kg, along with Furosemide 1 mg/kg (loop diuretic). He received Ondansetron 0.15 mg/kg (anti-emetic) and Omeprazole 1 mg/kg. His albumin level rose from 24 to 28 g/L (35-45 g/L). The ionogram normalised: the hyponatremia and hypocalcaemia on admission were caused by haemodilution on hypoalbuminaemia. Vomiting ceased during hospitalisation. He was discharged home after 15 days in hospital.

Dietary problems and iron, zinc and vitamin D deficiencies persisted for six months. A follow-up gastroscopy at three months showed a clear reduction in lesions. His albumin level at three months was 41 g/L (35-45 g/L). He was supplemented with iron, zinc and vitamin D, as well as nutritional supplements for six months. This period was necessary for him to regain his usual energy and appetite. To conclude, Ménétrier's disease is rare in children. Only about 50 cases are described. It is diagnosed clinic-pathologically. Its exact aetiology and pathophysiology have yet to be clarified. In children, it is often post-infectious in origin. Treatment is supportive and the condition usually resolves spontaneously. However, changes of weight loss and deficiencies caused by gastroenteropathy and hypoalbuminemia require close monitoring. Parents should be warned that symptoms may last for six months or more before healing completely.

- C05 -

BREAKING THE FLOW: BLEEDING BEYOND THE OBVIOUS IN A YOUNG ADULT. K. De Looze (1), K. Ferdinande (2), L. Levrau (1), U. Singfer (3), L. De Carvalho (4), A. Vantilborgh (5), M. Callens (6), A. Beyens (6), S. Raevens (1), A. Geerts (1), X. Verhelst (1), H. Van Vlierberghe (1) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology and hepatology, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [3] Ghent University Hospital, Ghent, Belgium, Department of Interventional Radiology, [4] Ghent University Hospital, Ghent, Belgium, Department of hepatobiliary surgery, [5] Ghent University Hospital, Ghent, Belgium, Department of Hematology, [6] Ghent University Hospital, Ghent, Belgium, Department of Medical Genetics.

A 19-year-old female with unremarkable medical history presented the emergency department with severe lower gastrointestinal bleeding, characterized by bright red blood loss per rectum and associated hemodynamic instability. Upon arrival, she was conscious but showed mild tachycardia and low-normal blood pressure. Physical examination revealed a slightly distended, non-tender abdomen. Laboratory findings showed a significant drop in haemoglobin level (7.1 g/dL) with pronounced iron deficiency, while other laboratory parameters were within normal range. The patient reported no medication use and led a healthy lifestyle. After initial hemodynamic stabilization, an urgent three-phase abdominal CT angiography was performed. CT revealed a large mesenteric arteriovenous malformation (AVM) originating from ileocolic branches of the superior mesenteric artery, with multiple dilated draining veins. Additional findings included thrombosis of the superior mesenteric vein extending to the portal vein, along with cavernous transformation of the portal vein, indicative of chronic portal vein thrombosis (PVT). No active gastrointestinal bleeding was detected on the CT. Subsequently, urgent catheter angiography confirmed the presence of an ileocecal AVM and extensive PVT. Two large AVM feeders were selectively embolized with glue in an urgent attempt to reduce the risk of rebleeding, while minimizing the chances of non-target embolization and ischemia. The presence of an AVM involving the superior mesenteric artery and vein is extremely rare and challenging to manage. Pathophysiologically, the PVT may have led to obstruction of the outflow tract of a high-flow AVM. This likely resulted in dilation of the venous high-capacitance system, which, under the influence of portal hypertension, may have progressively dilated and degenerated until gastrointestinal bleeding occurred. Most probably in this case, the PVT represents a second event leading to the decompensation of a pre-existing AVM. In light of the concomitant PVT therapeutic anticoagulation with heparin was initiated. Unfortunately, the patient experienced two subsequent episodes of significant lower gastrointestinal bleeding, necessitating additional embolization procedures. Following the final embolization, the patient developed acute abdominal pain, fever, and markedly elevated inflammatory markers (CRP >300 mg/L). Abdominal CT revealed diffuse mural thickening, mucosal hyperenhancement and submucosal oedema in the cecum, terminal ileum, mesocolonic oedema and ascites, compatible with enterocolitis. Colonoscopy confirmed significant ischaemic changes in this area. Blood cultures were positive for multidrug-resistant *E. coli*, prompting the initiation of high-spectrum antibiotics for sepsis due to bacterial translocation from the compromised bowel. Given the complexity and rarity of this case it was presented to an international panel of experts in gastrointestinal vascular malformations through the ERN Rare Liver CPMS platform. The consensus recommended the least invasive approach, with further discussion if the patient developed severe intestinal ischaemia, recurrent bleeding despite embolization, or acute abdominal deterioration. Potential interventions include surgical resection of the superior mesenteric vein, resection of the AVM and affected bowel segments, or, complete AVM occlusion followed by portal vein recanalization through TIPS procedure. Given the rarity of AVMs in the gastrointestinal tract, we consulted our medical genetic colleagues. Clinical examination identified prominent features such as macrocephaly (head circumference 61.5 cm; +3.7 SD), hypertelorism, down slanting palpebral fissures, low-set posteriorly rotated ears, and prominent eyebrows. Intraoral examination revealed gingival hypertrophy. Multiple trichilemmomas were observed on the forehead, along with café-au-lait spots on the back and freckling on the toes. These clinical features are strongly suggestive for Cowden syndrome, which may be correlated with mesenteric AVM's. Genetic testing for pathologic PTEN variants has been initiated, results are pending. To date, the patient has had no recurrence of bleeding. However, she remains hospitalised

due to persistent fever and elevated inflammatory markers, likely stemming from infected, compromised bowel segments requiring repeated courses of broad-spectrum antibiotics. Despite these challenges, the patient is otherwise stable.

Conclusion: We presented a rare and complex case of a young adult female with an ileocolic AVM that decompensated due to PVT, resulting in severe and recurrent episodes of lower gastrointestinal bleeding. Since the third embolization session, the patient has not experienced any further bleeding. The management of such cases requires a multidisciplinary approach, often incorporating international expert consensus due to the scarcity of literature. Therapy in this instance was guided by expert opinion from leading authorities in the field.

- C06 -

CASE REPORT: SIMULTANEOUS PORTOSYSTEMIC SHUNT AND PROXIMAL SPLENIC ARTERY EMBOLIZATION FOR PATIENTS WITH THERAPY-REFRACTORY HEPATIC ENCEPHALOPATHY AT RISK OF PORTAL HYPERTENSIVE COMPLICATIONS. A. Lemaitre (1), S. Nullens (2), M. Van Herck (2), T. Jardinet (3) / [1] University of Antwerp, Antwerp, Belgium, Gastroenterology/hepatology, [2] ZAS, Antwerp, Belgium, Gastroenterology/hepatology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Radiology.

Hepatic encephalopathy (HE) is a well-known complication of cirrhosis, usually precipitated by easily identified causes (e.g. infection, renal impairment...). When HE recurs despite optimal treatment or lacks clear precipitants, a portosystemic shunt may be the culprit. We present a case of therapy-refractory HE caused by a spontaneous portosystemic shunt (SPSS). Given the patient's history of prior variceal bleeding, a combined approach was undertaken to embolize the SPSS and the proximal splenic artery, aiming to manage HE and reducing portal hypertension (PHT). Case A 69-year-old man with MASLD-related cirrhosis (MELD 13) presented with his fifth episode of HE (West Haven grade 3) despite treatment with lactulose, rifaximin, and sodium benzoate. He had a medical history of variceal bleeding and biliopancreatic diversion (BPD). Laboratory investigations revealed no significant abnormalities, besides elevated ammonia levels (169 $\mu\text{mol/L}$). Full infection screen was negative. Abdominal CT scan identified a paraesophageal shunt, supplied by the coronary vein. To address HE, SPSS closure was planned. Because SPSS closure could increase PHT, this was combined with a proximal splenic artery embolization (pSAE), because of a history of variceal bleeding. The portal vein was accessed transhepatically, and the splenic artery cannulated via the femoral artery. SPSS embolization using Histoacryl-Lipiodol increased the hepatic vein pressure gradient (HVPG) from 17 to 21 mmHg. This was followed by pSAE using an Amplatzer vascular plug, reducing HVPG to 15 mmHg. HE symptoms resolved, pharmacological treatment was stopped, and paracentesis became less frequent. Weeks later, the patient was readmitted with abdominal pain, and CT confirmed splenic infarction. Recurrent spontaneous bacterial peritonitis necessitated splenectomy, which was complicated by haemorrhage, septic shock, and death.

Discussion: Portal hypertension is the main driver for several complications in cirrhosis, including variceal bleeding, ascites, hepatorenal syndrome and HE. SPSS form to decompress the portal system but can cause HE due to portal flow steal and decreased hepatocellular function. SPSS are present in up to 60% of cirrhosis patients and up to 40% of those develop HE. SPSS are associated with an increased risk of hepatic decompensation and mortality. SPSS embolization is a potential treatment of HE. It can improve liver perfusion and liver function, provided that liver function is still preserved (MELD score ≤ 11). However, in patients with a MELD score ≥ 15 , it is associated with increased mortality. For those with a MELD score of 11-15, careful patient selection is recommended. SPSS embolization can exacerbate PHT. Strategies to mitigate this include distal splenic artery embolization (dSAE) and proximal proximal splenic artery embolization (pSAE). dSAE reduces splenic vein outflow by inducing partial splenic infarction. Alternatively, pSAE lowers perfusion pressure while maintaining splenic blood flow through collaterals. pSAE less often leads to splenic infarction and subsequent infection as compared to dSAE. Combining SPSS closure with dSAE has been shown to decrease both HVPG and HE, but for pSAE and SPSS no previous cases have been described yet. For this case, pSAE was preferred over dSAE because of lower risk of splenic infarction. The procedure resulted in a significant decrease in PHT. Splenic infarction unfortunately occurred, probably due to altered vascular anatomy after BPD. The cause of recurrent infection, however, remains unclear. Possibly splenic infarction resulted in infection of the spleen. Infection however recurred after splenectomy. Another hypothesis is that initial remnant liver function before embolization was borderline (MELD 13), resulting in hepatic decompensation and increased vulnerability to infection.

Conclusion: In patients with therapy-refractory HE with SPSS, at risk of portal hypertensive complications, combining SPSS closure with a procedure to reduce PHT may be beneficial. This case highlights the potential of combining SPSS closure and pSAE to effectively reduce HE and HVPG, enabling cessation of anti-encephalopathic therapy and lowering paracentesis frequency. However, altered vascular anatomy can lead to complications such as splenic infarction. Despite this, a combined approach involving SPSS closure and pSAE can be a safe and effective strategy for selected patients. However further investigation is warranted.

- C07 -

SYSTEMIC MANIFESTATIONS OF MPOX PRESENTING AS MYOCARDITIS AND PROCTITIS: A CASE REPORT. J. Bekaert (1), A. Meuwissen (2), D. De Geyter (3), B. Vanmechelen (3), M. Surmont (4) / [1] Vrije Universiteit Brussel

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A 30-year-old man presented to the emergency department with retrosternal chest pain radiating to his left arm. His vital signs were normal, and he didn't report any fever. His medical history was unremarkable, though he was on Pre-exposure Prophylaxis (PrEP) as a man who has sex with men (MSM). He reported recreational drug use the previous day, specifically "poppers" and 3-methylmethcathinon (3MMC). Electrocardiography revealed ST-segment elevation in the anterior precordial leads. Cardiac markers were elevated, with troponin at 0.314 µg/L and creatine kinase at 242 U/L. Inflammatory markers were also mildly raised, including CRP at 40 mg/L and leukocytosis with a left shift. Urgent coronary angiography showed normal coronary arteries, and a follow-up transthoracic echocardiogram demonstrated no akinesia, pericardial effusion, or valvular abnormalities. A provisional diagnosis of myocarditis was made. Aspirin was initiated, and the patient was admitted for observation, a viral and autoimmune panel was taken to investigate potential causes of myocarditis. During four days of hospitalization, the patient developed severe, progressively worsening anal pain, without associated bleeding, mucus discharge, or changes in bowel habits. A urethral swab tested positive for gonorrhoea, and he was treated with a single intramuscular dose of ceftriaxone and a one-week course of oral doxycycline. Examination revealed a small posterior acute anal fissure, for which diltiazem ointment was prescribed. The patient was discharged but returned the following day due to worsening anal pain and new perianal nodules. Examination revealed two small pustules on the forearms and multiple clustered pustules in the perianal area. A digital anorectal examination was deferred due to the patient's pain. Swabs were taken in order to test for herpes and Mpox (formerly monkeypox), with Mpox Clade II confirmed as positive. Conservative management was initiated, focusing primarily on pain relief. An MRI of the heart was performed after a few weeks, which did not show any sequelae. Retrospective testing revealed no autoimmune or other viral pathogens to explain his perimyocarditis, leading us to suspect Mpox as the most evident underlying cause of his cardiac symptoms. In 95% of cases, the clinical presentation of Mpox typically begins with systemic prodromal symptoms, followed by the appearance of lesions within 7 days, as seen in this patient. Myocarditis has been reported as a systemic manifestation of Mpox in the literature. [1] Although vaccination offers approximately 80% protection, the patient was still infected, and vaccination did not prevent the development of systemic manifestations. Conclusion: Mpox is not limited to 2022; it continues to circulate and presents with typical symptoms, including severe anal pain, often preceding the appearance of lesions. This should be considered, especially when proctological examination findings do not correlate with severe pain, particularly in patients with risk factors such as young MSM, those with multiple sexual partners, or those engaging in chemsex, who are at increased risk for sexual transmissible infections. [2]

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- C08 -

AN UNUSUAL CASE OF SECONDARY ACHALASIA IN A PATIENT WITH KNOWN CARDIOMYOPATHY. S. Peeters (1), M. Van der Merwe (2), L. Debels (1), S. Kindt (1) / [1] UZ Brussel, Brussels, Belgium, Gastroenterology and Hepatology, [2] UZ Brussel, Brussels, Belgium, Internal Medicine.

Introduction: Chagas disease is an endemic, infectious disease caused by the protozoan parasite *Trypanosoma cruzi*. In the acute phase, symptoms are absent or mild and non-specific (1). However, during the chronic phase (1 to 3 decades after infection) the major manifestations are cardiomyopathy and digestive disorders (1,2). Once the disease becomes chronic, there are no established treatment guidelines, and therapeutic options become limited.

Case presentation: A 64-year-old woman of South American origin, with a history of Chagas-related cardiomyopathy, was admitted to the emergency room with epigastric pain and nausea for 3 days. Acalculous cholecystitis was the preliminary diagnosis based on ultrasound findings. In the absence of elevated inflammatory parameters and fever, additional testing was performed. Upper GI endoscopy revealed erythematous gastritis with multiple erosions and a normal but slightly tortuous appearance of the oesophagus. Biopsies were positive for *H. Pylori* but showed no abnormalities of the oesophagus. Eradication therapy was initiated and was successful. The patient, however, remained symptomatic reporting dysphagia for both solids and fluids. Additional oesophageal manometry and a barium oesophagram were compatible with achalasia type II. Endoscopic treatment by peroral endoscopic myotomy (POEM) is scheduled.

Discussion: An estimated 6–7 million people worldwide are infected with *T. cruzi* (1). In the acute phase, treatment with

antitrypanosomal drugs such as benznidazole and nifurtimox is effective. Chronic disease is characterised by cardiac involvement in up to a third of patients and digestive, neurological or mixed alterations in one tenth of cases (1,2,3). The digestive form consists of alterations in the motor, secretory, and absorptive functions of the gastrointestinal system, due to the destruction of enteric neurons in the submucosal and myenteric plexuses, mainly involving the oesophagus and the distal colon (4). This most frequently results in mega-oesophagus or megacolon (3,4). Oesophageal dysfunction from damage of the myenteric plexus manifests as secondary oesophageal achalasia. Treatment options remain limited to those of idiopathic achalasia, and consist of dietary and behavioural changes, POEM, pneumatic dilation of the lower oesophageal sphincter, laparoscopic Heller myotomy and oesophagectomy (4). This decision should be based on clinical presentation and severity. Treatment remains challenging but the real difficulty lies in the diagnosis. The World Health Organization recognised Chagas disease as a neglected tropical disease in 2005 with an underdiagnosis of up to 70% (1,5). Increased migration from Latin America to Europe will lead to this disease entity becoming more and more relevant to our routine practice with an estimated 1.8-2.8% of migrants being carriers (5). Future goals should include a standardised screening program for early diagnosis and treatment to avoid chronic complications (5,6).

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- C09 -

CELIAC DISEASE AND PORTAL HYPERTENSION: AN INTRICATE INTERPLAY. V. De Smet (1), L. Verset (2), M. Hodoul (3), J. Mulkay (4), T. Sersté (4) / [1] UZ Brussel, Brussels, Belgium, Department of Gastroenterology and Hepatology, [2] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Pathology, [3] CHU Saint-Pierre, Brussels, Belgium, Department of Radiology, [4] CHU Saint-Pierre, Brussels, Belgium, Department of Gastro-Enterology and Hepatology.

A 51-year-old male patient presented to the outpatient clinic of CHU Saint-Pierre, Brussels, with chronic diarrhoea since several years. The patient, an undocumented immigrant from Northern Africa, had been residing in Belgium for several months. His personal medical history was unclear, but an old medical report disclosed a potential coeliac disease with a poor compliance to regimen. He was not taking any prescribed medications and denied the use of alcohol, recreational drugs, substances, or herbal remedies. He also denied any history of upper gastrointestinal (GI) bleeding. The physical examination was normal, except for a BMI of 18.03. Blood tests revealed thrombocytopenia with a platelet count of $71 \times 10^3/\mu\text{L}$, elevated AST and ALT (49 IU/L and 63 IU/L, respectively), and iron deficiency without anaemia (TfSat 9%, ferritin 67 $\mu\text{g/L}$). HBsAg and HCV serologies were negative. Abdominal ultrasound showed signs of portal hypertension, including splenomegaly and peri-pancreatic collateral veins. More importantly, a complete portal vein thrombosis (PVT) and a large cavernoma were diagnosed. His ultrasound showed no signs of cirrhosis (no nodular aspect of the liver surface), focal lesions, or ascites. A complete thrombophilia work-up, including antiphospholipid antibodies, was normal. Upper GI endoscopy revealed the presence of grade III oesophageal varices, gastroesophageal varices (GOV) type 1 and type 2 and portal hypertensive gastropathy. Additionally, duodenal mucosal atrophy was observed. The patient tested positive for anti-gliadin IgG (191 U/mL) and anti-transglutaminase IgA (2951 U/mL) antibodies, and duodenal biopsies confirmed subtotal villous atrophy with a moderate increase in intraepithelial lymphocytes (Marsh IIIB), confirming the diagnosis of coeliac disease. A CT scan confirmed the presence of portal hypertension with splenomegaly and collateral veins, as well as the presence of the portal cavernoma associated with dilatation of the intra- and extrahepatic bile ducts. His Fibroscan® revealed a low liver stiffness (7.2 kPa) with no evidence of steatosis. A haemodynamic evaluation with measurement of the hepatic venous pressure gradient (HVPG) was performed and a liver biopsy was taken. The HVPG was measured at 3mmHg, consistent with the PVT. Pathological analysis of the liver biopsy disclosed a normal liver in the absence of significant fibrosis with reticulin staining being highly suggestive of nodular regenerative hyperplasia (NRH). Thus, a diagnosis of porto-sinusoidal vascular disorder (PSVD) with NRH and cavernoma was established in the context of coeliac disease. The patient was started on a gluten-free diet and an upper GI haemorrhage prophylaxis with non-selective beta-blockers was given. The chronic diarrhoea improved quickly.

UNEXPECTED CULPRIT: CONSTIPATION AND MESENTERIC CYSTS UNVEIL ABDOMINAL MYCOBACTERIUM BOVIS IN A YOUNG IMMIGRANT. K. Demeyer (1), L. Debels (1), D. De Geyter (2), S. Kindt (1) / [1] UZ Brussel, Brussels, Belgium, Gastroenterology & Hepatology, [2] UZ Brussel, Brussels, Belgium, Microbiology.

Introduction: *Mycobacterium bovis* (*M. bovis*), a member of the *Mycobacterium tuberculosis* complex, is predominantly transmitted through the consumption of products contaminated with bovine milk or via direct contact with infected cattle. Global epidemiological data demonstrates marked geographic heterogeneity in prevalence with elevated incidence rates observed in lower-income nations, exceeding 10% of all tuberculosis cases. The organism's primary route of transmission typically results in extrapulmonary tuberculosis, including abdominal involvement, distinguishing it from other *M. tuberculosis* complex members and limiting human-to-human transmission.

Case Presentation: A 20-year-old male Somali immigrant, with no prior medical comorbidities, initially consulted at an external medical facility with constipation, managed conservatively with laxatives. Over the following three weeks, the patient developed constitutional symptoms including pyrexia, anorexia and emesis. Upon presentation to the emergency department, the patient was admitted to the gastroenterology unit with a preliminary diagnosis of infected duplication cyst. Despite broad-spectrum antimicrobial therapy, the patient demonstrated no clinical improvement. A subsequent non-invasive diagnostic workup suggested an abdominal *M. tuberculosis* infection, which was ultimately confirmed via diagnostic laparoscopy revealing characteristic miliary peritoneal involvement. Both polymerase chain reaction (PCR) and culture results were positive for *M. tuberculosis* complex. Initial quadruple anti-tuberculosis therapy was initiated. However, subsequent molecular analysis at the reference laboratory (Sciensano) identified pyrazinamide resistance and confirmed the presence of *M. bovis*. Following these results, pyrazinamide was discontinued, and the treatment protocol was modified to a triple-drug regimen with an intended duration of nine months. Unfortunately, longitudinal follow-up was precluded due to the patient's visa application status.

Discussion: *M. bovis* represents an infrequent pathogen in high-income nations, often contributing to diagnostic delays, suboptimal antimicrobial selection, and inferior clinical outcomes. Global epidemiological data likely underestimate its true prevalence due to insufficient surveillance in endemic low-income regions and the requirement for molecular diagnostic techniques for species differentiation. A retrospective analysis of microbiological data from UZ Brussel (2014-2024) identified 13 *M. bovis* cases, constituting 6% of all registered *M. tuberculosis* complex isolates. The diagnosis of abdominal *M. bovis* infection presents significant challenges due to its heterogeneous clinical presentation and site-dependent manifestations. Neither clinical features nor radiological findings reliably differentiate between *M. tuberculosis* complex subspecies.

Conclusion: Diagnostic evaluations of extrapulmonary tuberculosis must systematically incorporate *M. bovis* assessment, particularly patient populations with specific risk factors (foreign-born, immunocompromised hosts, travel history to endemic regions, or documented pyrazinamide resistance).

ENDOMETRIOSIS IN DISGUISE: MYXOID LESIONS MASQUERADING AS LYMPHANGIOMA. A. Fahad (1), J. Noel (2), M. Zalcmán (3), M. Fastrez (4), A. Cremer (1) / [1] Erasme University Hospital, Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Erasme University Hospital, Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pathology, [3] Erasme University Hospital, Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Radiology, [4] Erasme University Hospital, Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gynaecology.

We report the case of a 49-year-old woman who presented to the outpatient clinic with a history of persistent right lower quadrant abdominal pain, bloating, and dyspepsia. The patient reported no fever, nausea, vomiting, or gynaecological symptoms and denied significant changes in bowel habits apart from two daily loose stools without blood. Her medical history was notable for fibromyalgia, hepatic steatosis, multinodular goitre, and sacroiliitis. Initial imaging in December 2018, prompted by her symptoms, revealed a 16 cm cystic abdominal mass with heterogeneous content. A subsequent CT scan confirmed the mass measured 17 × 16 × 11 cm. The cyst wall was thin and slightly irregular, with entirely liquid content and no evidence of internal septa. The lesion displaced intestinal loops without apparent continuity with surrounding organs, suggesting a peritoneal origin. Laboratory tests were unremarkable, except for slightly elevated CA 125 levels (78 U/mL, with a normal range <35 U/mL). The presumed diagnosis was cystic lymphangioma. Surgical intervention was recommended but declined several times by the patient, who instead underwent fluid drainage, which provided temporary symptom relief. Over the following years, the mass recurred, leading to worsening abdominal pain and the development of new symptoms, including diarrhoea. Imaging and laboratory results in 2023 revealed the persistence of the mass without any new alarming features. Despite two drainage procedures yielding thick, brownish fluid (2.9 L and 1.5 L), diagnostic uncertainty persisted. Cytological analysis revealed fibrin, erythrocytes, macrophages, and lymphocytes, consistent with a hematoma. Bacteriological analysis was negative, and cytology was

inconclusive. Ultimately, the patient consented to an exploratory laparotomy. Macroscopic examination revealed a 12 × 9 × 4.5 cm heterogeneous mass with cystic and haemorrhagic components. Histopathological analysis revealed irregular, inactive endometrial glands surrounded by myxoid stroma, consistent with myxoid endometriosis. This rare form of endometriosis, characterized by atypical histological features and a resemblance to malignancy, presented a significant diagnostic challenge, requiring careful correlation of clinical, radiological, and pathological findings for definitive diagnosis. The patient was referred to the gynaecology team and started on dienogest therapy, which led to substantial symptom improvement. This case underscores the importance of considering rare presentations of endometriosis, such as myxoid endometriosis, in the differential diagnosis of complex abdominal masses. It also highlights the necessity of a multidisciplinary approach to ensure accurate diagnosis and effective management.

- C12 -

DON'T ALWAYS JUDGE A LESION BY ITS COVER. G. Rasschaert (1), Q. Wu (1), O. Plomteux (2), F. Van Herpe (1), N. Bletard (3), P. Leclercq (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] Clinique MontLégia, CHC Groupe Santé, Liège, Belgium, Gastroenterology, [3] Clinique MontLégia, CHC Groupe Santé, Liège, Belgium, Pathology.

A trained endoscopist experienced in optical diagnosis can often make an accurate risk assessment for colorectal cancer (CRC) and invasion before attempting an endoscopic resection. This assessment is based upon the appearance of the lesion: like the diameter and a plethora of validated scoring systems like the Kudo classification of pit patterns, the Paris classification, Japan NBI Expert Team (JNET) classification and others.

We report the case of a 54-year-old man with Lynch syndrome, carrying a germline MLH1 mutation. He had a history of an extended right hemicolectomy for a pT4N1M0 CRC back in 2015. The endoscopic surveillance showed no lesion in 2016. In 2017 a millimetric tubular adenoma with low-grade dysplasia (TA-LGD) was resected. In 2019 two left-sided millimetric hyperplastic lesions were resected. However, in 2021 a lesion was observed in the sigmoid, estimated 10mm in diameter, optically assessed as both flat and elevated with a central depression, thus type 0-IIa+0-IIc according to the Paris classification. A diagnostic biopsy disclosed a TA-LGD on pathology reporting. An endoscopic full-thickness resection (eFTR) was attempted shortly after. No complications appeared during and after the procedure. The patient was discharged the same day. The pathology reporting of this eFTR specimen confirmed the previous diagnosis of a TA-LGD of about 10 mm. However, a mucinous submucosal adenocarcinoma with muscularis propria involvement of about 16 mm in diameter was found buried underneath both the TA-LGD region and the normal colonic mucosa disconnected from it. It was an R0 resection, classified as pT2. A CT thorax-abdomen was negative for distant metastases. After discussion with the patient, no further surgery was undertaken seen the history. The patient is well and alive and continues his regular follow up today.

This case demonstrates the usefulness of eFTR; an eventual other type of endoscopic resection might have compromised the outcome of this atypical case. Next, we emphasize that an optical diagnosis, even in expert hands and even with confirmed pathology diagnosis of a premalignant entity can still hold an unpleasant surprise underneath. On the other hand, the mucinous pathological character of the tumour here, with large mucin pools observed on H&E, might have made the lesion look bigger at this point in its natural disease course.

TO DINE OR NOT TO DINE: THE EFFECT OF A DAY-BEFORE LOW-FIBER DINNER ON BOWEL CLEANSING PRIOR TO COLONOSCOPY (DINNER1006 TRIAL). P. Sinonquel (1), I. Demedts (1), C. Camps (2), A. Luybaerts (2), H. Willekens (2), P. Roelandt (1), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, GI endoscopy trial centre.

Introduction: Bowel cleansing prior to colonoscopy is crucial to facilitate a high-quality colonoscopy. Current strict dietary restrictions may add an extra burden, potentially affecting patient compliance.

Aim: This study evaluates whether allowing a low-fiber dinner 2 hours prior to bowel cleansing the day before the colonoscopy affects bowel preparation quality and enhances patient experience.

Methods: This single-centre, prospective, investigator-blinded randomized controlled trial includes 525 patients who underwent bowel cleansing using a split-dose poly-ethylene glycol (PEG) regimen (NER1006, Norgine) taken the evening (6 or 8 pm) before and 5 hours before the colonoscopy. Participants were randomly assigned (1:1) to either a standard low-fiber regimen without or with dinner allowed up to 2 hours before the start of the bowel cleansing the day prior to colonoscopy. The primary endpoint assessed adequate bowel preparation (BBPS ≥ 6 , with no segmental score of 1 or 0) in both groups. The study also evaluated endoscopy quality through polyp (PDR), adenoma (ADR), advanced adenoma (aADR), and sessile serrated lesion (SDR) detection rates. Abdominal adverse events and patients' tolerance were evaluated via survey.

Results: Adequate bowel cleansing did not differ significantly between the control and interventional groups, with 247 of 262 (94.3%) and 248 of 263 (94.3%) patients achieving this outcome ($p > 0.9999$), respectively. Optimal bowel cleansing (BBPS 8-9) was achieved in 219 of 262 controls (83.6%; 95% CI: 0.807–0.864) and 214 of 263 patients following a lenient diet (81.4%; 95% CI: 0.767–0.861) ($p = 0.5662$). No significant differences were observed in quality metrics, with PDR at $68.7 \pm 5.6\%$ vs. $67.3 \pm 5.7\%$ ($p = 0.9097$), ADR at $46.6 \pm 6.0\%$ vs. $48.3 \pm 6.0\%$ ($p = 0.9296$), aADR at $14.1 \pm 4.2\%$ vs. $15.2 \pm 4.3\%$ ($p = 0.8743$), and SDR at $10.3 \pm 3.6\%$ vs. $9.9 \pm 3.6\%$ ($p = 0.7952$). Per-procedural abdominal complaints were comparable with $74.4 \pm 5.3\%$ vs. $72.2 \pm 5.4\%$ ($p = 0.7663$) of patients with maximum one event reported in the control vs interventional arm. Patients' experience and tolerance did not significantly differ between the control and interventional arm (regimen acceptability of $82.7 \pm 2.3\%$ vs $76.7 \pm 2.6\%$, $p = 0.4622$).

Conclusions: Allowing patients a more lenient dietary regime with a low-fiber dinner up to 2 hours before the start of the bowel cleansing the day before colonoscopy, does not significantly affect the adequacy of the bowel cleansing with a split-dose PEG regimen 12 and 5 hours before the procedure. Other endoscopy quality metrics and patient tolerance remain high.

A SELECTIVE RESECTION ALGORITHM FOR BARRETT'S NEOPLASIA OPTIMIZES ONCOLOGICAL OUTCOMES. S. Gupta (1), A. Bucalau (2), F. Vito Mandarino (1), B. Lam (1), M. Figueiredo Ferreira (2), P. Eisendrath (2), G. Losurdo (2), A. Sakiris (1), J. Gauci (1), A. Whitfield (1), O. Cronin (1), T. O'Sullivan (1), C. Kerrison (1), N. Shahidi (1), E. Lee (1), J. Devière (2), N. Burgess (1), A. Lemmers (2), M. Bourke (1) / [1] Westmead Hospital, Sydney, Australia, Department of Gastroenterology and Hepatology, [2] HUB Hôpital Erasme, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Introduction: Accepted oncological principles advise en-bloc, R0, excision of cancer to achieve a curative resection. In Barrett's neoplasia, this includes T1a and superficial-T1b disease. Treatment options include endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Recent data re-stratify the oncologic risk of high risk T1a, low and high risk T1b, with close endoscopic monitoring of those patients instead of surgical resection. Moreover, recent data confirm that endoscopists ability to optically discriminate between T1a and T1b disease lacks sensitivity. Altogether, the appropriate resection technique selection has not been described or validated

Aim: We conducted a prospective multi-centre observational study to evaluate the performance of a selective resection algorithm (SRA) for Barrett's neoplasia.

Methods: To achieve an en-bloc resection, ESD was selected if there was a suspicion for $\geq T1a$ disease and the lesion was >15 mm (January 2017 to April 2024). This was compared with a historical approach (HA), where ESD was only performed in cases suspicious for deep submucosal invasion (February 2013 to December 2016). The study was performed in two tertiary referral centres in Australia and Belgium.

Results: A total of 581 resections were performed in 542 patients. Median age was 70 (IQR 63-77) years. Median lesion size was 20 mm (IQR 10-30). Median Prague classification was C2 (IQR 0-6) M4 (IQR 2-8). EMR was performed in 354 (60.9%) and ESD in 227 (39.1%). ESD took longer (101.5 ± 54.9 mins) than EMR (41.6 ± 18.2 mins; $P < 0.001$). The

HA and SRA cohorts consisted of 189 (32.5%) and 392 (67.5%) resections, respectively. In the HA cohort, there were 170 EMR (89.9%) and 19 ESD (10.1%), and in the SRA cohort, there were 184 EMR (46.9%) and 208 ESD (53.1%). Histology was T1a adenocarcinoma in 177 (30.5%) and T1b in 94 (16.2%). For T1a disease, en-bloc resection (SRA 110 [83.3%] vs HA 22 [48.9%]; $P<0.001$), R0 excision (SRA 91 [68.9%] vs HA 17 [37.8%]; $P<0.001$) and curative resection (SRA 77 [58.3%] vs HA 14 [31.1%]; $P=0.002$) were higher in the SRA cohort. For T1b disease, en-bloc resection (SRA 70 [95.9%] vs. HA 9 [42.9%]; $P<0.001$), R0 excision (SRA 52 [71.2%] vs HA 2 [9.5%]; $P<0.001$) and curative resection (SRA 20 [27.4%] vs HA 0 [0%]; $P=0.005$) were higher in the SRA cohort. In the SRA cohort, the proportion of patients undergoing EMR for T1a and T1b disease was significantly lower than the HA cohort (T1a: 43 [32.6%] vs. 38 [84.4%], $P<0.001$, and T1b: 3 [4.1%] vs. 14 [66.7%]; $P<0.001$). Specifically in EMR groups, for T1a disease, the rates of en-bloc resection (SRA 23 [53.5%] vs HA 15 [39.5%], $P=0.207$), R0 excision (SRA 12 [27.9%] vs HA 11 [28.9%], $P=0.917$) and curative resection (SRA 9 [20.9%] vs. HA 10 [26.3%] $P=0.568$) were low but similar between both groups. There was no difference in recurrence (SRA 10 [23.2%] vs HA 7 [18.4%]; $P=0.594$). For T1b disease, the rate of en-bloc resection (SRA 1 [33.3%] vs HA 2 [14.3%], $P=0.465$) were similar between both groups. None of the cases were an R0 excision or curative resection. There was no difference in recurrence (SRA 2 [66.7%] vs HA 2 [14.3%]; $P=0.121$). With adoption of the selective resection algorithm, the proportion of ESD increased from 7.5% to 71.9% of cases annually. Among all T1a and T1b-SM1 cases with favourable histology, which underwent ESD, 86/99 (86.9%) were curative resections.

Conclusions: Our selective resection algorithm for Barrett's neoplasia performed better than the historical cohort utilizing a EMR-predominant approach, particularly pertaining to R0 excision and curative resection rates. We propose to change the recommendations by adopting ESD for neoplastic lesions ≥ 15 mm. This can be readily adopted by experienced endoscopists to facilitate resection planning and improve patients' outcomes.

- G03 -

CLINICAL IMPACT OF THE MISMATCH BETWEEN OPTICAL DIAGNOSIS AND HISTOLOGY: A POST-HOC SUB-ANALYSIS OF THE CAD-ARTIPOD TRIAL. P. Sinonquel (1), T. Eelbode (2), O. Pech (3), D. De Wulf (4), P. Dewint (5), H. Neumann (6), G. Antonelli (7), F. Iacopini (7), D. Tate (8), A. Lemmers (9), N. Pilonis (10), M. Kaminski (10), P. Roelandt (1), C. Hassan (11), I. Demedts (1), G. De Hertogh (12), F. Maes (2), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Electrical Engineering (ESAT/PSI), [3] Krankenhaus Barmhertzige Brüder, Regensburg, Germany, Gastroenterology and Hepatology, [4] AZ Delta, Belgium, Gastroenterology and Hepatology, [5] AZ Damiaan, Oostende, Belgium, Gastroenterology and Hepatology, [6] Gastrozentrum Lippe, Bad Salzuflen, Germany, Gastroenterology and Hepatology, [7] Ospedale del Castelli, Rome, Italy, Gastroenterology and Hepatology, [8] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and Hepatology, [9] CUB Hôpital Erasme, Belgium, Gastroenterology and Hepatology, [10] Centrum Onkologii-Instytut im Marii Skłodowskiej, Warsaw, Poland, Gastroenterology and Hepatology, [11] IRCCS Humanitas Research Hospital, Milan, Italy, Gastroenterology and Hepatology, [12] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Guidelines indicate that optical diagnosis can be employed during endoscopy for a leave-in-situ or resect-and-discard strategy of diminutive polyps. Additionally, it aids in determining the appropriate techniques for polyp resection.

Aim: Our objective was to assess the accuracy and the clinical impact of real-life optical diagnosis during real-time colonoscopy conducted in the context of a CAdE trial.

Methods: In this post-hoc sub-analysis we retrospectively compared optical diagnosis with histology results of 1608 polyps that were prospectively included in the CAD-ARTIPOD trial (NCT04442607). During CAD-ARTIPOD endoscopists (ADR 20-50%) provided optical diagnosis, polyps were resected, and histological examination was performed by two independent GI histopathologists. Mismatch was defined as a difference in polyp type (hyperplastic (HP) vs tubular adenoma (TA) vs tubulovillous adenoma (TVA) vs sessile serrated lesion (SSL) vs pseudopolyp vs carcinoma vs no polyp) or a difference in grade of dysplasia (high grade vs low grade vs no dysplasia). Clinical impact on surveillance interval per patient was consecutively evaluated according to ESGE standards.

Results: On a total of 1608 resected and histologically assessed specimens of 946 patients, 1026 (63.8%) showed a match and 582 (36.2%) a mismatch between optical diagnosis and histology. The optical diagnosis was 552 (34.3%) HP, 904 (56.2%) TA, 3 (0.2%) TVA, 119 (7.4%) SSL, 11 (0.7%) carcinoma, 6 (0.4%) inflammatory pseudopolyp and 13 (0.8%) unknown histology. Mismatch was present in 254 (43.6%) HP, 225 (24.9%) TA, 77 (64.7%) SSL, 7 (63.6%) carcinoma and 5 (83.3%) pseudopolyps. Clinical consequences occurred for 48 (8.5%) polyps in as many patients (5.3%), with 12 polyps leading to a prolongation of the surveillance interval and 7 polyps overestimated as carcinomas not truly requiring further treatment. Twenty-nine (4.9%) of the optically misdiagnosed polyps led to a shortened surveillance interval (12 polyps with HGD and 17 as fifth TA) and two (0.3%) required further surgical therapy. Of the 115 misdiagnosed hyperplastic polyps, 74 (64.4%) were left-sided and may have been left in situ when applying SODA criteria with correct optical diagnosis applied.

Conclusions: Even in the setting of a clinical trial with high detectors, where the focus was detection, rather than

optical diagnosis, discordance between optical diagnosis and histology occurred in approximately one out of three polyps. The clinical impact was significant with alterations in clinical management for 8.5% of affected polyps, in 5.3% of patients. This underscores the importance of training in optical diagnoses and the potential role of artificial intelligence to assist in a resect and discard strategy.

- G04 -

OUTCOME ASSESSMENT OF LUMEN-APPOSING METAL STENTS (LAMS) VERSUS DOUBLE PIGTAIL PLASTIC STENTS IN ENDOSCOPIC ULTRASOUND-GUIDED GALLBLADDER DRAINAGE: RESULTS OF A LARGE BICENTRIC RETROSPECTIVE STUDY. Y. Lamani (1), S. Hoibian (2), M. Poiraud (2), J. Ratone (2), Y. Dahel (2), M. Giovannini (2), S. Ouazzani (3), J. Devière (3), P. Eisendrath (3), F. Caillol (2), A. Lemmers (3) / [1] Erasme University Hospital, Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Institut Paoli-Calmettes, Marseille, France, Gastroenterology, [3] Erasme University Hospital, Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

Introduction: Endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) has emerged as a promising option in patients presenting with cholecystitis, deemed unfit for laparoscopic cholecystectomy. Since its inception, this technique has undergone significant evolution, incorporating alternative stent types such as double pigtail plastic stents (DPPS) and lumen-apposing metal stents (LAMS). Despite the increasing use of LAMS, there is limited comparative data on the efficacy and safety of LAMS versus DPPS in EUS-GBD. Existing studies often lack the robust evidence needed to inform clinical decision-making, with recommendations frequently based on low-quality data.

Aim: This study aims to fill this gap by comparing the clinical and technical outcomes of LAMS and DPPS. By analysing data from two expert centres, we seek to provide comprehensive insights that could refine procedural strategies and improve patient outcomes in EUS-guided gallbladder drainage.

Methods: We conducted a bicentric retrospective study on patients considered unfit for surgery by an experienced surgeon, presenting with acute cholecystitis. This study reviewed prospectively collected registries of all patients who underwent EUS-GBD using LAMS or DPPS between 2012 and 2023 at two European tertiary care centres. Primary outcomes included technical and clinical success (defined as symptom resolution 15 days post-intervention), and adverse events (using AGREE classification). Secondary outcomes were the reintervention rate, length of hospital stay, and 30-day mortality. Statistical non-parametric tests or Chi-square tests were used for comparisons and Kaplan-Meier analysis for survival and time-to-reintervention outcomes.

Results: Among the 55 patients included (66.7% men, median age 68 years (IQR, 55-81), 37 and 18 were treated with LAMS and DPPS, respectively. Technical success was similar with 97.3% in the LAMS group and 94.4% in the DPPS group ($p = 1.00$). No difference in clinical success was observed (78.4% for LAMS and 66.7% for DPPS ($p = 0.542$)). Adverse events within 30 days (AGREE classification 1–5) were also similar, with a rate of 31.4% for LAMS and 38.9% for DPPS ($p = 0.610$). There was no statistically significant difference in the occurrence of postprocedural peritonitis (16.7% LAMS vs. 8.3% DPPS, $p=0.388$) or in 30-day mortality (20% LAMS vs. 27.8% DPPS, $p=0.378$). However, the incidence of post-procedural septicaemia was significantly higher in the DPPS group (38.9% for DPPS vs. 8.3% for LAMS), without any impact on the post-intervention length of hospital stay (6 vs 7 days, $p = 0.478$). In terms of delayed complications (beyond 30 days), there was no difference in recurrent acute cholecystitis (9.4% for LAMS vs 11.1% for DPPS; $p = 1.00$), stent migration (3.7% for LAMS vs 11.8% for DPPS; $p = 0.549$), patency rates (88.9% for LAMS vs 82.4% for DPPS; $p = 0.662$), with similar reintervention rates (29.4% for LAMS vs 38.9% for DPPS; $p=0.54$).

Conclusions: This bicentric retrospective study is the first and largest to evaluate LAMS vs DPPS in EUS-GBD. The results are similar in terms of technical and clinical success, adverse events, and reintervention rates. We only observed a higher risk of postprocedural septicaemia in the DDPS group, without any impact on the postprocedural length of hospital stay. Given the cost difference between the two stent types, our findings challenge current recommendations for systematically favoring LAMS in this context.

- G05 -

PREDICTORS OF CLINICAL SUCCESS IN EUS-GUIDED DRAINAGE OF POSTOPERATIVE PANCREATIC FLUID COLLECTIONS. H. Hellinckx (1), M. Bronswijk (2), G. Vanella (3), H. Peeters (1), M. Noreillie (1), F. Frigo (3), R. Leone (3), H. van Malenstein (1), W. Laleman (1), R. Voermans (4), P. Arcidiacono (3), R. van Wanrooij (4), S. van der Merwe (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology and Hepatology, [3] Vita Salute San Raffaele University, Milan, Italy, Pancreatobiliary Endoscopy and Endosonography Division, [4] Amsterdam UMC, Amsterdam, The Netherlands, Gastroenterology and Hepatology.

Introduction: There has been a shift from percutaneous drainage towards endoscopic ultrasound (EUS)-guided

drainage for management of post-operative pancreatic fluid collections (POAFC). However, available series have been limited by sample size, and little is known about the factors that may influence clinical success.

Aim: Our aim was to evaluate the outcomes of EUS-guided drainage of postoperative collections following pancreatic surgery and identify predictors of clinical success.

Methods: We performed a retrospective review of patients who underwent EUS-guided drainage of POAFC between 2014 and August 2024 at three academic centres. Patients with a history of non-pancreatic surgery were excluded. LAMS or double pigtail plastic stents (DPPS) were used at the discretion of the endoscopist. Primary outcome was clinical success, defined as the complete radiological regression of the collection and resolution of symptoms without the need for additional drainage procedures. Secondary outcomes were technical success, defined as successful stent placement, and adverse events (based on the AGREE classification).

Results: In total, 270 cases were included (mean age 63 [SD±13.9] years, male 58%). Early drainage (≤14 days) was performed in 51% of cases (n=138). The most common reasons for surgery were pancreatic ductal adenocarcinoma (34.7%), NET (20.7%) and cholangiocarcinoma (6.3%). Majority of patients had a recent history of either pylorus-resecting pancreatoduodenectomy or distal pancreatectomy with splenectomy (35.9% and 33.7% respectively). DPPS were used in 213 cases (78.9%), whereas LAMS were used in 42 cases (15.6%). Clinical success with a single EUS drainage procedure was achieved in 163 cases (60%). Step-up interventions were required in 25.6% of patients (n=69). Of these, 41 cases required endoscopic revision only, with an overall median number of reinterventions of 0 (IQR 0-1, mean 0.42 [SD±0.95]). Technical success was achieved in 90% (n=243). Adverse events occurred in 46 cases (17%), with 3 cases requiring surgery (grade IIIB, 1%). When comparing LAMS and DPPS, a shorter median time to clinical success (60.5 vs. 160 days, p=0.018) was seen in the LAMS group, as well as a trend towards a higher reintervention rate (39% vs. 23%, p=0.055). After a median follow-up of 608 days (IQR 273-1126) recurrence rates were similar (9% vs. 2%, p=0.807). Univariate analysis did not reveal any major predictors of clinical success, including LAMS vs. DPPS (OR 0.61 [95% CI: 0.29-1.29], p=0.193), early vs. late drainage (OR 0.87 [95% CI: 0.53-1.41], p=0.565), splenectomy vs. no splenectomy (OR 0.92 [95% CI 0.55-1.53], p=0.752) or duodenal vs. transgastric route (OR 1.05 [95% CI: 0.25-4.50], p=0.947).

Conclusions: EUS-guided drainage of POAFC was effective in the majority of cases with a single procedure. No major predictors of clinical success were identified. When reintervention was required, a single endoscopic reintervention was sufficient in 54% of cases. These results further support the use of EUS-guided drainage for the management of postoperative collections.

- G06 -

ENDOSCOPIC ULTRASOUND-GUIDED BYPASS REVERSAL IN PATIENTS WITH ROUX-EN-Y GASTRIC BYPASS AND POSTPRANDIAL REACTIVE HYPOGLYCAEMIC SYNDROME: PROMISING INTERIM RESULTS OF A PROSPECTIVE PROOF-OF-CONCEPT STUDY. E. Gökce (1), B. Lapauw (2), C. Verroken (2), P. Hindryckx (1) / [1] University Hospital of Ghent, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospital of Ghent, Belgium, Department of Endocrinology.

Introduction: Postprandial reactive hypoglycaemic syndrome (PPRHS) is a common complication of Roux-en-Y gastric bypass (RYGB) surgery. A surgical bypass reversal is proposed to severe refractory cases but could lead to recurrence of obesity and the related health issues. Endoscopic ultrasound (EUS)-assisted placement of a large-diameter lumen-apposing metal stent (LAMS) between the stomach pouch and the excluded stomach has emerged as a promising minimally invasive alternative to surgical reversal.

Aim: We aim to investigate whether the creation of an EUS-guided gastro-gastrostomy using a large-diameter LAMS is an effective alternative to surgery in RYGB patients with invalidating PPRHS refractory to conservative treatment.

Methods: This is an interim analysis of a prospective proof-of-concept study in RYGB patients with severe PPRHS. After informed consent, they undergo EUS-assisted placement of a LAMS with a luminal diameter of 20 mm and a saddle length of 10 mm between the gastric pouch and the excluded stomach. Prospective follow-up is foreseen for 1 year. The main outcomes of interest are technical success, clinical success, and adverse events. Technical success is defined as the successful placement of the LAMS in the desired position. Clinical success is defined as resolution of PPRHS-related symptoms as reported by patients. Quality of life (QoL) before and after treatment is assessed with a visual analogue scale (VAS). The AGREE classification is used to grade adverse events.

Results: This interim analysis includes data from 6 RYGB patients (all women, mean age 44 years [range 34-56], mean BMI 22 [range 18-28]) with a median follow-up of 211 days [range 68-365 days]. Technical success was achieved in all patients, with a mean procedural duration of 18 minutes [range 10-38]. All patients could be discharged from the hospital the same day. Clinical success was seen in 5/6 patients, with a fast resolution of PPRHS-related symptoms and an associated improvement in QoL. One patient did not respond to the treatment and is currently under investigation to rule out other causes of hypoglycaemia. Adverse events occurred in 3 of the 6 patients (50%), all classified as minor. Two patients experienced temporary mild abdominal discomfort. One patient experienced an increase in reflux-associated symptoms, well-controlled by proton pump inhibitors. Importantly, the mean weight gain during follow-up was only 0.8 kg (range -3 to 4 kg).

Conclusions: EUS-guided LAMS placement between the stomach pouch and the excluded stomach appears to be a promising minimally invasive alternative to surgical gastric bypass reversal in RYGB patients with severely invalidating PPRHS. Interim analysis shows high technical and clinical success rates, without serious adverse events or significant weight gain.

- G07 -

INCIDENCE AND RISK FACTORS FOR DELAYED COMPLICATIONS (BLEEDING, PERFORATION AND ELECTROCOAGULATION SYNDROME) FOLLOWING ENDOSCOPIC SUBMUCOSAL DISSECTION: STUDY OF THE POTENTIAL PLACE FOR PREVENTIVE ENDOSCOPIC METHODS. P. El Nawar (1), V. Huberty (1), A. Bucalau (1), M. Figueiredo Ferreira (1), A. Lemmers (1) / [1] Hôpital Erasme, ULB, Belgium, Gastroenterology.

Introduction: Although technically challenging, endoscopic submucosal dissection (ESD) has been safely developed in Europe. New endoscopic methods are emerging to prevent delayed complications, such as delayed bleeding (DB), delayed perforation (DP) and post-ESD electrocoagulation syndrome (PEECS).

Aim: The aim of this study was to identify the incidence and the risk factors (RF) for the development of these complications to assess the potential place for preventive endoscopic methods.

Methods: This monocentric retrospective study was performed in a tertiary European centre, based on a systematic registry of prospectively collected cases treated by ESD from June 2015 to September 2024. To avoid confounding elements, cases with per-procedural perforation were excluded. No patient had any attempt to close the defect at the end of the ESD. Data on the follow-up (haemoglobin drop, pain and inflammatory syndrome, bleeding, transfusion, readmission, endoscopic haemostasis, surgery, death) were systematically collected in our hospital files and in the network of Belgian hospitals up to 30 days from the ESD. The primary outcome was the incidence of DC. Secondary outcomes were the risk factors of DC. Statistical analysis was performed using descriptive statistics, Kaplan-Meier for time from ESD to DC, univariate and multivariate analyses to identify predictive factors of DC.

Results: Of the 541 ESDs, 54 were excluded due to the need to place clips for per-procedural perforation or muscular tears. Among the remaining 487 cases (median age 67.76 ± 11.56 yo, male 61.4%, women 38.6%), 53% were performed in the upper GI (170 oesophageal, 85 gastric and 4 duodenal ESDs) and 47% in the lower GI (45 colonic and 183 rectal ESDs). A total of 19 patients (3.9%) developed DC (17 DB, one DP, one PEECS) within 30 days of ESD. Among DB, 7 happened in upper GI ESD (3 oesophagus, 4 stomach) and 10 in lower GI ESD (2 colon, 8 rectum). Although rare, DB is the most frequent complication of ESD, affecting only 3.5% (17/487) of patients in our cohort. Of these 17 patients, all cases of DB occurred within the first 14 days. 10 patients resumed antithrombotic therapy after ESD (59%) and 7 had no antithrombotic treatment (41%). Multivariate analysis showed that the predictive risk factors of a DB were oral anticoagulant ($p < 0.001$) and P2Y12 inhibitor ($p < 0.001$) use. DP and PEECS were virtual in our experience.

Conclusions: Our experience is associated with rare delayed post-ESD complications, accounting for only 3.9% of patients. DB is the most frequent complication, mainly in the population resuming antithrombotic therapy after ESD. Evidence and guidelines are needed to adjust the timeframe for resuming antithrombotic after ESD. Measures such as closure of the resection site or the use of haemostatic gels need to be assessed in high-risk patients, while assessing their cost-benefit balance.

- G08 -

CAN ARTIFICIAL INTELLIGENCE IDENTIFY HISTOLOGICAL SUBCLASSES OF HYPERPLASTIC POLYPS BASED ON THEIR ENDOSCOPIC FEATURES? A. Jans (1), B. Callaerts (2), P. Sinonquel (1), X. Sagaert (3), I. Demedts (1), P. Roelandt (1), T. Eelbode (2), F. Maes (2), S. Tejpar (1), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Department of Electrical Engineering (ESAT/PSI), [3] KUL - University of Leuven, Leuven, Belgium, Department of Pathology.

Introduction: Recent insights in polyp molecular biology have suggested that hyperplastic polyps (HP) are closely related to sessile serrated lesions (SSL). Their hallmark serrated crypts closely resemble those found in SSL. Furthermore, similar to SSL, specific subtypes of HP can harbour BRAFV600E-mutations. These findings, amongst others, have raised the hypothesis that some HP may have an intrinsic malignant potential through the serrated neoplasia pathway. However, in everyday clinical practice, no routine HP subdifferentiation is performed.

Aim: We aimed to develop a deep learning algorithm to classify molecular subclasses of HP, namely microvesicular hyperplastic polyps (MVHP) and goblet cell-rich hyperplastic polyps (GCHP), based on their endoscopic features.

Methods: In this single-centre trial 238 hyperplastic polyps from 159 patients were retrospectively selected. All polyps had high quality endoscopic video in white light endoscopy and virtual chromoendoscopy (i-scan) using Pentax EC38-i20c and EC34-i10 endoscopes. All histological slides were reviewed by an expert pathologist, updating diagnoses to MVHP, GCHP or mixed HP. We selected the polyps without mixed constitution for development of a deep learning

algorithm. These polyps were randomly split into 70% for training, 10% for validation and 20% for testing. Sequences of still images of the polyps were manually annotated and subsequently used to train a deep learning algorithm, with dataset imbalance addressed by randomly oversampling the MVHP.

Results: The 238 HPs were reclassified as 152 GCHP, 59 MVHP and 27 mixed HPs after expert histological review. We subsequently trained a convolutional neural network on the 211 HPs without mixed constitution. This resulted in a model with an AUC of 0.817, corresponding to a sensitivity of 80.0% for predicting MVHP and 78.4% for predicting GCHP. However, due to the low prevalence of MVHP (28%) the positive predictive value for MVHP is only 33.3%, whilst the positive predictive value for GCHP is 96.7%.

Conclusions: We successfully developed a deep learning algorithm capable of differentiating between molecular subclasses of hyperplastic polyps (MVHP vs GCHP) based on their endoscopic features. This model demonstrated a robust AUC of 81.7% with a sensitivity of 80.0% and 78.4% for predicting MVHP and GCHP respectively. However, the low prevalence of MVHP (28%) limited its positive predictive value (33.3%) for predicting MVHP. Despite these challenges, this pilot study serves as a proof of concept that artificial intelligence is capable of predicting hyperplastic polyp subclasses based on endoscopic appearance. Furthermore, it highlights the potential of artificial intelligence to enhance the diagnostic precision, which could contribute to more tailored surveillance and management strategies in the future.

- G09 -

UPDATE ON THE EFFICACY AND SAFETY OF ESD IN BARRETT'S ESOPHAGUS OVER THE LAST 5 YEARS.

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Introduction: Endoscopic submucosal dissection (ESD) is currently considered the treatment of choice for superficial Barrett's oesophageal tumours larger than 15 mm. However, there is a risk of complications such as perforation, bleeding and stricture. In our last study published in 2015, the risk of oesophageal stricture reached 60 % of patients.

Aim: The study aimed to evaluate the effectiveness of endoscopic treatment, and its risk of complications.

Methods: We reviewed the last 100 consecutive patients undergoing ESD for superficial Barrett's esophageal tumours (05/2017-12/2023), in a prospective database of Barrett's endoscopic treatment (Cliniques universitaires Saint-Luc). We analysed demographic, procedure, pathology, admission length, complication data.

Results: Eighty percent of patients were men with a mean age of 67y, and BMI 28.6kg/m². The mean Barrett's oesophagus size was C3 M5 (0-21), and tumour size 22 mm (15-40). Prior histological diagnosis revealed high-grade dysplasia in 58 patients and adenocarcinoma in 42 patients. Twenty-six (26%) patients had previously undergone endoscopic treatment, such as endoscopic mucosal resection (EMR) and/or radiofrequency ablation (RFA), or surgery (n=5). Resection was performed with the Dualknife in most cases, with a mean resection time of 90 minutes (18-250), en-bloc in all patients. Haemostasis was performed with a hot biopsy forceps in 29 patients and clips (1-5) in 51 patients. The specimen size was 43 mm (14-88), mean circumference was 56% (20-100), with free deep margins in all patients. Final diagnosis was adenocarcinoma in 80pts, HGD in 17 and LGD in 3 pts. The resection was not considered curative in a total of 14 patients (11 patients presented sm2 histological grade, and 14 patients lymphovascular infiltration), and further treatment discussed at MDT. There were no cases of perforation, 3 cases of bleeding required additional endoscopic haemostatic treatment, 1 patient requiring 24h of intensive care, no mortality. The mean hospitalization time was 2.2 days (2-8). Steroids were used to prevent stenosis in 18 patients (18%): 3 with local triamcinolone injection (2 combined with budesonide), 12 with systemic steroids (1 combined with budesonide), and 3 with budesonide alone, the decision left to the discretion of the endoscopist. During endoscopic follow-up, 13 strictures (13%) occurred, all treated endoscopically by balloon dilation, with a first dilation time of 5 weeks (3-12), a mean of 2.9 sessions (1-9), and reaching an of 15.9 mm (15-18). No complications related to endoscopic dilation of the strictures were reported.

Conclusions: ESD for superficial Barrett's tumours may now be considered as an effective and safe technique with a stricture rate of 13%, lower than previously published.

Reference: Chevaux, Jean-Baptiste; Piessevaux, Hubert; Mourin, Anne; Yeung, Chun-Ping Ralph; Danse, Etienne; Deprez PH. Clinical outcome in patients treated with endoscopic submucosal dissection for superficial Barrett's neoplasia. Endoscopy 2015, 47:103-112.

- G10 -

EFFICACY AND SAFETY OF A GEL HEMOSTATIC POWDER (GHP) IN PREVENTING DELAYED BLEEDING AFTER ENDOSCOPIC RESECTION (ER) IN HIGH-RISK PATIENTS: A MULTICENTRIC PROSPECTIVE STUDY.

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Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are widely used to remove neoplastic lesions in the gastrointestinal tract, offering organ preservation and reducing morbidity. However, delayed bleeding (DB) is a common complication, especially in patients needing to resume anticoagulant or antithrombotic therapy. This study evaluates the efficacy and safety of a new gel haemostatic powder (GHP) (Nexpowder™) in preventing DB after EMR or ESD in high-risk patients.

Aim: The study aimed to determine whether applying the GHP at the end of ER can reduce the DB rate compared to the literature-reported mean 16% rate to less than 5% in high-risk patients undergoing EMR or ESD for lesions ≥ 20 mm.

Methods: A prospective, multicentric, open-label study was conducted at seven Belgian hospitals from September 2023 to June 2024. A sample size of 50 patients was computed using statistical test based on the data provided in different cohorts of the literature. Patients with indications of endoscopic resection for (1) upper or lower GI lesions ≥ 20 mm, either on anticoagulant or anti-P2Y12 therapy, or (2) duodenal EMR even without antithrombotic therapy, were enrolled prospectively in all participating centres. The GHP was applied at the end of the procedure to cover the entire resection field. The primary endpoint was the rate of DB within four weeks post-procedure, DB was defined as clinical bleeding or haemoglobin drop of ≥ 2 g/dL. Secondary endpoints included the safety profile of GHP, the duration of the endoscopic procedure and GHP spraying duration, the length of hospital stay, post-procedural pain, and the incidence of adverse events. Kaplan-Meier curves analysed the probability of bleeding over time, and Cox regression identified factors influencing bleeding risk. Data were prospectively collected in an anonymized e-CRF. The study protocol was registered under the number NCT06096948 (clinicaltrials.gov).

Results: Fifty patients (74% male, median age 73 (IQR 66-79)) were effectively enrolled and treated by endoscopic resection (46% by ESD, 54% by EMR) and GHP application at the end of the resection. 60% resumed anticoagulants and 8% anti-P2Y12 therapy after the ER procedure, with a median of 5 days for anticoagulants (NOAC) and 7 days for anti-P2Y12 therapy. Lesion location was distributed as follows: duodenum (40%), colon (20%), oesophagus (18%), stomach (12%) and rectum (10%); with a median maximal size of 30mm (IQR 20-40mm). Among them, 22% (11/50) experienced DB. This complication was most frequently observed for rectal ESD (3/5, 60%) and duodenal EMR (6/19; 30%). DB typically occurred within the first 10 days post-procedure, with a median onset on day 7 (3/11 (27%) patients experienced DB on day 7). A full 100% covering of the resection field by the GHP was achieved in 84% of the cases with no post-procedural bleeding and in 73% of the cases that experienced bleeding ($p=0.3$). Perprocedural bleeding and attempt to close the defect did not significantly influence the delayed bleeding outcomes. The hypothesized reduction in DB from a mean 16% rate (extracted from the literature focussed on high-risk patients after ER) to below 5% was not achieved ($p=0.2472$). On univariate analysis, the only factor associated with DB risk was the lesion size ($p=0.042$). Comparing our DB rates after GHP application by organ stratification (duodenum 30%, colorectum 26.7%, stomach 16.7%) to the reported literature (without GHP application), we observed similar rates with no organ-specific effect. The secondary outcomes of the study showed that pain levels were minimal, with median scores of 0.0 across all patients. The median hospital stay was 1 day, with no significant difference between the bleeding and non-bleeding groups. The duration of GHP application was longer in the bleeding group but did not reach statistical significance. No significant association was found between adverse events and delayed bleeding, and no adverse events related to GHP were reported.

Conclusions: In our prospective study involving high-risk patients, applying GHP following endoscopic resection did not significantly lower the rate of DB, with the observed rate reaching 22%. Lesion size was a key predictor of DB. Further studies are needed to find optimal preventive treatment after endoscopic resection.

- G11 -

RISK FACTORS FOR POST-ERCP INFECTION, INDICATIONS FOR SINGLE-USE DUODENOSCOPES AND COST-BENEFIT ANALYSIS OF THEIR USE. M. Lucion (1), V. Putzeys (2), D. Blero (1), H. Piessevaux (1), P. Deprez (1) / [1] UCLouvain, Cliniques Universitaires St Luc, Belgium, Hepatogastroenterology, [2] Hospital CHR de la Citadelle, Liège, Belgium, Hepatogastroenterology.

Introduction: Epidemics of multi-resistant infections transmitted by reusable duodenoscopes have led to the development of single use duodenoscopes (SUDs). The use of SUDs, now proven to be effective and safe, nevertheless remains economically and ecologically costly, while the real incidence and cost of these duodenoscope-associated infections (DAI) remain unclear.

Aim: The aim of our study was, firstly, to determine the indications for single-use duodenoscope (SUD) based on a large cohort of patients who had undergone ERCP with a reusable duodenoscope, and secondly, to calculate the cost-benefit balance for SUD use in different ERCP practice scenarios.

Methods: We conducted a retrospective longitudinal study including all ERCPs performed in an academic and in a non-academic centre between July 1, 2021 and June 30, 2022, based on a prospective registry. Potential risk factors for post-ERCP infections, infectious data, and technical data were recorded at inclusion. Post-ERCP infection was defined as any infection occurring within 30 days of ERCP, in the absence of a more likely infectious aetiology and of pre-ERCP infection. Type of infection, AGREE classification, pre- and post-ERCP length of stay, germ type and its antibiogram, and duodenoscope serial number were also recorded. A link between germ type, duodenoscope serial number, and ERCP date was sought. Extra-cost of post-ERCP infections was calculated on the basis of hospital bills. Following different incidences of duodenoscope-associated infections (DAI), the first scenario envisaged SUD use for all patients at risk of infection, while the second scenario envisaged SUD use only for MDRO-carrying or -infected patients.

Results: In these 654 ERCPs, including 539 academic and 115 non-academic procedures, 14 patients were MDRO-carriers or -infected. 54 post-ERCP infections were identified, while a germ was found in 23 of these. Most of the germs (n=27) were gram-negative bacteria (n=22), with different antibiograms. Two cases of Vancomycin-Resistant Enterococci septicaemia were observed, while no Pseudomonas infections were detected. Multivariate analysis showed that the presence of a Klatskin tumour, haematological disease, chemotherapy, and benign biliary stricture were significantly associated with post-ERCP infection. Considering HIV, Covid and MDRO-carriers or -infected patients, the total theoretical indications for SUD use was 37.8% of all ERCPs. However, no correlation could be seen between germ type and antibiogram in pre- or post-ERCP infection and the duodenoscope serial number, nor according to ERCP date. The cost-benefit analysis showed that the acceptable additional cost of using SUD compared with using reusable duodenoscope ranged from €50 to €2,923, varying considerably according to the prevalence of patients at high risk of infection and MDRO-carriers or -infected patients, and DAI incidence.

Conclusions: We found no correlation in favour of a DAI in our cohort. Based on risk criterias for post-ERCP infection, indication rate for SUD is 37.8%. Cost-benefit analysis showed that the "acceptable" additional cost of SUD-use varied considerably. Assuming a MDRO carriage of 2.14% and a 1% DAI incidence, the acceptable extra cost of SUD use would be around €2046.

- G12 -

EUS-GUIDED GALLBLADDER DRAINAGE FOR ACUTE CHOLECYSTITIS IN THE WESTERN WORLD: EXPLORING HETEROGENEITY IN CURRENT PRACTICE AND THE RELATION WITH PATIENT OUTCOME. L. De Wispelaere (1), H. Degroote (2), T. Billiet (3), C. Snauwaert (4), D. De Wulf (5), E. De Volder (5), L. D'Souza (6), A. Siddiqui (7), M. Bronswijk (8), S. van der Merme (8), R. Voermans (9), P. Hindryckx (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [2] Vrije Universiteit Brussel (VUB), Jette, Belgium, Gastroenterology, [3] AZ Groeninge, Kortrijk, Belgium, Gastroenterology, [4] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology, [5] AZ Delta, Belgium, Gastroenterology, [6] Stony Brook University Hospital, New York, United States, Gastroenterology, [7] Inova Fairfax Hospital, Falls Church, United States, Gastroenterology, [8] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [9] Amsterdam UMC, Amsterdam, The Netherlands, Gastroenterology.

Introduction: Endoscopic ultrasound guided gallbladder drainage (EUS-GBD) with lumen-apposing metal stents (LAMSs) is a well-accepted treatment option for acute cholecystitis in patients who are not (immediately) suitable for surgery. However, little is known on the optimal algorithm after LAMS placement, which may be influenced by prognosis of the patient and potential future operability.

Aim: The aim of the study is to examine heterogeneity in patient profiles and treatment protocols for EUS-GBD in Western countries, and to assess the relation to patient outcome.

Methods: An international multicentre retrospective cohort study at 18 institutions in Europe, the United States of America and Canada is currently conducted. All consecutive patients (> 18 years) who underwent EUS-guided gallbladder drainage with LAMS for acute cholecystitis are included. Demographic, medical, procedural and outcome data are captured in a predefined data extraction file. Adverse events (AEs) are graded following the AGREE classification (endoscopy-related AEs) and the Clavien Dindo classification (surgery-related AEs).

Results: At the moment of abstract submission, only preliminary data from 4/18 centres were available for analysis. Sixty-two patients were included, with a follow-up period of 165 days (median, range 1-1241 days). The vast majority (56/62, 90.3%) of LAMS placements were performed from within the duodenum using a 10/10 or a 15/10 size (52/62; 83.9%). In the majority of cases (37/62; 59.7%), a coaxial stent (DPPS) was placed. The technical success rate of EUS-GBD was high (60/62; 96.8%). In 59/62 (95.2%) patients, clinical and biochemical improvement was observed after a median of 2 days (range: 1-10 days). Patients were discharged from the hospital after a median of 8 days (range: 1-129 days). AEs were observed in 17/62 patients (27.4%, 5 AGREE II, 8 AGREE IIIa and 1 AGREE V). Six AEs (9.7%) were related to recurrence of biliary disease, all in the patient group treated for calculous cholecystitis and with incomplete gallbladder stone clearance. Only 3 AEs (4.8%) were LAMS-related adverse events: 1 lumen occlusion by food, 1 lumen occlusion by a stone and 1 perforation with the tip of device through the contralateral gallbladder wall. Seven patients (11.3%) received EUS-GBD as bridge to future surgery. In all patients, the LAMS was removed and

exchanged to double pigtailed, if possible. Two patients have not yet received cholecystectomy at the time of writing. Four cholecystectomies were performed laparoscopically. One patient received laparotomy because of a need for concomitant surgical ampullectomy. Adverse events after cholecystectomy were seen in 3/5 cases (60%) but none of them could be linked to the previous EUS-GBD.

Conclusions: This preliminary analysis of an ongoing international multicentre retrospective cohort study confirms that EUS-GBD is an effective treatment option for acute cholecystitis in patients that are temporally or permanently unfit for surgery, with an acceptable safety profile and a low rate of biliary disease. The completion of this large multicentre cohort study will likely provide further insights into the optimal protocol for EUS-GBD in different patient settings (e.g. bridge to surgery or non-fit for future surgery, poor or better prognosis,...).

- G13 -

IMPACT OF COMBINED AUDIOVISUAL INFORMATION COMPARED WITH VERBAL INFORMATION ALONE PRIOR TO UPPER GASTROINTESTINAL ENDOSCOPY ON PATIENT COMFORT AND ANXIETY: A RANDOMIZED CONTROLLED TRIAL. S. Zaouga (1), E. Salma (1), S. Ben Hamida (1), H. Elloumi (1), I. Cheikh (1) / [1] Habib Bougatfa Hospital, Tunisia, Gastroenterology.

Introduction: Oesophagogastroduodenoscopy is gold standard procedure for detecting upper gastrointestinal disorders. However, little is known about how to most effectively deliver relevant information to patients scheduled for endoscopy.

Aim: The aim of our study was to assess the effects of audiovisual information compared with oral information alone on the levels of anxiety before and after the procedure, tolerance and the quality of information.

Methods: We conducted a prospective study in Both Habib Bougatfa University hospital and Military hospital of Bizerte which enrolled consecutive patients scheduled for endoscopy over a month period. Patients were randomized either to receiving, an explanatory video about the upcoming examination, or oral information delivered by each patient's doctor. Evaluation of quality of information was rated on scales between 0 (none received) and 10 (excellent). Evaluation of anxiety was performed by the STAI-Y questionnaire. Tolerance of the procedure was rated on a scale between 0 to 4 : 0 if the patient was still throughout the procedures, may retch at intubation; 1: when minimal retching <25% of procedure time; 2: when frequent retching >25% of procedure time; 3: when the patient attempts to handle and/or remove gastroscope; 4: if the patient extubates themselves or withdraws consent. The analysis of outcome variables was performed by Spss Version 26.

Results: Our study included 40 patients with a female-to-male sex ratio of 1.8, comprising 20 patients who received only verbal information (Group 1) and 20 who received audiovisual information (Group 2). The mean age of participants was 46.2 ± 12 years. Both groups were comparable in terms of age, gender, comorbidities, and educational level. In Group 1, the mean pre-procedure STAI score was 47, decreasing to 34.7 after the procedure. The overall evaluation of the quality of information was 5.17. Regarding tolerance, 6 patients (30%) had a tolerance score <2, while 14 patients (70%) had a score ≥ 2 . In Group 2, the mean pre-procedure STAI score was 45, dropping to 30 after the procedure. The overall evaluation of the quality of information was 7.9. Regarding tolerance, 15 patients (75%) had a tolerance score <2, while 5 patients (25%) had a score ≥ 2 . Patients who received audiovisual information reported lower pre-endoscopic anxiety levels than those who received only verbal information, although this difference was not statistically significant (mean STAI score for Group 1: 47 vs. Group 2: 45, $p = 0.6$). However, the reduction in post-procedure STAI scores compared to pre-endoscopic values was more significant in the group that received audiovisual information (12 points vs. 16 points, $p < 0.01$). Tolerance during the examination was better in patients who received audiovisual information (Group 1: 1.7 vs. Group 2: 1.1, $p = 0.05$). Additionally, the relevance of the information was rated higher in the group receiving audiovisual information, with a statistically significant difference ($p < 0.001$).

Conclusions: Audiovisual information led to more favourable assessments of the quality of information and had an impact on patient anxiety and on the overall assessment of the endoscopy. Because structured and comprehensive audiovisual information is perceived as beneficial by patients, gastroenterologists should consider using it as a daily basis.

- G14 -

THE CLINICAL VALIDATION OF A COMPUTER-AIDED POLYP DETECTION MODEL INTEGRATED AS A PLUG-AND-PLAY ENDOSCOPY DEVICE (ALTER-EGO TRIAL). P. Sinonquel (1), D. De Wulf (2), D. Tate (3), D. Wyffels (4), T. Eelbode (5), B. Callaerts (5), C. Camps (6), H. Willekens (6), A. Luypaerts (6), F. Maes (5), E. D'Agostino (4), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] AZ Delta, Belgium, Gastroenterology and Hepatology, [3] University Hospital Ghent (UZ Gent), Ghent, Belgium, Gastroenterology and Hepatology, [4] Easics, Leuven, Belgium, R&D, [5] KUL - University of Leuven, Leuven, Belgium, Electrical Engineering (ESAT/PSI), [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, GI endoscopy trial centre.

Introduction: The development of a computer-aided detection (CAdE) model into a clinically reliable plug-and-play device is a complex and challenging process.

Aim: This study evaluates the performance, stability, and robustness of a new all-in-one plug-and-play device, integrated with a previously in-house developed and clinically validated AI algorithm for colorectal polyp detection.

Methods: The ALTER-EGO trial is an investigator-initiated operator blinded multicentre trial conducted in 3 Belgian centres. The AI model performing real-time polyp detection during real-time endoscopy was developed using deep learning on a high-resource/cost graphics processing unit (GPU)-based hardware platform and validated to achieve enhanced adenoma detection. The model was integrated into a lower-cost/resource field-programmable gate array (FPGA)-based hardware device, necessitating implementation adjustments and retraining to account for technological differences between both platforms. The new FPGA-based CAdE system was evaluated in the exact same study set-up as the original GPU-based system, using a second observer and real-time unblinding. We evaluated the number of polyps detected, the extra detection and miss rates in comparison to expert endoscopists and performed analysis of false positive rate and technical failures to reflect system stability. Sample size analysis calculated 660 polyps required for non-inferiority analysis (margin 5%) with the original validation outcomes (CAdE sensitivity 0.946 +/- 0.03).

Results: A total of 843 polyps were identified in 291 patients, of which 776 (92.1%) were detected by both endoscopist and CAdE, 41 (4.8%) were detected by endoscopist alone, 26 (3.1%) were solely detected by CAdE. Sensitivity of the CAdE was 95.1% (95%CI: 93.6-96.6) versus 96.6% (95%CI: 95.7-98.1) for the expert endoscopists. In comparison to the original GPU-based CAdE system, detection was non-inferior with a $\Delta 0.005$ (95%CI: -0.04487 – 0.0548) ($p=0.02$) and margin at 5%. Due to hardware-related adjustments, false positive rate increased from 1.7 to 8.8 per minute ($p<0.001$). Technical failure occurred in 49 patients; 109 events of technical deficiencies were reported.

Conclusions: Integration of an originally GPU-based AI model into a FPGA-based plug-and-play hardware device resulted in stable performances, non-inferior to the GPU-based algorithm. The required technical adjustments of the FPGA-based algorithm however resulted in a significantly higher false positive rate and increased number of technical failures.

- G15 -

ACETIC ACID CHROMOENDOSCOPY: A SIMPLE, CHEAP, EFFECTIVE AND EFFICIENT TOOL TO IMPROVE THE VISIBILITY AND DELINEATION OF COLONIC SESSILE SERRATED POLYPS IN DAILY PRACTICE. S. Arnaert (1), A. Billiet (1), M. Cool (1), G. Lambrecht (1), M. Tresinie (1), S. Van Avermaet (1), D. Persyn (1), P. Dewint (1), G. Deboever (1) / [1] AZ Oostende, Oostende, Belgium, Gastroenterology.

Introduction: Post-colonoscopy colorectal cancer (PCCR) remains a significant problem despite better detection tools, and accounts for 3-9% of all colorectal cancers. Missed lesions and incomplete removed polyps account for the majority of PCCR. Especially the detection and delineation of sessile serrated lesions (SSLs) remains a challenge in daily clinical practice. In academic settings, it has been shown that acetic acid (AA) might improve the visualization of SSL. Interestingly, this new technique has not penetrated our daily clinical practice.

Aim: To investigate whether AA might be an efficacious and user-friendly tool in daily practice for better delineation of SSL in a non-academic, peripheral centre.

Methods: AA, in different concentrations, was sprayed on SSLs, which were detected with light endoscopy. All colonoscopies were performed with High-Definition endoscopes. Most of the colonoscopies were performed water-aided in unsedated or minimally sedated patients. Different AA concentrations were made by diluting commercially available AA (7%) with NaCl 0.9%. After cleansing the SSLs with the water jet, AA was injected with a syringe of 10 or 20 ml through the biopsy channel of the endoscope. The patient turned into the position that optimised contact of the AA solution with the surface of the polyp.

Results: The study included 40 patients with SSLs. All SSLs were situated in the right colon. Lower concentration of AA (0.7%) induced less visible demarcation of the borders and a lower whitening effect in the SSLs than a concentration of 1.4%. After staining, the polyp surface and borders were examined with High-Definition White Light (HD WL) and Narrow Band Imaging (NBI). The whitening effect quickly appeared within 5-10 seconds and the SSLs remained stained for 2-3 minutes. The normal surrounding mucosa also became whiter, but clearly less than the polyps, and the whitening disappeared quickly, usually within a minute. The use of AA extended the total procedure time by only 30 sec. There were no secondary effects nor immediate or late complications.

Conclusions: AA chromoendoscopy on colonic SSLs induces a concentration-dependent whitening that optimises the visibility of the polyps and their delineation. AA chromoendoscopy is easy to apply through the biopsy channel, cheap, safe, universally available and only minimally prolongs the procedure time. Future research should define the place of systemic irrigation of the proximal colon in order to improve detection and delineation of SSLs (thereby decreasing the PCCR in daily routine colonoscopies).

- G16 -

ARTIFICIAL INTELLIGENCE-BASED ASSESSMENT OF ENDOSCOPIC TIP-CONTROL CORRELATES WITH HUMAN SUBJECTIVE IMPRESSION IN A SIMULATION ENVIRONMENT. T. Tornai (1), L. Debels (2), M.

Argenziano (1), L. Desomer (3), M. Montori (1), P. Poortmans (1), A. Sorge (1), S. Smeets (1), D. Tate (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Dienst Gastro-enterologie en Hepatologie, [2] UZ Brussel, Brussels, Belgium, Dienst Gastro-enterologie en Hepatologie, [3] AZ Delta, Belgium, Campus Rumbeke, Roeselare Dienst Gastro-enterologie en Hepatologie.

Introduction: The quality of tip manipulation in endoscopy (tip-control) is akin to hand steadiness in surgery where correlation with surgical complications and morbidity is established. The subjective opinion of tip-control given by blinded human raters can accurately classify endoscopy provider profile and therapeutic experience. However, to remain unbiased, videos must be read by multiple human observers in a blinded environment adding time, cost and a delay to obtaining results.

Aim: We aimed to train an artificial intelligence (AI) model to assess tip-control and compare its performance to evaluations by blinded human raters on the same endoscopic videos.

Methods: 13 endoscopists applied margin ablation on four shapes two times, printed onto a ham with STSC in an ex-vivo model [1]. Procedural videos were blindly, anonymously, and randomly evaluated 3-times each by a pool of 7 human raters using an online tool. Outcome of ratings was accuracy (%), speed (mm/sec) and subjective tip-control score (%). An AI model was trained on video data to detect the proximity between the endoscope and the printed line (validation accuracy 88.5%). An unsupervised computer vision model analysed motion data, generating variables related to speed, online/offline periods, and motion peaks. We fitted two generalized linear mixed models to predict the subjective tipcontrol score. The first model was based on performance metrics including speed, hit frequency, hit density, and accuracy. The second model utilized twelve AI derived metrics. We selected predictors by ranking all possible combinations using the Akaike Information Criterion, then retained those in the final models that were included in at least 4 out of 5 folds in cross-validation. Model performance was evaluated by comparing predictions to the subjective tip-control ratings using Spearman rank correlation.

Results: Human raters agreed on subjective tip-control scores (intraclass correlation coefficient 0.86 [0.76-0.92]). The performance metric-based model including speed (OR:1.03 [1.01-1.05], $p=0.002$), accuracy (OR:1.07 [1.04-1.09], $p<0.001$) and number of correct hits per minute (OR:1.05 [1.02-1.07], $p<0.001$) predicted subjective tip-control scores with high accuracy ($r=0.88$, [0.83-0.92]). The AI based model included five predictors: number of offline periods (OR:1.01 [1-1.3], $p=0.041$), duration of offline periods (OR: 0.99 [0.99-0.99]), median height of motion speed peaks during offline (OR:1.61 [0.94-2.76], $p=0.082$) and online periods (OR:0.48 [0.2-1.15], $p=0.101$) and median prominence of peaks during simulation (OR: 0.01 [0.001-0.18], $p=0.002$). The model based on AI derived metrics predicted subjective tip-control scores also with good accuracy ($r=0.78$ [0.68-0.84]).

Conclusions: An AI model reliably predicted blinded human rater subjective impression of endoscopist tip-control using a standardized ex-vivo simulator. The AI model was comparable to structured human performance-metric rating which involves significantly more time and effort. The AI approach offers potential real-time, unbiased assessment of endoscopic technical skills.

- G17 -

IMPROVING CELLULAR YIELD DURING ENDOSCOPIC BRUSH SAMPLING IN PATIENTS WITH BARRETT ESOPHAGUS USING A SIMPLE MODIFICATION BY NOT RESHEATHING. M. Wyckmans (1), A. Driessen (2), S. Krishnadath (1) / [1] Antwerp University Hospital, Edegem, Belgium, Gastroenterology, [2] Antwerp University Hospital, Edegem, Belgium, Pathology.

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Introduction: Brush cytology is a technique that allows sampling of broad mucosal areas. It has various gastrointestinal indications such as malignancy, Barrett's oesophagus and *Helicobacter pylori* infection. During endoscopy, the brush bristles exit a protective sheath. After sampling, the bristles retract back into the sheath. While few studies have explored the role of the plastic sheath on cellularity, loss of cellularity during retraction of the sheath is observed in the literature. [1, 2] As diagnostic accuracy depends on cellularity yield, this study investigated whether not retracting the bristles into the sheath is feasible and results in better cellular yield.

Aim: As diagnostic accuracy depends on cellularity yield, this study investigated whether not retracting the bristles into the sheath is feasible and results in better cellular yield.

Methods: Patients undergoing standard-of-care endoscopy were included at the Antwerp University Hospital. Endoscopy was performed by two experienced gastroenterologists. Cellularity results were defined as 'insufficient', 'low', 'moderate' and 'high'. [3] Cellularity results were bundled in two groups 'insufficient-to-low' and 'moderate-to-high' in order to facilitate statistical analysis using Chi-squared test at 95% confidence interval.

Results: A total of fourteen patients with Barrett oesophagus were included during a one-year period with a total of 26 brush samples. Prior diagnoses were 'no dysplasia' in five patients, 'low-grade dysplasia' in two patients,

‘high-grade dysplasia’ in four patients and ‘intramucosal carcinoma’ in three patients. When brush retraction was performed, cellularity was insufficient-to-low in 47.4% (nine brushes) and moderate-to-high in 52.6% (10 brushes). When brush retraction was not performed, cellularity was moderate-to-high in 100% (7 brushes), there were no brushes that yielded insufficient-to-low cellularity. When comparing the two techniques, there is more cellular yield when not retracting ($p = 0.0243$).

Conclusions: This small-scale study points towards better diagnostic performance of brush cytology by not retracting the brush into the sheath after brush sampling during endoscopy. More research is needed to confirm better diagnostic accuracy and whether these findings can be applied for other indications of brush cytology.

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- G18 -

ACCURACY OF THE MUSCLE RETRACTION SIGN FOR DETERMINING DEEP SUBMUCOSAL INVASION DURING ENDOSCOPIC RESECTION OF RECTAL LESIONS. M. Argenziano (1), A. Sorge (2), M. Montori (1), P. Poortmans (1), T. Tornai (1), S. Smeets (1), S. Al-Dury (1), L. Debelts (3), L. Desomer (4), D. Tate (1) / [1] Ghent University Hospital, Ghent, Belgium, Gastrointestinal and liver diseases, [2] University of Milan, Italy, Department of Pathophysiology and Transplantation, [3] UZ Brussel, Brussels, Belgium, Gastrointestinal and liver diseases, [4] AZ Delta, Roeselare, Belgium, Gastroenterology.

Introduction: Accurate assessment of submucosal invasion (SMI) depth is crucial for selecting the appropriate endoscopic resection technique for large non-pedunculated colorectal polyps ≥ 20 mm (LNPCPs). Traditional imaging modalities including magnetic resonance imaging, endoscopic ultrasound and endoscopic imaging alone, often fail to precisely predict SMI depth.

Aim: This study aimed to determine the accuracy of using the pocket detection method (PDM) and identification of the muscle retraction sign (MRS) to detect the presence of deep SMI in rectal LNPCPs.

Methods: Consecutive patients who underwent endoscopic resection of rectal LNPCPs using PDM in a tertiary care centre were prospectively included from August 2023 to October 2024. First a pocket was created under the lesion, with initial directionality targeted towards the area of most disordered vascular pattern. Within the pocket, the presence of the muscle retraction sign (MRS) - defined by an area of submucosa non-staining with indigo carmine combined with the inability to extend the pocket into this area - was used to assess the presence of deep SMI [particularly if this correlated with the position of the detected worst mucosal vascular pattern]. If MRS was absent endoscopic submucosal dissection (ESD) was performed; if present in the distal rectum endoscopic intermuscular dissection (EID) was performed; in the proximal rectum, non-anterior position, knife-assisted full-thickness resection (kFTR) was performed. Deep SMI was defined as $\geq 1000\mu\text{m}$ invasion from the muscularis mucosa at histopathology. Fibrosis was classified according to Matsumoto classification.

Results: 23 patients were included, median lesion size 25 mm (IQR: 20-40). 78.3% were located in the distal rectum and 69.7% on the posterolateral wall. 47.8% of lesions contained JNET 3 vascular pattern. 60.9% of lesions contained a Paris 0-Is component. Grade F1 and F2 fibrosis were present in 17.4% and 4.3% respectively. Deep SMI was confirmed in 47.8% ($n=11$) of lesions. Pocket creation was successful in all 23 LNPCPs with MRS detected in 10/23 (43.5%). The accuracy of MRS for the detection of deep SMI was 78.3%, [95% CI 58.1-90.3], with sensitivity of 72.7% [95% CI 43.4-90.2] and specificity of 83.3% [95% CI 55.2-95.3]. The median time to detection of MRS (where present) was 19.5 minutes (IQR 10-34). 13 ESDs (56.5%) were performed, along with 6 (26.1%) EIDs and 4 (17.4%) kFTRs. The overall R0 rate was 95.6% ($n=22$). When MRS was present, using this finding to guide therapeutic approach led to R0 in 9/10 (90%). When MRS was absent, using ESD to complete resection was successful in 3/3 cases (R0 100%) despite deep SM. (sm2). Intraprocedural bleeding occurred in 47.8% of cases, unintentional intraprocedural perforation in 10% with no cases of clinically significant post-endoscopy bleeding or postprocedural perforation.

Conclusions: The pocket detection method, utilizing the presence of MRS, accurately predicts the presence of deep SMI in rectal LNPCPs. This finding could assist in the selection of optimal resection technique. Specifically, in cases of deep SMI where MRS is absent ESD is likely to achieve R0 resection without resorting to more complex, resource-intensive techniques with higher rates of adverse events.

CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN A LARGE WESTERN COHORT. F. Kungu (1), R. Garces Duran (1), H. Dano (2), R. Yeung (1), C. Snauwaert (1), T. Moreels (1), Y. Deswysen (3), G. Van Ooteghem (4), M. Van Den Eynde (1), H. Piessevaux (1), P. Deprez (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Anatomopathology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Digestive Surgery, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Radiotherapy.

Introduction: Studies on the efficacy and prognosis of superficial oesophageal squamous cell carcinoma are rare in the Western World.

Aim: Our aim was to analyse the results of endoscopic resection combined, if indicated in high-risk endoscopic resections, with surgery or chemoradiotherapy (CRT).

Methods: Retrospective review of a prospective endoscopic database, including demographic data, comorbidities, previous treatments, type and size of lesion, technique of resection, pathological assessment (horizontal and vertical margins, grade of differentiation, lymphovascular invasion), “adjuvant” treatment, relapse rate, treatment of relapses, and final outcome.

Results: 283 lesions (ESD 218, EMR 65) were resected in 208 patients, 64% males, with a history of alcohol in 75%, smoking in 71%, and ENT cancer in 25%. Lesions were located in the upper mid and lower oesophagus in 22, 56, 22% of patients, respectively. Median size of lesion was 25mm (range: 3-100mm), and median circumference of the lesion was 33% (range: 5-100%). Half of the patients (139/283) had a previous treatment (ESD/EMR, CRT). 151 (53%) were $\leq$ m2, 102 (36%) m3-sm1, 30 (10.6%) deeper. The resection was R0 (vertical) in 248 (88%), R0 (horizontal for cancer) in 251 (89%). Lymphovascular invasion was observed in 32 (14%), G3 in 18 lesions (6.4%). R0 and curative resection rates were therefore 87.6% and 44.9%, respectively. Lesions at high risk for recurrence were calculated at 35% (99/283). However local recurrence was observed in only 19/208 patients (9.1%) and distant metastasis in 12/208 patients (5.7%), with a mean follow-up of 56 months (4.7y). Indeed, adjuvant treatment was proposed after MDT to 103 patients and effectively achieved in 58 patients (18 surgery and 40 CRT or immunotherapy). Complications of endoscopic resection were as follows: 1 bleeding (0.3%), 13 perforations (4.6%), 73 strictures (25.8%), and mortality 90 days in 2 patients.

Conclusions: Endoscopic resection for superficial oesophageal squamous cell carcinoma seems a valid proposal in Western countries, with low rates of local recurrence (9.1%), and distant metastases (5.7%), when combined with surgery or CRT after multidisciplinary discussion, in the high-risk resections.

KNIFE-ASSISTED FULL-THICKNESS RESECTION GUIDED BY THE POCKET-DETECTION METHOD FOR POSTERIOR DEEPLY INVASIVE RECTAL CANCER: A NOVEL ENDOSCOPIC APPROACH (WITH VIDEO). M. Argenziano (1), A. Sorge (1), A. Hoorens (2), M. Montori (1), P. Poortmans (1), S. Smeets (1), T. Tornai (1), L. Debelts (3), L. Desomer (4), D. Tate (1) / [1] Ghent University Hospital, Ghent, Belgium, Gastrointestinal and Liver diseases, [2] Ghent University Hospital, Ghent, Belgium, Pathology, [3] UZ Brussel, Brussels, Belgium, Gastroenterology & Hepatology, [4] AZ Delta, Roeselare, Belgium, Gastroenterology.

Introduction: Histologically complete (R0) resection rates using endoscopic submucosal dissection (ESD) for lesions with deep submucosal invasion are suboptimal (62%–64% for Sm 2-3), even in expert centres [1]. Currently available techniques for the local resection of deeply invasive rectal cancer include Transanal Minimally Invasive Surgery (TAMIS), endoscopic device-assisted full-thickness resection (FTRD) [2] and endoscopic intermuscular dissection (EID) [3]. These techniques have limitations in specific situations such as lesion size, location, or poor ability to delineate margins.

Aim: We aimed to evaluate the feasibility of endoscopic knife-assisted full-thickness resection (kFTR) guided by the pocket-detection (PDM) method for deeply invasive rectal cancer.

Methods: Consecutive lesions on the posterior rectal wall with suspicion of deep submucosal invasion on magnification chromoendoscopy and/or magnetic resonance imaging/endoscopic ultrasound were retrospectively included. kFTRs guided by PDM were performed at a tertiary centre for interventional endoscopy, between February and October 2024 by a single operator with extensive experience (>500 ESDs as the first operator). A multidisciplinary team (MDT) discussed the cases and agreed on endoscopic resection due to patient preference or unsuitability for surgery due to comorbidities and/or advanced age. kFTR guided by PDM involved creating a submucosal pocket to detect and isolate the invasive component (muscle-retracting sign), followed by muscularis propria incision and full-thickness resection. A 5-day course of empiric antibiotics was administered to all patients.

Results: Technical success, accuracy of detecting deep submucosal invasion and en-bloc resection rates were 100%. The median procedure time was 141.5 [IQR 123.7-179.5] minutes and the median hospitalization was 1 [IQR 1-7] day. No peri- or post-procedural adverse events occurred. Histopathology showed R1-vertical margin in patient 1 (pT2 adenocarcinoma) and R0 resection in patients 2, 3 and 4 (pT1bsm3) after refinement of the procedure to include a $\geq$ 3mm

muscularis propria margin around the suspected invasive component. There was no recurrence at the first endoscopic follow-up of patients 1, 2 and 4. Patient 3 was sent to surgical low anterior resection due to multiple high-risk histological features. The previous kFTR did not impair surgery (no residual rectal carcinoma and 1/17 positive lymph nodes).

Conclusions: Endoscopic kFTR guided by the PDM may be a feasible organ-preserving treatment for the detection and resection of deeply invasive posterior rectal cancer. Future studies are needed to ascertain whether kFTR could represent a viable alternative to conventional surgical local excision techniques in the rectum.

- G21 -

SAFETY AND FEASIBILITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION IMPLEMENTATION FOR ALL GASTROINTESTINAL TRACT ORGANS IN A EUROPEAN MEDIUM-VOLUME NON-ACADEMIC CENTRE.

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Introduction: Endoscopic submucosal dissection (ESD) is an endoscopic resection technique used for en-bloc removal of dysplastic and early cancerous lesions throughout the gastrointestinal (GI) tract. Compared to snare-based resection techniques, it allows for higher R0 resection rates, better histopathological staging and thus a reduced recurrence risk as well as fewer unnecessary surgeries for lesions with a low risk of recurrence. ESD is now a well-established procedure in developed countries but its implementation across different centres is challenging due to the long and demanding training process associated with a steep learning curve. While indications for gastric, esophageal and rectal lesions are now firmly established, the indications for ESD versus EMR (Endoscopic mucosal resection) for large nonpedunculated colonic polyps are still debated. As the indications for ESD continue to expand and ensuring equitable access to optimal care for all patients remains a priority, the next challenge lies in disseminating ESD practice across different centres and operators with a sufficient case volume, supported by high-quality training programs.

Aim: Our aim was to assess the safety and feasibility of ESD implementation for all GI tract organs in a European medium-volume non-academic centre.

Methods: All ESD performed between December 5, 2022, and November 12, 2024 at the Centre Hospitalier de Wallonie Picarde (CHWAPI) in Tournai, Belgium were included and data regarding patients and lesions characteristics as well as the procedure were retrospectively analysed. There were two endoscopists performing the ESD (either individually or together), both trained by French or Belgian recognized experts in ESD.

Results: During this period, 122 lesions (116 patients) were resected by ESD. There were 62 colic (including 3 ESD/FTRD and 5 ESD/EMR hybrid resections), 37 rectal (including 1 ESD/EMR hybrid and 3 EID resections), 15 oesophageal, and 8 gastric (including 1 ESD/EMR hybrid and 1 EID resections) lesions. The mean age of the patients was 68,7years (range: 36 -94). The mean hospital stay was 1.53 day. Overall en-bloc resection rate was 95% (colon 94%, rectum 97%, oesophagus 100%, stomach 88%), overall R0 resection rate was 85 % (colon 87%, rectum 86%, oesophagus 87 %, stomach 63%), overall curative resection rate was 79,51% (colon 84%, rectum 76 %, oesophagus 80%, stomach 63%). Mean dissection rate was 19.02 mm²/min (colon 18.81, rectum 21.63; oesophagus 15.47; stomach 15.33 mm²/min). Histopathological analysis showed 37,7% of benign or low-grade dysplastic lesions, while the rest (62,3%) presented with high grade dysplasia or carcinoma. Regarding complications, there was no immediate bleeding that led to procedure interruption. There were 3 case of delayed rectal bleeding which were treated endoscopically (overall delayed bleeding rate 2,5 %, rectal bleeding rate 8,1%). There was one late colonic perforation after 3 days which necessitated surgical treatment (overall perforation rate 0,8%, colic perforation rate 1,6%). One rectal ESD was considered a failure, and the resection was completed surgically without any surgical complications.

Conclusions: Consistently with recent literature, our findings align with the ESGE (European Society of Gastrointestinal Endoscopy) recommendations for ESD training with en-bloc resection rates that are > 90%, perforation rate < 3% and < 1% overall need for surgery because of complications. The ideal goal of 80-85% R0 resection rate suggested by the ESGE guidelines was achieved for every site except the stomach which might be explained by the small number of gastric lesions included. In conclusion, we consider the implementation of ESD for all GI tract organs to be feasible and safe in a medium-volume centre with experienced operators, after adequate training with recognized experts. A precise and appropriate selection of lesions is essential to minimize the risks associated with the procedure, especially for colonic lesions. Finally, considering the expanding number of indications for ESD, particularly in the colonic field, the number of trained operators and centres of expertise must increase. However, high-quality and validated training is essential to ensure the quality and safety of procedures.

- G22 -

DELINEATION OF RECURRENCE AMONG NON-EXPERT ENDOSCOPISTS IS LESS ACCURATE THAN EXPERTS BUT IS READILY TRAINABLE BY A SHORT LEARNING INTERVENTION. S. Smeets (1), M. Argenziano (2), P. Poortmans (3), L. Debels (4), M. Montori (2), A. Sorge (5), T. Tornai (3), C. Schoonjans (6), L.

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Introduction: Incorrect decision making regarding the endoscopic resection scar after EMR risks unrecognized residual or recurrent adenoma. Residual or Recurrent Adenoma (RRA) propagating into post-colonoscopy colorectal cancer. Despite expert series suggesting that scar recognition and interrogation are well performed with a high negative predictive value, the performance of non-experts remains unknown.

Aim: We aimed to investigate the diagnostic performance of endoscopic imaging in detecting RRA at an endoscopic resection scar amongst non-experts and the impact of a learning intervention.

Methods: A survey containing 15 paired High-Definition White Light (HD-WL) and virtual chromoendoscopy (VC) images, a learning intervention on detection of RRA (LT), followed by 15 different HD-WL & VC images was circulated to the GIEQs foundation mailing list. Images were selected from a prospective database of surveillance after EMR. For each image the same questions were asked: Is this a resection scar? Is there evidence of RRA? What is your confidence? Demographic data collected included participant number of EMRs performed, current grade and years of experience. Comparisons were made to expert opinion derived at a consensus meeting of the senior authors regarding the appearances of the images using the approach set out in Desomer et al. 2017.

Results: 82 participants completed the survey (response rate: 4.1%) resulting in 2,460 observations. 15 (18.3%) participants were experienced (had performed >100 EMRs ever). The overall accuracy of RRA detection pre-LT was 75.3% (95%CI 73.5-77.2) vs post-LT: 79.5% (95%CI 77.2-82.0, $p = .006$). Specificity was significantly improved after the LT (50.0% [95%CI 44.1-55.4] pre vs 94.0% [95%CI 90.0-98.0] post, $p < .001$). Both accuracy and specificity were significantly higher amongst experienced endoscopists (acc: 83.6%, spec 67.3%) versus inexperienced endoscopists (acc: 74.0% $P < .001$, spec: 46.7% $P < .003$) prior to the LT. Specificity improved in both groups after the LT (experienced 67.3% vs 97.6%, $P < .001$ and inexperienced 46.7% vs 93.5%, $P < .001$). Furthermore, the difference in specificity disappeared after the LT (spec experienced 97.6% vs inexperienced 93.5% $p = .440$). RRA smaller than 10 mm was more likely to be missed (<10mm 77.5%, <5mm 58.9% of missed detections). RRA occupying $\leq 20\%$ of the scar accounted for two-thirds of missed detections (66.4%). RRA located on the edge of a scar (versus centrally) accounted for the vast majority of missed RRA (88.1%).

Conclusions: The accuracy of RRA detection in non-experts is low compared to previously published expert series, even amongst endoscopists performing EMR regularly. Low accuracy predominantly resulted from low specificity, which was mitigated by the training intervention. These results suggest the potential negative effects of missing RRA at an endoscopic resection scar (propagation between surveillance procedures and the potential for development of RRA) can be mitigated by training.

- G23 -

ENDOSCOPIC TREATMENT OF SPHINCTER OF ODDI DYSFUNCTION IN PATIENTS WITH ROUX-EN-Y GASTRIC BYPASS: TECHNICAL AND CLINICAL OUTCOMES. T. Moreels (1), L. Monino (2), P. Deprez (2), H. Piessevaux (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology and Hepatology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology and Hepatology.

Introduction: Sphincter of Oddi dysfunction (SOD) is a common pathology in women who underwent cholecystectomy. It is characterized by typical colic pain of biliary and/or pancreatic origin, in association with disturbed liver and/or pancreatic function tests and with radiological stigmata of poor transpapillary drainage (SOD type I). In SOD type II typical pain is associated with either biochemical or radiological abnormalities and in SOD type III only typical colic pain is present.

Aim: We studied technical and clinical outcomes of endoscopic SOD treatment (biliary and/or pancreatic sphincterotomy) in Roux-en-Y gastric bypass (RYGB) patients.

Methods: Retrospective analysis of a prospective cohort of RYGB patients who underwent ERCP between 2014 and 2024.

Results: A total of 19 patients (17 female, aged 47 ± 3 years) were referred for endoscopic SOD treatment. 84% ($n=16$) had undergone cholecystectomy. Mean time between RYGB surgery and endoscopic SOD treatment was 6 ± 1 y. All patients underwent enteroscopy-assisted endoscopic retrograde cholangiopancreatography (entero-ERCP) using single-balloon enteroscopy, except for 1 case with the motorized spiral enteroscope. In case of technical failure endoscopic ultrasound-guided transgastric ERCP (EDGE) was performed. Technical success as defined by endoscopic sphincterotomy during one-stage entero-ERCP reached 79% ($n=15$) and increased to 90% ($n=17$) with 2 successful multi-stage EDGE procedures. For 2 entero-ERCP failures a wait-and-see approach was conducted. Clinical success as defined by pain relief and biochemical improvement during follow-up was significantly higher (86%) in 14 SOD I patients as compared

to 5 SOD II and III patients (40%, $p=0.046$ Chi-square). There were 2 adverse events related to the ERCP procedure: 1 post-ERCP pancreatitis (AGREE II) and 1 fausse guidewire route during biliary cannulation (AGREE I). There were no serious adverse events.

Conclusions: Entero-ERCP using single-balloon enteroscopy is a very effective and safe procedure to treat RYGB patients suffering from SOD type I. Clinical outcome of endoscopic sphincterotomy in SOD II and III RYGB patients remains questionable.

- G24 -

EUROPEAN CONSENSUS RECOMMENDATIONS FOR DIRECT CHOLANGIOSCOPY AND PANCREATOSCOPY USING A MODIFIED DELPHI PROCESS. E. Göke (1), E. Palmeri (1), S. Stefanovic (2), V. Ascenti (3), A. Anderloni (4), V. Cennamo (5), F. Prat (6), G. Webster (7), D. Joshi (8), J. Potts (9), T. Wong (10), R. Sturgess (11), K. Oppong (12), M. James (13), M. Huggett (14), J. Portal (15), M. Ellrichmann (16), J. Vila (17), I. Fernandez-Urien (18), M. Udd (19), L. Kylänpää (19), W. Laleman (20), J. Poley (21), P. Karagoyozov (22), F. Van der Heide (23), J. Koornstra (24), E. Aljahlili (25), C. Gerges (26), R. Voermans (27), G. Goodchild (28), A. Inderson (29), P. De Jonge (30), S. Crinò (31), M. Bruno (32), D. David (32), P. Hindryckx (33) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology, [2] Diagnostic Centre Bled Group, Bled, Slovenia, Department of Gastroenterology and Hepatology, [3] University of Milan, Italy, Postgraduate School of Radiology, [4] Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy, Rome, Italy, Gastroenterology and Endoscopy Unit, [5] Azienda USL di Bologna, Bologna, Italy, Department of Gastroenterology and Interventional Endoscopy, [6] Beaujon Hospital, APHP, Paris Cité University, , France, Service d'Endoscopie Digestive, [7] University College London Hospitals, London, United Kingdom, Department of Gastroenterology, [8] King's College Hospital London, London, United Kingdom, Institute of Liver Studies, [9] Royal London Hospital, London, United Kingdom, Royal Free Sheila Sherlock Liver Centre, [10] Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, Department of Gastroenterology, [11] University of Liverpool, Liverpool, United Kingdom, Department of Gastroenterology, [12] Newcastle Upon Tyne NHS Foundation Trust, Newcastle, United Kingdom, Department of Gastroenterology and Hepatology, [13] NIHR Nottingham Biomedical Research Centre, Nottingham, United Kingdom, NIHR Nottingham Biomedical Research Centre, [14] St James's University Hospital, Leeds, United Kingdom, Department of Gastroenterology, [15] University hospital of Bristol NHS foundation Trust, United Kingdom, Department of Gastroenterology, [16] University Hospital Schleswig-Holstein, Campus Kiel, Germany, Interdisciplinary Endoscopy, Medical Department 1, [17] Hospital Universitario de Navarra, Pamplona, Spain, Endoscopy Unit, Gastroenterology Department, [18] Hospital Universitario de Navarra, Pamplona, Spain, Department of Gastroenterology and Hepatology, [19] Helsinki University Central Hospital and Biomedicum, Helsinki, Finland, Department of Gastrointestinal Surgery, [20] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Liver and Biliopancreatic disorders, [21] Maastricht University Medical Centre, Maastricht, The Netherlands, Department of Gastroenterology and Hepatology, [22] Acibadem City Clinic University Hospital Tokuda, Sofia, Bulgaria, Clinic of Gastroenterology, [23] University Medical Centre Groningen, Groningen, The Netherlands, Department of Gastroenterology and Hepatology, [24] University Medical Centre Groningen, Groningen, The Netherlands, Department of Gastroenterology, [25] King Abdulaziz University Hospital, Jeddah, Saudi Arabia, Jeddah, Saudi Arabia, Department of Gastroenterology, [26] University Hospital Essen, Essen, Germany, gas, [27] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology, [28] Royal London Hospital, London, United Kingdom, Department of Gastroenterology and Hepatology, [29] Leiden University Medical Centre (LUMC), Leiden, The Netherlands, Department of Gastroenterology and Hepatology, [30] Erasmus MC, University Medical Centre Rotterdam, The Netherlands, Department of Gastroenterology, [31] University of Verona, Verona, Italy, Department of Gastroenterology, [32] Erasmus MC, University Medical Centre Rotterdam, The Netherlands, Department of Gastroenterology and Hepatology, [33] University Hospital of Ghent, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Direct cholangioscopy and pancreatoscopy have become widely implemented techniques in the diagnostic or therapeutic algorithm of several pancreaticobiliary disorders. Currently, no widely accepted guidelines exist.

Aim: This study aimed to generate general and indication-specific European consensus recommendations on cholangioscopy and pancreatoscopy.

Methods: Supported by the available literature evidence, statements were formulated and grouped into the following categories: 1) pre-procedural considerations, 2) general technical aspects, 3) biliopancreatic stones, 4) biliary strictures, and 5) other indications. The evidence level of each statement was determined using the GRADE methodology. European cholangioscopy experts were invited to participate in a modified Delphi process. When no 80% consensus was reached, the statement was modified based on expert feedback and subjected to a second Delphi round. Statements were rejected if no consensus was reached after the second Delphi round.

Results: Thirty-four cholangioscopy experts throughout Europa completed the Delphi process. Forty (97.5%) of 41 generated statements were accepted, of which 39 (95.1%) in the first Delphi round. Supported by moderate-to-high level evidence, 100% consensus was reached on the need for prophylactic antibiotics and NSAIDs before cholangioscopy. Despite low to very low level of evidence, expert consensus was reached on several aspects related to training and

technique (eg. the need for sphincterotomy and guidewires, handling of the elevator and the steering wheels, and methods of irrigation during the procedure). No consensus was achieved on the use of simethicone during cholangioscopy. Specific recommendations for biliopancreatic stones covered the position of cholangioscopy in the therapeutic algorithm of biliopancreatic stones and the optimal technique of lithotripsy. Regarding biliary strictures, consensus definitions to differentiate 'unexplained biliary strictures' from 'indeterminate biliary strictures' were generated. Other recommendations concerned the position of cholangioscopy in the therapeutic algorithm of unexplained biliary strictures and primary sclerosing cholangitis, the value of standardized visual evaluation criteria, the minimal number of targeted biopsies and the preferred specimen fixation medium. The remaining consensus recommendations related to the use of cholangioscopy a) for selective guidewire placement, b) for retrieval of internally migrated biliary or pancreatic stents, c) to identify the bleeding source in hemobilia and d) to perform diagnostic pancreatoscopy.

Conclusions: Using a modified Delphi process within a large group of European experts, we developed general and indication-specific consensus recommendations for cholangioscopy to guide clinical practice.

BELGIAN SOCIETY FOR GASTROINTESTINAL ENDOSCOPY - VIDEO SESSION (BSGIE)

- GV01 -

MEDICAL MALPRACTICE LITIGATIONS AGAINST GASTROENTEROLOGISTS IN BELGIUM. T. Moreels (1), N. Meyten (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology and Hepatology, [2] Ziekenhuis aan de Stroom Antwerpen, Antwerpen, Belgium, Cardiology.

Introduction: Medical malpractice litigations represent an important reality for clinical physicians. However, no data are available about their impact on gastroenterologists in Belgium. There is currently no national database on endoscopy-related complications or malpractice litigations.

Aim: We tried to estimate the number of malpractice litigations against gastroenterologists in Belgium based on the annual reports of the Fund for Medical Accidents (FMA), residing under the Belgian national social security service (RIZIV-INAMI).

Methods: The annual reports of the FMA are available online in the public domain. The FMA was established in 2010 by the RIZIV-INAMI aiming to financially compensate patients filing against their treating physician because of medical malpractice, as a cheaper and faster alternative to legal law suits. We performed a retrospective review of all available annual reports from 2012 onwards, focussing on results within the fields of Gastroenterology and Cardiology.

Results: From 2010 to 2023 a total of 6884 applications for malpractice litigations were filed resulting in a final decision for 3185 care providers between 2014 and 2023. In this 10 years period claims were filed against 92 gastroenterologists, with a mean of 9 claims per year, putting gastroenterologists steadily in the top 10 of care providers at risk for malpractice litigations (ranging from position 6 to 9 during the 10 years period), led by far by orthopaedic surgeons (28% of all malpractice litigations). Gastroenterology is the only non-surgical speciality in the top 10 next to Emergency Medicine. There are currently 777 practicing gastroenterologists in Belgium (in 2022), indicating that over 10 years' time the cumulative risk of malpractice litigation through the FMA alone is as high as 12%. The subject of the litigations (diagnostic error, endoscopic complication...) is not mentioned in the FMA annual reports and therefore remains unknown. Compared to Cardiology, another interventional speciality within the field of Internal Medicine, gastroenterologists are more prone to malpractice litigations. Only 73 (6%; $p < 0.001$ Chi-square) on a total of 1237 practicing cardiologists faced malpractice litigations through the FMA, excluding cardiologists from the top 10 specialities at risk.

Conclusions: Although the currently obtained results are still incomplete, exclusively based on the annual reports of the FMA, they reveal that gastroenterologists in Belgium are considerably at risk of malpractice litigations reaching 12% over a 10 years' period, as compared to only 6% cumulative risk of practicing cardiologists during the same study period. Endoscopy-related complications are supposedly the most common reason of malpractice litigation and Belgian gastroenterologists should be aware of this considerable risk.

- GV02 -

ENDOSCOPIC TREATMENT OF ESOPHAGO-BRONCHIAL OR TRACHEAL FISTULA. P. Deprez (1), T. Moreels (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology and Hepatology.

Esophago-bronchial or tracheal fistula are rare but serious complication after oesophageal or thoracic surgery. They can cause respiratory failure, pulmonary sepsis, and finally septic shock and death. We report several cases (videos) with failure of closure (post-Nissen chronic fistula, patient operated by Nissen himself, but neoplastic fistula at the end), and successful closure either with clips, OTSClips, suture, or ESD plus application of biosynthetic tissue.

- GV03 -

ENDOSCOPIC TREATMENT OF A COMPLEX COLORECTAL ANASTOMOTIC LEAK WITH A PELVIC ABSCESS AND RECTOVAGINAL FISTULA. L. Monino (1), P. Deprez (1), R. Bachmann (2), C. Remue (2), E. Danse (3), T. Moreels (4) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology and Hepatology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Colorectal Surgery, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Radiology, [4] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology and Hepatology.

A 56-year-old woman was diagnosed with rectal adenocarcinoma and underwent laparoscopic anterior resection of the rectum with lymph node dissection and colorectal anastomosis. She presented 1 month later with anastomotic leakage complicated by a presacral abscess and a rectovaginal fistula. The collection was initially surgically drained without success. Endoscopy was performed and demonstrated a two-third circumferential dehiscence of the colorectal

anastomosis, associated with a complex pelvic collection and a rectovaginal fistula. The multiloculated pelvic collection was internally drained by placing multiple double-pigtail stents in association with a sponge connected to an external vacuum container. The sponge was endoscopically replaced every 3–4 days and after 9 sponges the leak was successfully closed without need for further surgical intervention. Endoscopic and radiologic follow-up at 2 and 9 months showed a normal colorectal anastomosis without recurrence of the pelvic collection or rectovaginal fistula. The endoscopic treatment and the evolution of the anastomotic leak is shown in this case video.

- GV04 -

LOCKING DOWN PERFORATIONS: ADVANCED ANCHORING TEETH CLIPS FOR ESOPHAGEAL REPAIR.

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Zenker's diverticulum (ZD) is a rare pharyngoesophageal disorder often presenting with dysphagia and regurgitation. We report the case of a 65-year-old male with a 3 cm ZD who underwent CO₂ laser marsupialization performed by the ENT team. The postoperative course was complicated by an oesophageal perforation on day 1, confirmed by imaging as an extraluminal leak with a peri-oesophageal collection. Upper endoscopy revealed a large perforation covering 50% of the circumference at the oesophageal opening, allowing the endoscope to pass into the superior mediastinum. The perforation was successfully closed using 10 LOCKADO™ 11-mm clips (Micro-Tech). Originally designed for haemostasis, these clips are proving effective for managing perforations due to enhanced compression force, ten anchoring teeth for improved tissue anchoring, and unlimited repositioning before deployment for precise placement. Their short luminal projection minimizes risk of injury to opposing tissues, and multiple sizes options allow adaptability to complex anatomy. Post-procedure imaging demonstrated significant resolution of the peri-oesophageal collection and absence of further contrast leakage. The patient gradually resumed oral intake and was discharged in stable condition. Follow-up imaging confirmed complete healing of the perforation with no residual fistula or secondary stricture, and the patient remained asymptomatic. This case demonstrates the successful use of anchoring teeth clips in managing a complex oesophageal perforation following ZD surgery. While primarily designed for haemostasis, the innovative design and functionality of these clips make them a valuable tool for tissue stabilization and closure of perforations, emphasizing their role in the minimally invasive management of gastrointestinal surgical complications.

- GV05 -

ENDOSCOPIC EXPLORATION OF THE EXCLUDED GASTRODUODENAL SEGMENT IN PATIENTS WITH ROUX-EN-Y GASTRIC BYPASS: INDICATIONS AND FINDINGS.

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Introduction: The gastroduodenal segment in patients with Roux-en-Y gastric bypass (RYGB) is excluded from conventional endoscopic access, rendering its diagnostic and therapeutic endoscopic exploration challenging. Device-assisted enteroscopy (DAE) enables endoscopic access of the excluded gastroduodenal segment in RYGB patients.

Aim: We studied indications and findings of DAE-assisted procedures in the excluded gastroduodenal segment in RYGB patients.

Methods: Retrospective analysis of a 5-year (2020-2024) prospective cohort of RYGB patients who underwent DAE of the excluded gastroduodenal segment.

Results: A total of 29 RYGB patients (16 female, age 58±2 years) were referred for endoscopic exploration of the excluded gastroduodenal segment because of overt or occult bleeding (n= 16; 55%) or because of abnormal radiological CT-findings (n=13; 45%). All DAE procedures were performed under general anaesthesia with endotracheal intubation and with fluoroscopic guidance. The bleeding group contained significantly more male patients (69%) and the time interval between the RYGB surgery and the bleeding was significantly shorter (7±1 year) as compared to the CT-findings group with only 15% of male patients (p=0.0040) and a longer time interval (14±2 years) between RYGB surgery and CT-findings (p=0.0029). DAE in the bleeding group reached the excluded stomach in 94% of the procedures, whereas in the CT-findings group the excluded stomach was only reached in 62% (p=0.0332), and in the remaining 38% the excluded duodenum was reached. In 38% of the bleeding group endoscopic findings were normal as compared to 23% in the CT-findings group (p=0.4037). Positive findings in the bleeding group were ulcers at the Roux-en-Y anastomosis (13%) or at the gastroduodenal level (27%), duodenal angiodysplasia (13%) and diversion gastritis of the excluded stomach (7%). Haemostasis was successfully performed when indicated using haemostatic clips and argon plasma coagulation. Positive findings in the CT-findings group were ulcers at the gastrojejunal anastomosis (15%), duodenal adenoma with high grade

dysplasia (8%), pyloric hypertrophy with prolapse (46%) and one case of poorly differentiated adenocarcinoma of the excluded stomach (8%). Endoscopic polypectomy was performed as well as endoscopic biopsy sampling. A total of 16 patients (55%) underwent biopsies of the excluded stomach in search of *Helicobacter pylori*, but all samples turned out negative. No DAE-related adverse events occurred.

Conclusions: High-impact pathology (bleeding ulcers and neoplastic lesions) may occur in the excluded gastroduodenal segment in RYGB patients. Bleeding occurs more often in male patients at an earlier postoperative time interval as compared the pathological radiological CT-findings occurring more often in a later phase with a female predominance. Although neoplastic lesions were found, the majority of suspected tumoural CT-findings turned out to be a benign prolapse of hypertrophic pyloric mucosa. DAE also enables therapeutic interventions like successful hemostasis, polypectomy and tissue sampling. DAE should be considered as a first-line endoscopic approach to diagnose and treat suspected pathology in the excluded gastroduodenal segment in RYGB patients.

- GV06 -

ENDOSCOPIC HELIX TACKING SYSTEM FOR THE MANAGEMENT OF COLONIC ANASTOMOTIC DEHISCENCE (X-MAN) AFTER A LAPAROSCOPIC LEFT COLECTOMY. V. VandenDriessche (1), E. Kaya (1), P. Yengue (1), M. Lefebvre (1) / [1] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastroenterology. We present the case of a 69-year-old patient who underwent laparoscopic left colectomy with an end-to-end colorectal anastomosis. Within 2 months, he developed an anastomotic dehiscence (AD), connected to a cavity measuring 20 mm in diameter. Initially treated by endoluminal vacuum therapy, the cavity size was reduced from 20 to 10 mm within 2 weeks. However, complete closure was ultimately achieved using an endoscopic helix tacking system. Closure was accomplished by placing 4 tacks around the defect in a "Z" pattern, pulling the thread attached to the tacks, and securing the suture with a cinch device. 6-week follow-up confirmed successful closure, demonstrating the safe and effective management of an AD using X-MAN.

- GV07 -

CONTRAST MEDIA GUIDED-VACUUM THERAPY FOR THE TREATMENT OF LOWER-GI LEAKAGE. S. Ouazzani (1), M. Fernandez y Viesca (1), M. Arvanitakis (1), F. Bouazza (2), J. Devière (1), P. Eisendrath (1), A. Lemmers (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Institut Jules Bordet, Brussels, Belgium, Digestive Surgery.

Leakage after rectal cancer surgery significantly jeopardizes patient's prognosis. Endo-vacuum therapy appears to be effective and safe to treat this complication. Sponges placement is performed through an overtube, without direct visual endoscopic control, potentially compromising their precise placement, since they are not visible under fluoroscopy. For improving sponges placement accuracy, we aimed to make them radio-opaque by simply immersing them in contrast media, allowing us to visualize their precise placement in the abscessed cavity under fluoroscopy. We present here a case of complete and circumferential leakage after rectal surgery for an adenocarcinoma, treated by neoadjuvant immunotherapy and radiotherapy, and complicated by severe bleeding, treated by arterial embolization. This leakage was treated by contrast media guided-Endosponge placement method, helping placement of serial multiple sponges, cut before placement according to the shape of the large cavity. After 8 sessions, we observed complete re-epithelialization, with leak healing and restoration of digestive continuity.

- GV08 -

ENDOSCOPIC ULTRASOUND-GUIDED GASTROENTEROSTOMY TO TREAT AN OBSTRUCTIVE GASTRIC TWIST AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY. L. Monino (1), Y. Deswysen (2), M. Thoma (2), P. Deprez (1), T. Moreels (3) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hépto-Gastroentérologie, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Upper Gastrointestinal Surgery, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépto-Gastroentérologie.

A 69-year-old woman underwent sleeve gastrectomy. One month later, she presented symptoms of gastric outlet obstruction. Endoscopy showed severe reflux esophagitis associated with a mid-gastric twist confirmed by CT scan. Three sessions of endoscopic balloon dilatation were performed without any clinical improvement. An endoscopic ultrasound (EUS)-guided gastroenterostomy was proposed to "bypass" the mid-gastric twist. An oroenteric catheter was placed over a guidewire to fill the jejunal lumen. Next, the target jejunal limb was identified by EUS and punctured with the electrocautery-enhanced lumen-apposing metal stent (LAMS) in pure cut mode using the WEST free-hand technique. The LAMS (20*10 mm) was deployed connecting the proximal gastric and jejunal lumen without adverse events. There was a rapid clinical improvement with disappearance of the gastric outlet obstruction symptoms and confirmed by radiology and endoscopy at 1 and 3 months and 1 year.

PERSISTENT DYSPHAGIA POST ANTI-REFLUX SURGERY TREATED WITH EUS-GUIDED FISTULA FORMATION BETWEEN GASTRIC FUNDUS AND CORPUS J. Sleurs (1), J. Lesaffer (2), C. Snauwaert (3) / [1] KUL - University of Leuven, Leuven, Belgium, Student Medicine, [2] AZ Sint-Jan Brugge, Brugge, Belgium, Digestive Surgery, [3] AZ Sint-Jan Brugge, Brugge, Belgium, Gastroenterology and Hepatology.

We present a case of persistent dysphagia following anti-reflux surgery, caused by pouch formation of the gastric fundus. The usual treatment for persistent dysphagia involves redo surgical intervention. Considering the severity of the patient's symptoms, an innovative approach was chosen by EUS-guided fistula formation between the fundus pouch formed by the cuff created during the anti-reflux surgery and the corpus of the stomach. This intervention resulted in significant improvement of the patient's symptoms of dysphagia and frequent vomiting.

BELGIAN HELICOBACTER AND MICROBIOTA STUDY GROUP (BHSMG)

- H01 -

BREATH UNTARGETED PROFILING REVEALS NOVEL BIOMARKERS OF GUT MICROBIOME-DRIVEN PROCESSES. M. Autuori (1), A. Neyrinck (1), L. Lengelé (1), E. Viera Olivera (1), M. Rombaux (1), J. Rodriguez (1), P. Cani (2), J. Walter (3), L. Bindels (4), N. Delzenne (1) / [1] Université catholique de Louvain (UCLouvain), Belgium, Metabolism and Nutrition Research Group, Louvain Drug Research Institute, [2] Université catholique de Louvain (UCLouvain), Belgium, Metabolism and Nutrition Research Group, Louvain Drug Research Institute; Welbio department, WEL Research Institute; Institute of Experimental and Clinical Research (IREC), [3] University College Cork, Cork, Ireland, APC Microbiome Ireland, School of Microbiology, and Department of Medicine, [4] Université catholique de Louvain (UCLouvain), Belgium, Metabolism and Nutrition Research Group, Louvain Drug Research Institute; Welbio department, WEL Research Institute.

Introduction: Gut microbiota ferments dietary fibre – the undigested fraction of ingestion food – leading to the production of various metabolites that influences conditions such as obesity, cardiovascular diseases, and cancer (1). In recent years, breath metabolomics has emerged as a promising non-invasive tool for investigating human metabolism (2). Recently, our team highlighted the potential of breath analysis to monitor gut microbiota fermentation of an insoluble dietary fibre called chitin-glucan (3).

Aim: In the present analysis, we seek to identify a broad range of volatile bioactive compounds that reflect the complex interactions between various dietary fibres and the gut microbiome.

Methods: 14 healthy volunteers (21 ± 0.5 years old; 7 men/7 women) participated to two test days at a one-month interval, where they received either a low-fibre (2.6g, LF) or high-fibre (16.1g, HF) breakfast. Before test days, stools were collected to evaluate the microbiota composition by Illumina sequencing (V5-V6 region of 16S rRNA). All along test days, breath samples were analysed using Selected-Ion Flow-Tube Mass Spectrometry (SIFT-MS). A sparse Partial Least Squares-Discriminant Analysis (sPLS-DA) identified the 30 most discriminating signals from breath samples between the test days and related compounds were identified from the SIFT library (LabSyft®) and quantified at each time point.

Results: The gut microbiota composition was not significantly different between both test days. Eighty-six potential novel biomarkers of gut microbiota activity were identified, most of them (77) being increased at post absorptive state 5 to 10 hours after ingestion of the HF versus LF breakfast. Forty nine out of the 77 compounds have already been identified in breath, blood, faeces and/or saliva in humans. Among those, some are known to be produced by gut microbes (e.g., methanol, lactic acid) while others have not yet been related to the gut (e.g., dimethyl disulfide, heptanal). Finally, some compounds neither measured in the breath nor linked to the gut microbiota before (e.g., acrylic acid, phenylacetaldehyde) might be of noteworthy interest.

Conclusions: This study established a list of potential metabolites in the breath that will be of interest to unravel the gut microbiota activity in response to dietary fibre intake. Breath analysis has the potential to advance our understanding of the microbiome activity in a non-invasive, dynamic, and sustainable way. Further analysis of the relationship between gut microbiota and novel highlighted metabolites are ongoing.

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- H02 -

IMMUNOHISTOCHEMICAL POSITIVITY RATE OF HELICOBACTER PYLORI IN GASTRIC BIOPSIES IN THE KORTRIJK REGION IN THE PERIOD 2012-2023 IN RELATION TO PATIENT AGE. L. Libbrecht (1), A. Vanneste (2) / [1] AZ Groeninge, Kortrijk, Belgium, pathology, [2] AZ Groeninge, Kortrijk, Belgium, Pathology.

Introduction: there exists a plethora of studies on *Helicobacter Pylori* (HP) epidemiology, including the importance of birth and age cohorts effects, but there are no studies that have looked at this subject via upfront immunohistochemistry (IHC) for HP on gastric biopsies on a large number of patients over a long period of time, taking into account the patient age at the time of biopsy.

Aim: to extract upfront IHC HP data stored in the laboratory information system (LIS) of the pathology department of AZ Groeninge Kortrijk over a long period of time and to analyse this data, especially in relation to patient age.

Methods: upfront HP IHC data is present in the LIS of the AZG Kortrijk pathology department since 2012 and extraction of this data was performed in an anonymous fashion for the period 2012-2023, together with info regarding the patient age at the time of biopsy. The study was approved by the local ethical committee.

Results: of the 38955 gastric biopsies received at our department in the period 2012-2023 from gastroenterologists working in the Kortrijk region, 17% was HP IHC positive. The overall positivity rate, i.e. independent of patient age, declined in a linear way from 29% in 2012 to 10% in 2023. If a similar linear decline would further occur in the coming years, the positivity rate would become 0% in 2032. Overall, and mainly in the first 3/4 of the period 2012-2023, the HP IHC positivity rate showed an increase from the first to fourth decade of life, leading to a maximum of 30%, followed by a plateau to a decrease with further increasing age of the patients. Mainly in the last 1/4 of the period 2012-2023, the shape of this curve flattened, due to the continuous decrease of the HP IHC positivity rate in all age groups during the overall study period. This decrease is therefore not primarily due to a birth cohort effect. Furthermore, especially in the first 2/4 of the evaluated period, the above described shapes of the curves of the graphs of HP IHC positivity rate in relation to patient age are very similar to those in the study of Sonnenberg et al., *Gastroenterology* 2010, who looked at upfront HP IHC positivity rate in gastric biopsies of 78985 patients taken throughout the United States in the 1-year period between 1/4/2007 and 31/3/2008. This illustrates that such curves based on HP IHC positivity rates in gastric biopsies can be useful to study regional-geographical differences and similarities in the epidemiology of HP, albeit indirectly.

Conclusions: our findings illustrate that analysing positivity rates of HP IHC performed in an upfront fashion on gastric biopsies of a large number of patients over a long time period in relation to the patient's age yields valuable novel information regarding HP epidemiology, albeit indirectly. Collecting and analysing such type of data can become an extra tool to study.

CONTRASTING OUTCOMES OF DIETARY INTERVENTIONS AND FMT ON COLONIC AND ILEAL INFLAMMATION IN HUMANIZED IBD MODELS. S. Deleu (1), K. Vidmar (2), S. Troisi (3), H. Wargo (2), L. Masi (3), J. Williams (2), S. Artone (2), S. De Santis (2), C. De Salvo (2), V. Petito (3), L. Lopetuso (4), F. Cominelli (5), T. Pizarro (2), F. Scaldaferri (3) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, DEPARTMENT OF CHRONIC DISEASES, METABOLISM AND AGEING, [2] Case Western Reserve University, Cleveland, United States, Pathology, [3] Fondazione Policlinico Universitario “A. Gemelli” IRCCS, Rome, Italy, Rome, Italy, CeMAD Translational Research Laboratories, Digestive Disease Centre (CeMAD), Department of Medical and Surgical Sciences, [4] “G. d’Annunzio” University of Chieti-Pescara, Chieti. Chieti, Italy, Centre for Advanced Studies and Technology (CAST), [5] Case Western Reserve University, Cleveland, United States, Gastroenterology and hepatology.

Introduction: Faecal microbiota transplantation (FMT) has been shown to be a promising approach to treat active ulcerative colitis (UC). However, its use as a treatment for Crohn's disease (CD) is in its early stages, and scientific evidence for its effectiveness is currently limited. Also, diet plays a crucial role in shaping the gut microbiome and might affect the efficacy of FMT.

Aim: Therefore, we aimed to investigate the additive effects of dietary interventions on multidonor FMT efficacy in preclinical humanized IBD models.

Methods: Age/sex-matched inbred ileitis-prone SAMP and C57BL/6 mice were treated with broad-spectrum antibiotics followed by humanization with either CD or UC multidonor patient-derived microbiota, and subsequently randomized to either Western, Mediterranean or Control diet in combination with healthy donor multidonor FMT or sham (n= 8/ experimental grp; Fig1A). After one week, mice were subjected to DSS to induce acute colitis (7d, 2-2.5%), followed by another 7d of recovery. Disease activity indices (DAI) were determined and evaluated by area under the curve (AUC). Feces were collected every other day for 16S sequencing. At sacrifice, colonic lengths were measured, and blood and different tissues collected for histology, RNA and protein analysis.

Results: Independently from diet, FMT was shown to improve disease activity (Fig 1; $p=0.047$) in SAMP mice. Whereas independently from FMT, the Mediterranean diet showed significantly lower disease compared to control and Western diet for SAMP and C57BL/6 (all $p<0.001$). Dietary regimen seems to affect the disease activity most, as within each diet no significant effect of FMT could be observed (Table 1). Nevertheless, C57BL/6 receiving FMT in addition to the Mediterranean diet had significantly higher survival rates ($p=0.0096$) compared to all other groups. Moreover, in SAMP higher histologic ileal inflammation was observed for animals receiving FMT (Fig1; $p=0.0119$), while the opposite was observed for colonic inflammation with a trend towards lower inflammation ($p=0.0729$). Further, a trend towards lower histologic ileal inflammation was observed for the Mediterranean compared to the Western diet ($p=0.080$), which was not observed for colonic tissue. Microbial analysis and RNA sequencing data might explain these findings (ongoing).

Conclusions: In conclusion, independently from each other, both FMT and Mediterranean diet lower disease activity in two humanized mouse models of IBD. Although a trend towards increased efficacy is observed when combining FMT and diet, the additive effect of FMT within each diet seems to be rather limited. Yet, FMT may decrease the severity of colitis, while surprisingly it may worsen ileitis in SAMP mice. Hence, further analyses are required to elucidate the specific mechanisms behind these findings.

TOTAL EMULSIFIER INTAKE, BUT NOT ULTRA-PROCESSED FOOD CONSUMPTION IS HIGHER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE COMPARED TO HEALTHY CONTROLS: A BELGIAN CROSS-SECTIONAL COHORT STUDY. J. Wellens (1), M. Debrauwere (2), S. Hoekx (1), J. Vanderstappen (1), E. De Maegd (2), E. Vissers (2), M. Ferrante (1), B. Verstockt (1), S. Vermeire (1), J. Sabino (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, Translational Research Centre for Gastrointestinal Disorders (TARGID).

Introduction: Our Western diet is typically high in ultra-processed foods (UPFs), which have been linked to inflammatory bowel disease (IBD) incidence and progression. UPFs often contain emulsifiers that might affect the intestinal barrier and microbiota.

Aim: We aimed to assess the intake of UPFs, emulsifiers, and macronutrient in patients with IBD and healthy. controls.

Methods: We compared the dietary intake of patients with ulcerative colitis (UC) and Crohn's disease (CD) to healthy controls previously recruited in the FOAM study (NCT06552156). Patients were recruited at the infusion unit of a tertiary care hospital. Dietary intake was assessed using Food Frequency Questionnaires (FFQs) for all individuals, as

well as two 24-hour dietary recalls for IBD patients, and two prospective food logs for the controls. Macronutrients and energy intake were calculated from FFQs and food logs. UPF and emulsifier intake were calculated from food logs. Kruskal Wallis with post-hoc Dunn test was used for continuous data, and Fisher exact test for proportions, with multiple testing correction using Bonferroni.

Results: We included 186 subjects (N=65 healthy controls, N=59 CD, and N=62 UC). In the total cohort of 101 participants (54.3%) were female, including 52 females (80%) in the healthy subgroup, and 25 (42.3%) and 24 females for CD and UC respectively. Median (IQR) age was 26 (23 - 33) years for healthy controls, while this was 41 (32 - 51) and 46 (35 - 55) years old for CD and UC respectively. Median (IQR) Body Mass Index was 22.2 kg/m² (20.7 - 25.1) in healthy controls, 25.9 kg/m² (22.7 - 29.7) in CD, and 24.9 kg/m² (22.5 - 27.6) in UC. For CD 45.7% had a history of bowel surgery, compared to 1.6% in UC patients. UPF intake was similar in all groups, yet emulsifier intake was higher in UC and CD compared to controls (p=0.03 and p=0.0004, respectively). Compared to controls, higher intakes of E402 (UC p=0.02, CD p=0.002), E411 (both p=0.01), E471 (UC p=0.02, CD p=0.0009), as well as carrageenan E407 (UC p=0.001, CD p=0.002), and xanthan gum E415 (UC p=0.03, CD p=0.01) were seen. Intake of E476 was higher in patients with CD compared to controls (p=0.02), while intake of E412 was higher in patients with UC compared to controls (p=0.02). The proportion of non-consumers of E402 was higher in controls (100%) compared to patients with IBD (CD 83%, UC 67%, p=0.03). Food logs showed a higher sugar intake in UC (p=0.004) compared to controls. When comparing FFQs, two participants were excluded due to incomplete data. A higher intake of deli meat in CD was seen, compared to UC (p=0.04). Compared to controls, patients with IBD had higher intakes of soft drinks (UC p=0.0005, CD p=0.001), meat (UC p=0.02, CD p=0.04), and butter (UC p=0.03, CD p=0.005). However, intake of breakfast cereals (UC p=6e-13, CD p=1e-10), legumes (UC p=2e-04, CD p=1e-05), meat substitutes (UC 0.0006, CD p=0.02), whole grain pasta and rice (UC p=2e-6, CD p=4e-5), and fibre (UC p=0.01, CD p=0.002) was lower in UC and CD. Coffee (p=0.03), potato (p=0.01), deli meat (p=0.0003), and sodium intake (p=0.02) was higher in CD than controls, while nut and seed intake was lower (p=0.0003). For UC, polysaccharide intake was lower in UC than controls (p=0.007). There was no correlation between C-reactive protein and intake of UPFs, emulsifiers, macronutrients or total energy intake (p>0.1).

Conclusions: We show higher intakes of emulsifiers in patients with IBD compared to controls, while UPF intake was comparable. The concomitant increased intake of specific emulsifiers such as carrageenan and guar gum that have previously been associated with disruption of the intestinal barrier, warrant further investigation into their role in the propagation and maintenance of gut inflammation.

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METAGENOMIC OUTCOMES OF FAECAL MICROBIOTA TRANSPLANTATION IN ULCERATIVE COLITIS ARE INFLUENCED BY BASELINE MICROBIAL COMPOSITION AND DONOR-RECIPIENT RICHNESS DISPARITY. S. Deleu (1), J. Vazquez Castellanos (2), S. Andreu-Sánchez (2), C. Caenepeel (1), S. Verstockt (1), K. Arnauts (1), F. Baert (3), F. Mana (4), L. Pouillon (5), T. Lobaton (6), E. Louis (7), D. Franchimont (8), B. Verstockt (9), M. Ferrante (9), J. Sabino (9), J. Raes (2), S. Vermeire (9) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology and Immunology, [3] AZ Delta, , Belgium, Gastroenterology and hepatology, [4] UZ Brussel, Brussels, Belgium, Gastroenterology and hepatology, [5] Imelda Hospital, Bonheiden, Belgium, Gastroenterology and hepatology, [6] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and hepatology, [7] CHU Liege, Liège, Belgium, Gastroenterology and hepatology, [8] Erasme Hospital, Brussels, Belgium, Gastroenterology and hepatology, [9] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and hepatology

Introduction: Rigorous donor preselection, strict anaerobic processing, and repeated faecal microbiota transplantation (FMT) administration did not improve outcomes for induction of clinical remission in the RESTORE-UC trial1.

Aim: We studied the luminal, and mucosal microbiota composition as well as gene expression throughout the RESTORE-UC study, to further understand the results and instruct future FMT trial design.

Methods: The RESTORE-UC trial was a multi-centric double-blind, sham-controlled randomized trial. Patients with moderate to severe UC (total Mayo 4-10) were randomly allocated to receive 4 anaerobic-prepared allogenic or autologous donor FMT. Mucosal biopsies were collected for RNA and 16S sequencing at week 0 and 8. Quantitative microbiota profiling was performed on donor samples, and in patients at weeks 0, 1, 2, 3, 4, 8, 12, 26, and 52 (n=756). Clinical success (steroid free clinical remission) and -response (≥ 3 points or $\geq 50\%$ reduction in combined Mayo subscores for rectal bleeding and stool frequency) were evaluated at w8. Metagenomic success (w8) was defined as restoration of eubiosis (Bacteroides 2 (B2) to non-B2 enterotype) and failure was considered with subtypes being no transition, non-B2 to other non-B2 transition, lead dysbiosis (non-B2 to B2), and maintenance of dysbiosis (B2 to B2).

Results: Baseline microbiota composition was significantly associated with future clinical and metagenomic success (resp. p=0.035; p=0.003). Similar trends were observed at week 8 (resp. p=0.056; p=0.001). Restoration of eubiosis was characterized by a rapid increase in bacterial richness after the first FMT administration, which was maintained up to 12 months after intervention. A greater difference in richness between donor and recipient determined the metagenomic success (p=0.06) and clinical response (p=0.01), while this was not observed for clinical success (p=0.16). Metagenomic

success was accompanied by increased engraftment after FMT ($p < 0.01$). Independently from clinical success, patients with dysbiotic faecal communities (w0) had distinctive mucosal communities in their intestinal biopsies ($p < 0.01$), which were significantly changed in samples where eubiosis was restored ($p = 0.012$), but not in those where clinical success was observed ($p = 0.34$). However, this could be explained by the low overall response rate. No specific transcriptomic profiles in mucosal biopsies at baseline were reminiscent of metagenomic ($p = 0.24$), nor clinical success ($p = 0.22$).

Conclusions: Patient and donors should be rigorously selected in future FMT trials, and selection should be based on microbial composition and by obtaining a great difference in richness between receptor and donor. Ref.1 Caenepeel*, Deleu*, Vazquez* et al., 2024.

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MULTIOMIC ANALYSIS REVEALS THREE DISTINCT SUBTYPES WITHIN PERIANAL CROHN'S DISEASE, INDEPENDENT OF CONCOMITANT PROCTITIS. S. Abdurahiman (1), J. Sabino (2), S. Verstockt (3), M. Ferrante (2), M. Lenfant (2), J. Raes (4), A. D'Hoore (5), S. Vermeire (2), G. Bislenghi (5), B. Verstockt (2) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium., [3] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium. , [4] KUL - University of Leuven, Leuven, Belgium, Laboratory of Molecular Bacteriology, Department of Microbiology and Immunology, Rega Institute, Katholieke Universiteit Leuven, Leuven, Belgium., [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery, Colorectal Surgery, UZ Leuven, KU Leuven, Leuven, Belgium.

Introduction: Perianal fistulization (pCD) affects approximately 20% of Crohn's disease (CD) patients, often necessitating a combination of medical and surgical interventions. Patients with colonic involvement are at an increased risk of developing pCD. However, the molecular mechanisms underlying its development remain poorly understood, with epithelial-to-mesenchymal transition (EMT) frequently proposed as a key process. Despite significant progress in management of luminal CD, pCD continues to pose a major unmet need, emphasizing the importance of understanding the molecular and environmental drivers and to discover new therapeutic targets.

Aim: To investigate the molecular mechanisms driving perianal fistulization (pCD) in Crohn's disease (CD), with an emphasis on transcriptional and microbial factors, aiming to identify novel therapeutic targets and enable patient stratification based on distinct molecular phenotypes.

Methods: Paired biopsies from the fistula tract and rectal orifice of 81 pCD patients underwent 16S rRNA and RNA sequencing, generating multiomic profiles. Multiomics Factor Analysis (MOFA) was applied to integrate transcriptomic and microbiome data, capturing distinct sources of variation across multiple data types. MOFA factors were ranked by the variance explained, and hierarchical clustering based on MOFA factor values enabled comprehensive integration of all omic layers into a unified structure for patient stratification. To identify key molecular drivers associated with each axis of variation, the top 100 genes with the highest and lowest MOFA weights at the extremes of each factor were selected. These genes were derived from the dataset contributing most to the variance of each corresponding MOFA factor (fistula transcriptomics for Factor 1 and rectal transcriptomics for Factor 2). Gene over representation analysis was then performed using the Molecular Signature Database (MSigDB) to highlight the most biologically relevant features. Gene module scores were derived using Seurat and mapped onto a publicly available single-cell RNA sequencing (scRNA-seq) dataset (GSE228421) to explore relevant gene signatures and visualize expression patterns.

Results: The MOFA model showed minimal contribution from the microbiota but accounted for over 80% of transcriptomic variance. Unsupervised clustering based on MOFA identified three distinct patient clusters (C1, C2, C3) with unique molecular phenotypes, independent of concomitant or prior proctitis ($p = 1.0$). C3 was associated with positive end of the primary axis of variation, showing a keratinization signature in the fistula, without signs of epithelial-mesenchymal transition (EMT) or rectal keratinization. In contrast, C1 and C2 were at the opposite extreme of this axis, characterized by EMT signatures in the fistula and an absence of keratinization. However, the rectal profiles differed between C1 and C2 clusters. C1 lacked keratinization in the rectum, while C2 exhibited concurrent keratinization in the rectum. The enrichment of EMT-related genes at one end and keratinization-related genes at the other end of the primary axis of variation (Factor 1) in fistula suggests that these processes are distinct and mutually exclusive in the pathology of fistulas. Analysis of publicly available scRNA-seq data from psoriasis patients (a keratinization-hallmark disease) revealed significant upregulation of the pCD-specific keratinization gene signature in lesional keratinocytes compared to non-lesional samples, indicating a psoriasis-like keratinization process in pCD. Finally, microbial profiling showed no significant associations between bacterial genera and any of the identified clusters in either rectum or fistula (adj. $p > 0.05$).

Conclusions: Our analysis identified three distinct patient clusters in pCD, revealing diverging keratinization and EMT phenotypes in fistula. This stratification was independent of proctitis and there was little to no contribution of the microbiota. Comparing the expression profiles with the ones observed in patients with psoriasis suggests a psoriasis-like keratinization process in a subset of patients. These findings uncover potential novel mechanisms in pCD pathogenesis.

THE COURSE OF CROHN'S DISEASE IN THE BIOLOGICS ERA: AN IN DEPTH SINGLE-CENTRE TERTIARY COHORT STUDY IN BELGIUM. C. Vuckovic (1), A. Cremer (1), L. Amininejad (1), C. Minsart (1), J. Bottieau (2), D. Franchimont (1), C. Liefferinckx (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology, [2] Laboratoire de Gastro-Entérologie Expérimentale (LGE), Université Libre de Bruxelles, Anderlecht, Belgium, Gastroenterology.

Introduction: Since 1999, Biologics have become a cornerstone in the management of Crohn's Disease (CD), enabling complete mucosal healing in a significant proportion of patients, with measurable changes in major outcomes in large phase III/IV clinical trials. This holds true particularly when patients were exposed early at diagnosis to biologics, as reported in the recent PROFILE study. However, their real-world impact on the long-term course of the disease remains uncertain.

Aim: This retrospective study aims to characterize the natural history of CD before and during the Biologics Era, through a large cohort of CD patients followed in one tertiary centre in Belgium.

Methods: A total of 1,262 patients diagnosed with Inflammatory Bowel Diseases (IBD) were screened from the 3000+ IBD patients' clinics. Patients with unconfirmed CD diagnosis, missing data, and patients diagnosed before 1990 were excluded. A total of 516 CD patients were included and stratified in two subpopulations, according to the date of CD diagnosis (before or after 1999). All events were recorded from date of diagnosis to maximum follow-up (FU), to achieve high granularity, from demographics (sex, tobacco use) and disease characteristics (CD phenotype based on Montreal Classification, presence of extra-intestinal manifestations, associated IMIDs, first degree familial history of IMIDs or IBD) to treatment adaptations (immunomodulators, biologics, surgeries). Continuous variables were presented as medians (IQR25-75). Categorical data were expressed as absolute numbers and percentages. Subpopulation comparisons were conducted using Fisher's exact test and Mann-Whitney test, as appropriate. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using Prism.

Results: Among the 516 CD patients included, 87 were diagnosed before 1999 and 429 were diagnosed after 1999. No significant differences were observed in demographics or disease characteristics at diagnosis between the two groups. At maximum FU, however, a greater proportion of patients diagnosed before 1999 had progressed to B2/B3 phenotypes (69% vs. 39%, $p < 0.0001$). This difference at maximum FU likely reflects the longer disease duration in patients diagnosed before 1999 (Median FU 27 years [22–30] vs. 12 years [6–15], $p < 0.0001$), as evidenced by a similar progression rate from luminal B1 to B2/B3 phenotypes after 10 years of FU in both groups (27% vs. 23%, $p = 0.6$). Changes in CD phenotypes were diagnosed sooner in patients diagnosed after 1999 compared to patients diagnosed before 1999 (Median time from B1 phenotype to B2/B3 phenotypes: 4.8 years [1.8–9.9] vs 12.3 years [6–16.8], respectively, $p < 0.0001$). Similarly, surgeries for CD complications occurred sooner in patients diagnosed after 1999 compared to patients diagnosed before 1999 (Median time to first surgery after CD diagnosis: 5.9 years [2.1–10.2] vs. 12.5 years [6.6–18.2], $p < 0.0001$). This trend may indicate a shift toward proactive medical management (e.g greater access to TDM and MRI imaging) and advances in surgical techniques, enabling earlier diagnosis of B2/B3 phenotypes and reducing surgical burden. As expected, patients diagnosed after 1999 were exposed to biologics for a larger portion of their FU compared to those diagnosed before 1999 (Median proportion of their FU exposed to biologics: 51% [15–79] vs 11% [0–37], $p < 0.0001$).

Conclusions: The proportion of patients progressing to a B2/B3 phenotype at 10 years of disease course is similar for CD patients diagnosed before and during the Biologics Era. The detection of complications occurred earlier in the follow-up of patients diagnosed after 1999, which suggests a shift toward more proactive monitoring since the advent of biologics. Based on these findings, it remains uncertain whether biological therapies have significantly altered the course of the disease and progression to B2/B3 phenotypes in CD patients. However, while these results are based on objective outcomes, they do not fully capture the impact of biological treatments on patients' quality of life and disease burden.

THERAPEUTIC ANTIBODY CLEARANCE BETTER PREDICTS ENDOSCOPIC OUTCOMES THAN TROUGH CONCENTRATIONS IN PATIENTS WITH CROHN'S DISEASE. Z. Wang (1), Y. Hoffert (1), W. Zhang (1), W. Kantasiripitak (1), V. Bram (2), J. Sabino (2), M. Ferrante (2), P. Declerck (1), G. D'Haens (3), D. Laharie (4), S. Vermeire (2), E. Dreesen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology and Hepatology, [4] Hôpital Haut-Lévêque, Université de Bordeaux, France, Department of Gastroenterology, Hepatology and Digestive Oncology.

Introduction: Monitoring of monoclonal antibody (mAb) clearance has been suggested for prediction and follow-up of treatment outcomes in patients with inflammatory bowel diseases. We investigated clearance monitoring in patients with Crohn's disease (CD) using data from clinical trials.

Aim: We aimed to investigate clearance monitoring in patients with Crohn's disease (CD) using data from clinical trials.

Methods: Data from patients with moderate-to-severe CD starting infliximab (n=108; TAILORIX trial [1]) and ustekinumab (n=80; a real-life cohort study [2]) therapy were repurposed. Endoscopic remission (CD Endoscopic Index of Severity <3) was assessed at week (w)12 and w54 of infliximab therapy. Endoscopic response ($\geq 50\%$ reduction in Simple Endoscopic Score for CD from baseline) was assessed at w24 of ustekinumab therapy. We performed Bayesian forecasting to estimate time-varying mAb clearance using measured drug concentrations, covariates, and population pharmacokinetics models (NONMEM 7.5). Generalized linear mixed-effects models with binomial logistic regression were used to predict the probability of endoscopic outcomes based on single predictors: Ctrough, mAb clearance, C-reactive protein (CRP), and faecal calprotectin. A novel software tool for clearance monitoring of infliximab and ustekinumab was developed using the Shiny and mapbayr packages in R.

Results: During standard 5 mg/kg infliximab induction therapy, patients achieving endoscopic remission at w12 had significantly higher infliximab serum trough concentrations (Ctrough) and lower infliximab clearance at w2 and w6 of treatment ($p < 0.01$). During infliximab maintenance therapy with eventual dose optimizations, infliximab Ctrough was not significantly different between patients with and without endoscopic remission at w54 (median [interquartile range IQR]: 5.7 [4.1–9.3] mg/L and 6.5 [3.9–8.5] mg/L, respectively) ($p = 0.92$). However, infliximab clearance during maintenance therapy was significantly lower ($p < 0.01$) in patients with endoscopic remission than in patients without endoscopic remission at w54 (0.25 [IQR 0.22–0.29] L/day and 0.28 [IQR 0.25–0.33] L/day, respectively). Moreover, infliximab clearance during maintenance had similar discriminative ability as faecal calprotectin (area under the receiver operating characteristics curve AUROC 0.63 [95% confidence interval PI 0.57–0.69] vs. 0.67 [95%PI 0.61–0.73], respectively). During ustekinumab induction therapy, ustekinumab clearance and faecal calprotectin, but not Ctrough and CRP, could discriminate between patients with and without endoscopic response at w24. During ustekinumab maintenance therapy, neither ustekinumab Ctrough nor CRP could discriminate between patients with and without endoscopic response at w24. However, ustekinumab clearance during maintenance could predict endoscopic response at w24 with discriminative ability similar to faecal calprotectin (AUROC 0.70 [95%PI 0.57–0.83] vs. 0.70 [95%PI 0.54–0.85]). An infliximab clearance of 0.25 L/day during maintenance therapy was identified as an optimal cut-point to classify patients with and without endoscopic remission at w54 of infliximab therapy (sensitivity=0.48, specificity=0.75). A ustekinumab clearance of 0.22 L/day during maintenance therapy was identified as an optimal cut-point to classify patients with and without endoscopic response at w24 (sensitivity=0.71, specificity=0.70). We developed an evidence-based interactive software tool that can predict the probability of achieving endoscopic outcomes in a clinical setting based on the estimated clearance of infliximab and ustekinumab (https://lpmx.shinyapps.io/clearance_monitoring/).

Conclusions: While Ctrough loses its ability to predict treatment response when doses are optimized or not administered by bodyweight, mAb clearance remains a reliable predictor. Our interactive clearance monitoring tool can provide valuable information to forecast the chance of achieving endoscopic outcomes and distinguish between exposure-driven and mechanistic failure when patients with CD are dose-optimized.

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STUDY OF THE ROLE OF THE EPITHELIUM IN THE INITIATION AND PROGRESSION OF INTESTINAL FIBROSIS IN ULCERATIVE COLITIS M. Stepniak (1), P. Adam (1), C. Salée (1), C. Massot (1), C. Shadouh (1), S. Vieujean (2), C. Reenaers (2), C. Coimbra Marques (3), J. Loly (2), E. Decker (3), N. Blétard (4), P. Delvenne (4), S. Specq (5), S. Beq (6), E. Louis (2), M. Meuwis (1) / [1] GIGA Institute, University of Liège, Liège, Belgium, Translational Gastroenterology Research, [2] University Hospital CHU of Liège, Belgium, Hepato-gastroenterology and digestive oncology, [3] University Hospital CHU of Liège, Belgium, Abdominal surgery, [4] University Hospital CHU of Liège, Belgium, Pathological anatomy, [5] University of Lille, Inserm, CHU Lille, France, Infinite unit, [6] Thabor Therapeutics, France, R&D.

Introduction: Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by diffuse inflammation of the colonic mucosa, starting in the rectum. However, fibrosis features in the submucosa and muscularis mucosae have been described even in the absence of active inflammation, while fibrosis in UC remains underexplored. Currently, no anti-fibrotic treatment exists for IBD. As in other fibrotic diseases, pro-inflammatory and pro-fibrotic cytokines (TGF- β) promote fibroblast proliferation and transition into myofibroblasts (FMT), leading to excessive extracellular matrix deposition. In IBD, endoplasmic reticulum stress (ERS) and inflammation increase the expression of ER chaperone proteins such as AGR2. When secreted, extra-cellular AGR2 (eAGR2) is capable of inducing FMT on an intestinal fibroblast model, suggesting its role in intestinal fibrosis

Aim: Our objective is to better understand the role played by the epithelium in UC intestinal fibrosis initiation and progression. We aim to develop a model of apical out organoid4 showing a profibrotic phenotype and to characterise the molecular changes of such induced apical-out organoids derived from UC and the paracrine mediator(s) implicated in fibrosis.

Methods: Organoids derived from healthy and UC patients, when grown without matrix, reverse polarity (apical-out) and differentiate. On such UC organoids, we induced transient ERS using Tunicamycin (Tm), followed by a recovery period in fresh culture medium, allowing observations of the epithelial post-stress response. RNA, protein extracts and culture supernatants were analysed to assess ERS markers, epithelial-mesenchymal transition (EMT), pro-fibrotic markers (TGF- β 1, eAGR2). Organoids were also evaluated by immunofluorescence (IF) targeting AGR2 and XBP1. Pre-conditioned culture supernatants were used in a functional assay where intestinal fibroblasts (CCD18-Co) were exposed to assess FMT by IF (α -SMA increase). This FMT initiation allows for the demonstration of the pro-fibrotic phenotype of apical-out organoids and the characterization of UC epithelium response after ERS. 44 patients (198 IHC slides) were graded for inflammation using the Geboes score and fibrosis, and AGR2/BiP staining were performed to also assess ERS

Results: Apical-out organoids demonstrated, after 12h of transient Tm stimulation and a 32h recovery period, an increased expression of all established ERS markers (BIP/CHOP/sXBP1) in RT-qPCR. The respective fold changes ranged from 6 to 16, 4 to 9.5, and 3 to 8. AGR2 was consistently elevated in stimulated conditions compared to the control condition, with fold changes ranging from 2 to 10 depending on the patients. No pro-inflammatory cytokines nor TGF- β were increased during the recovery period. In WB, eAGR2 was present in all culture supernatants and was increased under stimulated conditions compared to vehicle with absence of cellular lysis. In cellular extracts, AGR2 show an increase which is dose-response dependent in some patients with an increase compared control condition. BIP was consistently present only under Tm stimulation. Functional tests on CCD18-Co demonstrated an increase in α -SMA IF in all patients, culture supernatants of inverted organoids under ERS conditions show a pro-fibrogenic effect on fibroblasts. The active form of eAGR2 was also quantified in these supernatants, and eAGR2 concentration of stimulated conditions ranged between 1.5 to 3 times higher than those in the control conditions. Organoids were assessed by IF after the recovery period with double staining for AGR2 and XBP1. Compared to the control condition, the AGR2 and XBP1 signals were increased and AGR2 localization was more diffuse throughout the organoid and in the cytoplasm of the cells compared to vehicle condition. We also confirm that ERS is present in UC tissues, with both chaperone IHC signals found increased with higher levels of concomitant inflammation and fibrosis.

Conclusions: We developed a translational model for studying the role of UC epithelium in intestinal fibrosis, and this by applying transient ERS and evaluating the response of the intestinal epithelium following ERS. Apical-out organoids derived from UC, when induced with ERS, are capable of producing a pro-fibrotic paracrine effect independent of a pro-inflammatory phenotype. This suggests that ERS observed in IBD could influence the development of intestinal fibrosis independently of inflammation. The role of eAGR2 in this phenotype is currently under characterization, as the transcriptomic and secretomic molecular changes, that accompany this ERS response within UC organoids and, consequently, the UC epithelium.

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CHARACTERISATION OF REMISSION LEVELS IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH 5-AMINOSALICYLATES: RESULTS OF THE CARUC-ASA PROSPECTIVE MULTICENTRE STUDY. C. Reenaers (1), C. Caenepeel (2), G. Lambrecht (3), L. Pouillon (4), F. Baert (5), A. Cremer (6), A. Colard (7), C. Claessens (8), T. Billiet (9), J. Gedolf (10), B. Strubbe (11), E. Humblet (2), A. De Zutter (12), J. Rahier (13), M. Somers (14), D. Reynders (15), L. Vansteenkiste (16), I. Arijis (16), A. Raeves (16), E. Louis (17), B. Verstockt (18) / [1] CHU Liege, Liège, Belgium, gastroenterology, [2] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology, [3] AZ Damiaan, Oostende, Belgium, Gastroenterology, [4] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [5] AZ Delta, Belgium, Gastroenterology, [6] Erasme Hospital, Brussels, Belgium, Gastroenterology, [7] CHC, Liège, Belgium, Gastroenterology, [8] AZ Turnhout, Turnhout, Belgium, Gastroenterology, [9] AZ Groeninge, Kortrijk, Belgium, Gastroenterology, [10] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [11] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology, [12] Sint Andries ziekenhuis Tiel, Tiel, Belgium, Gastroenterology, [13] CHU Dinant Godinne, Yvoir, Belgium, Gastroenterology, [14] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [15] University Hospital Ghent (UZ Gent), Gent, Belgium, Statistic, [16] BIRD Office, Belgium, BIRD Office, [17] CHU Liege, Liège, Belgium, Gastroenterology, [18] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology.

Introduction: The treatment goals for chronic inflammatory bowel diseases are increasingly ambitious, targeting steroid-free remission, mucosal healing, and biomarker normalisation. In ulcerative colitis (UC), histological remission lowers risks of hospitalisation, cancer, and relapse.

Aim: This study aims to describe remission levels in UC patients in symptomatic remission on first-line 5-aminosalicylic acid (5-ASA) and factors associated with remission.

Methods: This national, multicentre, prospective, phase 4 interventional study (ClinicalTrials.gov: NCT05992142) included UC patients in symptomatic remission, defined by a stool frequency score ≤ 1 and no rectal bleeding, on 5-ASA monotherapy (oral and/or rectal) for at least 6 months. Patients on corticosteroids, immunomodulators, biologics, or small molecules were excluded. Assessments included stool frequency, rectal bleeding, urgency, rectosigmoidoscopy (Mayo score, UCEIS), biopsies with the Geboes score assessed by central reading, faecal calprotectin (FCP), and MARS

(Medication Adherence Report Scale) questionnaire. The different levels of remission were defined as followed: Complete Symptomatic Remission (CSR: PRO-2 = 0, no urgency), Endoscopic Remission (ER: Mayo 0–1, UCEIS 0–1), Complete Endoscopic Remission (CER: Mayo 0, UCEIS 0–1), Histological Remission (HR: Geboes 0–1), and FCP <150 µg/g; and Deep Remission as combined CCR, CER, and HR. In the absence of CER, physicians completed a questionnaire to investigate the reasons for not altering therapy.

Results: From December 2022 to February 2024, 198 UC patients (median age 50, 41% female) were enrolled from 14 centres. Montreal classifications were E1 (37%), E2 (44%), and E3 (18%). Treatment included oral 5-ASA (n=134, 68%), rectal 5-ASA (n=19, 9%), and a combination (n=45, 23%) with a median duration of 2.0 years (1.0 – 4.0). Among patients on oral 5ASA monotherapy 20% received <2g/d, 63% 2 to 3 g/d and 17% >3 g/d. The median MARS-5 score was 24. ER was observed in 172/198 patients (87%), CER in 138/198 (70%), and HR in 156/196 (80%). Among those in ER, CER, 151/172 (88%) and 127/137 (93%) also had HR, respectively. Normal FCP was seen in 152/194 (78%) and in 128/153 (83%) of the HR subgroup. 5-ASA administration form was significantly associated with ER (p=0.5, OR=2.9, 95%CI 1.1-7.3) for oral against combined. Deep remission was achieved in 47/197 (24%) of patients. The main reason for absence of deep remission was the absence of CSR (63%). In case of absence of CER, only 37% of physicians answered the questionnaire. The main reason for not altering treatment, was physician reluctance in 36% of cases, low compliance of patient according to the physician in 11%, and patient not willing to change in 1.8%.

Conclusions: In UC patients in clinical remission on 5-ASA, the majority achieved endoscopic and/or histological remission, suggesting that higher remission levels beyond clinical remission alone are attainable in selected, highly adherent patients on first-line therapy.

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ESTIMATED BENEFITS AND WILLINGNESS OF REMOTE MONITORING IN IBD PATIENTS UNDER MAINTENANCE THERAPY. D. Beeckmans (1), S. Brams (1), S. Delen (2), L. Fierens (3), M. Vanhaverbeke (3), J. Sabino (1), B. Verstockt (1), S. Vermeire (1), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Department of Gastroenterology and Hepatology, [3] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism.

Introduction: Following STRIDE II guidelines, patients with inflammatory bowel diseases (IBD) are tightly monitored evaluating effectiveness of the IBD-therapies and predicting flares accurately. In many centres, patients on stable conventional therapy typically have annual outpatient visits with their IBD physician, while patients on advanced therapies are seen every six months. However, the growing number of IBD patients in active follow-up is straining outpatient clinic capacity and increasing time pressures on healthcare professionals. Furthermore, many patients do not require specialised interventions during these visits, and those in long-term remission often prefer less frequent follow-up to reduce absenteeism from work or school. New care models answering these challenges are therefore needed.

Aim: We aimed to evaluate the potential optimization of resources of remote monitoring for IBD patients in a large-volume referral centre.

Methods: An anonymous survey was conducted in 300 adult patients with IBD, either untreated or on stable subcutaneous or oral maintenance therapy for at least two years, to assess their interest in a remote monitoring program and gather insights into their preferences for its implementation and into their cost and time savings.

Results: Of the 300 patients, 48% were male, 68% had Crohn's disease, 31% ulcerative colitis and 1% IBD type unclassified. Forty-one percent of patients had a disease duration of more than 20 years. Additionally, 17% were without any IBD-related therapy, 9% were on conventional therapy only, and 74% were receiving advanced subcutaneous or oral therapy. Most patients (68%) were actively employed, 70% of whom worked full-time. Notably, 77% (n=230) expressed interest in significantly reducing their outpatient clinic visits in favour of remote monitoring. Most patients that did not want to reduce outpatient clinic visits mentioned that they first need more information on the remote monitoring program or that they prefer face to face contact. The study also identified cost and time savings for patients, as an outpatient visit takes approximately 3 hours (range 2-4 hours). Also, 14% (n=41) used public transport and the median cost to attend the clinic was 12 euros (range 0-56EUR). Moreover, 86% travelled by car or motorcycle (n=258) and the median travel distance was 35 km (range 18-60km). The use of a home-base stool analysis twice a year would be an additional cost for patients on remote monitoring, however this tool could save time for the patient. Patients on remote monitoring can also choose to bring their stool sample to a local lab for faecal calprotectin analysis. In this case, costs are equal for patients on remote monitoring and patients visiting the clinic every six months. Costs considering transport, parking and consultation will decrease with a factor four in a time frame of two years for patients on remote monitoring. Among the patients interested in remote monitoring, 94% were willing to complete three-monthly questionnaires taking about 10 minutes, and 94% agreed to annual blood analyses. Regarding faecal calprotectin, 66% were open to conducting home-based stool analyses every three months, while 72% would agree to bring a stool sample to their general practitioner or local hospital. Also, 79% were willing to attend biennial outpatient clinic visits. Patients also emphasized the importance of personal contact in establishing a trustworthy and safe remote monitoring system. We expect the reduced number of

outpatient clinic visits to result in a direct cost benefit for RIZIV-INAMI. Secondly, the decreased waiting times (a rough estimation of two months due to remote monitoring) for new or more urgent patients are expected to result in a reduction of emergency admissions and hospitalisations. This will result, in turn, in a cost benefit for RIZIV-INAMI. From a societal perspective, we expect that the strongest benefit will be observed in a reduced absenteeism. Remote monitoring is aiming for better health care and for an economic advantage on the level of different perspectives.

Conclusions: Remote monitoring is a promising program for IBD patients in stable remission, offering potential financial and time savings for employers, patients, and society. However, further research is required to evaluate the safety and feasibility of this approach.

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IMPROVED HISTO-ENDOSCOPIC OUTCOMES WITH VEDOLIZUMAB IN EARLY VERSUS LATE CROHN'S DISEASE REGARDLESS OF DISEASE LOCATION: INSIGHTS FROM THE LOVE-CD TRIAL. M. Lenfant (1), G. De Hertogh (2), F. Baert (3), P. Bossuyt (4), M. Löwenberg (5), E. Clasquin (5), F. Hoentjen (6), T. Molnár (7), G. D'Haens (5), S. Vermeire (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology, [3] AZ Delta, Belgium, Gastroenterology, [4] Imelda General Hospital, Belgium, Gastroenterology, [5] Amsterdam University Medical Centres, The Netherlands, Gastroenterology, [6] University of Alberta, Alberta, Canada, Gastroenterology, [7] University of Szeged, Szeged, Hungary, Internal Medicine.

Introduction: Achieving deep remission, encompassing clinical, endoscopic, and biological remission, is a long-term goal in Crohn's disease [CD] according to the STRIDE-2 guidelines. The role of histological remission in CD remains unclear.

Aim: We evaluated the efficacy of vedolizumab [VDZ] for inducing combined endoscopic and histological remission in early versus late CD in the prospective, open-label LOVE-CD trial conducted in Belgium, the Netherlands and Hungary.

Methods: In the LOVE-CD trial, patients with moderate-to-severe disease (Crohn's Disease Activity Index 220-450 and presence of ulcers at baseline endoscopy) received intravenous vedolizumab over a 52-week period. Early CD was defined as a diagnosis <24 months (treatment-naïve or history of corticosteroid and/or immunomodulator use), and late CD as a diagnosis >24 months with prior anti-TNF exposure (and corticosteroids and/or immunomodulator use). Ileocolonoscopies were performed at three timepoints (baseline, week 26, week 52) during which biopsies were systematically collected in the terminal ileum and colon. Both the endoscopies and biopsies were centrally scored by experienced readers for the simple endoscopic score for Crohn's disease [SES-CD], Roberts' histopathology index [RHI], and Geboes score [GS]. Endoscopic remission, histo-endoscopic mucosal improvement [HEMI], and histo-endoscopic mucosal remission [HEMR] were defined as SES-CD <4, GS ≤3B.1, and GS <2B.1 respectively. The association between histologic and endoscopic scores was studied with Spearman's rank correlation coefficient. Intention-to-treat analysis with non-responder imputation was used to handle missing data.

Results: Out of 260 patients included in LOVE CD (86 early CD, 174 late CD), data from 440 biopsies (336 colon, 114 ileum) obtained from 179 patients were available at week 26, and 435 biopsies (323 colon, 112 ileum) from 177 patients were available at week 52. There was a strong correlation between the endoscopic and histological assessment (colon r 0.69, ileum r 0.64, total r 0.64, $p < 0.001$). Patients with early CD were more likely to achieve histological remission than patients with late CD at week 52 (38.4 % vs. 14.9%, $p = 0.00004$). Endoscopic and histological healing rates at week 26 (endoscopic remission 36.9%, HEMI 30.4%, HEMR 24.2%) and week 52 (endoscopic remission 35%, HEMI 30%, HEMR 22.7%) were comparable. When looking at disease location, histological remission rates in the colon and ileum did not significantly differ (35.2% vs. 27.8%, $p = 0.15$).

Conclusions: Vedolizumab was more effective at inducing endoscopic and histological remission in early CD as compared to late CD, with most of the histo-endoscopic healing occurring during the first 26 weeks. Histo-endoscopic healing rates under vedolizumab were comparable in colonic and ileal disease. Histological scores (RHI, GS) are also applicable for the evaluation of ileal and colonic CD.

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ENDOSCOPIC REMISSION IN CROHN'S DISEASE, THE CREDO TRIAL: INTER-READER VARIATION STUDY OF THE DETECTION OF ENDOSCOPIC LESIONS ASSUMED CONSENSUALLY TO BE RELATED TO REMISSION. P. Bossuyt (1), J. Mary (2), E. Louis (3), F. Baert (4), L. Caillio (5), N. de Suray (6), P. Dewint (7), M. Ferrante (8), J. Filippi (9), D. Laharie (10), C. Reenaers (3), M. Simon (11), C. Stefanescu (12), C. Trang (13), L. Vuitton (14), S. Vermeire (8), Y. Bouhnik (12) / [1] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology, [2] Hospital Saint Louis, France, UMR1153 Inserm CRESS- équipe ECSTRRA- SBIM, [3] CHU Liege, Liège, Belgium, Department of gastroenterology, [4] AZ Delta, Roeselare, Belgium, Department of gastroenterology, [5] CHU Nimes, Nimes, France, Department of gastroenterology, [6] Grand Hôpital de Charleroi, Charleroi, Belgium, Department of gastroenterology, [7] Maria Middelaers Ziekenhuis, Gent, Belgium, Department of gastroenterology, [8] University

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Introduction: There is no clear consensus on the definition of endoscopic remission in Crohn's disease (CD). Indeed, existing endoscopic scoring systems for CD focus primarily on disease activity rather than on remission. The CREDO programme aims to define an objective measure (depth or grade) of endoscopic remission in CD.

Aim: This inter-reader variation study aims to assess reproducibility in identifying endoscopic lesions that are assumed broadly agreed to be associated with remission.

Methods: Sixteen centres in Belgium and France were involved in the study of patients with CD in clinical and biochemical remission (CDAI <150 and CRP <5 mg/l and faecal calprotectin <250 µg/g). Lesions potentially related or not to remission in CD were predefined by the principal authors, then discussed and refined during a consensus meeting with 12 central readers (CRs) and the local endoscopists. Fifteen patients per centre were planned to be selected with an endoscopy representing equally complete remission, almost complete remission, not complete, nor an almost complete remission according to local endoscopist appraisal. Finally, 210 patients were enrolled with 15 endoscopy videos recorded within each of the 14 centres. The 14 centres and 12 CRs were splitted in two balanced groups. Within each group, readings of the 15 videos per centre were randomly assigned to the 6 CRs using a balanced incomplete block design, each video being read by 4 CRs and each CR reading 10 videos. In each group, this design was replicated 7 times leading to 105 videos randomly assigned to 6 CRs, 4 CRs reading each video and 70 videos being read by each CR (efficiency factor of 0.90). Inter-reader reproducibility level of each lesion was evaluated within each group by the intraclass correlation coefficient (ICC) (a). Benchmark ICC limits widely accepted are 0.4-0.6, 0.6-0.8, 0.8-1.0 to define moderate, substantial, almost perfect agreement, respectively (b).

Results: Highly variable inter-reader reproducibility level was observed for the different lesions in group 1. Level of reproducibility was substantial for passable stenosis, pseudopolyp type white and red, mucosal defect and ulcer. It was moderate for stenosis, ulcerated stenosis, surelevated scarred lesion, raised trabecular scar, erosion with halo, erosion, punctiform lesion, deep ulcer, superficial ulcer and alteration of vascular pattern type white. Results of reproducibility levels estimated in group 2 were similar despite less frequent lesions.

Conclusions: Our inter-reader variation study findings provide a foundation for developing an objective and standardized definition of endoscopic remission in CD.

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LONG TERM REAL-WORLD EFFECTIVENESS AND SAFETY OF UPADACITINIB IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE: A BELGIAN MULTI-CENTRIC REFRACTORY COHORT. A. Pavlidi (1), B. Verstockt (2), S. Vieujeun (3), V. Desmedt (4), F. Couturier (5), J. Rahier (6), F. Baert (7), M. Somers (8), O. Dewit (9), P. Bossuyt (10), A. Hoyois (11), T. Holvoet (12), R. Ouziel (13), B. Willandt (14), G. Lambrecht (15), M. Salamé (16), A. Verreth (17), M. Lenfant (2), D. Franchimont (1), A. Cremer (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology, [3] University Hospital CHU of Liège, Belgium, Department of Gastroenterology, [4] University Hospital of Ghent, Belgium, Department of Gastroenterology, [5] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Department of Gastroenterology, [6] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Department of Gastroenterology, [7] AZ Delta, Belgium, Department of Gastroenterology, [8] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology, [9] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Gastroenterology, [10] Imelda General Hospital, Belgium, Department of Gastroenterology, [11] CHU Saint-Pierre, Brussels, Belgium, Department of Gastroenterology, [12] Vitaz, Sint-Niklaas, Belgium, Department of Gastroenterology, [13] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Department of Gastroenterology, [14] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Department of Gastroenterology, [15] AZ Oostende, Oostende, Belgium, Department of Gastroenterology, [16] CHR De la Haute Senne, Soignies, Belgium, Department of Gastroenterology, [17] AZ Voorkempen, Malle, Belgium, Department of Gastroenterology.

Introduction: The therapeutic options for inflammatory bowel disease (IBD) have expanded with the introduction of JAK inhibitors. However, real-world data on upadacitinib (UPA) in patients with moderate to severe Crohn's Disease (CD) are scarce.

Aim: Our aim was to assess the long-term effectiveness and safety of UPA in multi-refractory Belgian patients.

Methods: Data from all patients with active CD initiating UPA between September 2022 and January 2024 were retrospectively collected from 17 Belgian centres. Effectiveness endpoints were evaluated at week 24 and 52. Steroid-free clinical response and remission were defined using the two-component patient-reported outcome. Endoscopic response was defined as a decrease in baseline Simple Endoscopic Score (SES-CD) with $\geq 50\%$, and endoscopic remission as SES-CD ≤ 4 or absence of ulcers. Adverse events (AE), treatment discontinuation, CD-related hospitalization and surgery were assessed throughout follow-up. Non-response imputation was applied for clinical evaluation.

Results: A total of 140 patients were included with a median follow-up of 33 weeks (IQR: 3-97). Patients were predominately female (57%), median age at baseline was 40 years old (IQR: 14-70) and median disease duration was 13 years (IQR: 0-45). 23% of the patients had ileal CD, 18% colonic CD, 59% ileocolonic CD with 16% concomitant upper gastrointestinal CD and 38% concomitant perianal disease. The majority of the patients (89%) was exposed to ≥ 3 biologics and 59% had previously undergone a CD-related surgery. At week 24, 53% and 40% of patients achieved steroid-free clinical response and remission, respectively. At week 52, these numbers were 37% and 29%. Endoscopic data were available in 48/140 patients at week 24, of whom 52% and 27% reached endoscopic response and remission. At week 52, these numbers were 63% and 37%. Of patients with active articular extra-intestinal manifestations at baseline 37% and 34% had a quiescent articular disease by week 24 and 52, respectively. 5 out of 9 patients with active perianal disease at baseline and on UPA by week 52, had persistent perianal active disease. Overall, 66 patients (47%) discontinued UPA during follow-up: 23 due to primary non-response, 13 due to secondary loss of response, 16 due to AE, 3 due to patient's choice and 11 due to CD-related surgery. 16 patients required CD-related hospitalization within 52 weeks. AEs occurred in 60% of patients (84/140). Of these patients 11% experienced serious AE of which 2 cardiovascular events: 1 transit ischemic attack and 1 deep venous thrombosis. The most common reported AEs were herpes simplex reactivation (5/140), respiratory tract infection (7/140), cutaneous reactions (7/140) and acne (17/140). Only 3 patients had reactivation of herpes zoster infection.

Conclusions: In this real-world cohort of highly refractory CD patients, UPA effectively induced both steroid-free clinical remission and endoscopic remission by week 52. UPA was relatively well tolerated with respect to adverse events.

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A MINDFULNESS-BASED INTERVENTION HAS SIGNIFICANT EFFECTS ON DEPRESSION, STRESS AND PERCEIVED CONTROL BUT NOT ON DISABILITY IN PATIENTS WITH CROHN'S DISEASE. B. Keersmaekers (1), D. Beeckmans (1), S. Brams (1), K. Vanderbist (1), M. Van den Bosch (2), S. Vermeire (3), B. Verstockt (3), J. Sabino (3), I. Van Diest (4), M. Ferrante (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Leuven Mindfulness Centre, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] KUL - University of Leuven, Leuven, Belgium, Department of Health Psychology.

Introduction: Crohn's disease (CD) is often associated with significant disability and psychological distress, significantly reducing patients' quality of life.

Aim: We evaluated the impact of a mindfulness-based intervention on disease-related disability in patients with CD on stable maintenance therapy. Additionally, we wanted to assess the impact of mindfulness on anxiety, depression, stress, disease acceptance, perceived control, and disease activity.

Methods: We conducted a monocentric randomized controlled trial (RCT), where participants were randomly assigned to either an immediate intervention group or a waitlist control group that received the same intervention after six months. The IBD Disability Index at screening (IBD-Disk ≥ 40 or <40) was used as a stratification factor. Disease activity was measured through patient-reported outcomes (PRO-2) and biomarkers, including faecal calprotectin and C-reactive protein (CRP), which were all assessed at baseline, as well as at 1.5- and 3-months follow-up. IBD-related disability was evaluated using the IBD-Disk, while psychological factors including anxiety, depression, and stress were assessed using the DASS21 scale. Disease acceptance and perceived control were measured using the SHE model, and mindfulness levels were evaluated with the FFMQ-SF. The intervention consisted of four mindfulness group sessions of three hours each over six weeks. The primary outcome was the mean change in the total IBD-Disk score at three months and was analysed using a constrained longitudinal data analysis (cLDA). Based on power calculation ($\alpha=0.05$, power=0.80), 54 patients had to be randomized.

Results: Out of the 58 patients that were screened, 52 patients (38% male, median age 49.5 years) were randomized into the immediate intervention group (n=26) or the six-month waitlist control group (n=26) and included in the full analysis set. Baseline characteristics were comparable between both groups with 38% vs. 38% male, median age 51 vs. 49 years, disease duration 27 vs. 20 years, prior surgery 73% vs. 73%, clinical remission based on average daily liquid stool frequency ≤ 2.8 and abdominal pain score ≤ 1 11% vs. 14%, median C-reactive protein 1.1 vs. 1.4 mg/L, and median faecal calprotectin 59 vs. 58.5 mg/kg. None of the patients were on steroids or immunomodulators, while anti-TNF agents were used by 46% vs. 35%, anti-interleukins by 15% vs. 31%, vedolizumab by 8% vs. 12% and JAK inhibitors by 4% vs. 0%. Compared to the waitlist, participants in the intervention group showed significant improvements in depression (-5.27 vs. -0.97, $p = 0.0118$), stress (-8.09 vs. -1.30, $p = 0.0026$), perceived control (0.82 vs. 0.09, $p = 0.0119$),

and mindfulness after three months (8.87 vs. 0.92, $p = 0.0002$). Although improvements in disease-related disability (-8.07 vs. -4.37, $p=0.3240$), anxiety (-3.25 vs. -1.29, $p=0.2532$), and disease acceptance (0.74 vs. 0.40, $p=0.3846$) showed positive trends, these items did not reach statistical significance. No changes were observed in clinical and biochemical markers of disease activity.

Conclusions: A 6-weeks mindfulness-based intervention can significantly improve depression, stress, perceived control, and mindfulness in patients with CD, with effects sustained 3 months post-intervention. Although numerically better, no significant effects were found on disease-related disability. Further research is warranted to explore the long-term benefits and underlying mechanisms of mindfulness in CD management.

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LOW REMISSION RECAPTURE AFTER USTEKINUMAB DOSE OPTIMIZATION IN CROHN'S DISEASE: RESULTS OF THE RANDOMIZED PLACEBO-CONTROLLED DOUBLE-BLIND RESCUE STUDY. P. Bossuyt (1), J. Rahier (2), F. Baert (3), E. Louis (4), E. Macken (5), T. Lobaton (6), J. Busschaert (7), H. Peeters (8), P. Dewint (9), D. Franchimont (10), J. Dutré (11), B. Willandt (12), C. Claessens (13), O. Dewit (14), M. Ferrante (15), S. Vermeire (15) / [1] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology, [2] Centre Hospitalier Universitaire Mont-Godinne, , Belgium, Department of Gastroenterology, [3] AZ Delta, Belgium, Department of Gastroenterology, [4] CHU de Liège, Liège, Belgium, Department of Gastroenterology, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology, [6] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology, [7] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Department of Gastroenterology, [8] AZ Sint-Lucas, Ghent, Belgium, Department of Gastroenterology, [9] AZ Maria Middelaers, Ghent, Belgium, Department of Gastroenterology, [10] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, [11] ZNA Jan Palfijn, Merksem, Belgium, Department of Gastroenterology, [12] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Department of Gastroenterology, [13] AZ Turnhout, Turnhout, Belgium, Department of Gastroenterology, [14] UCL Saint Luc, Brussels, Belgium, Department of Gastroenterology, [15] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: In Crohn's disease (CD), an exposure-response relationship exists for ustekinumab, with higher serum levels associated with better outcomes. Although several retrospective and observational studies demonstrate dose-escalation of ustekinumab can be effective in case of secondary loss of response (LOR), prospective placebo-controlled data are lacking.

Aim: The aim of the REScUE study (NCT04245215) was to investigate the effect of 2 different re-induction regimens with ustekinumab on clinical, endoscopic, biological and pharmacological outcomes in patients with CD.

Methods: This Belgian multicentre prospective double-blind randomized placebo-controlled trial included adult patients with CD treated with ustekinumab who presented with secondary LOR to ustekinumab after documented primary response. Secondary LOR was defined by PRO-2 (abdominal pain score > 1 AND liquid or very soft stool frequency > 3) and confirmed by either an elevated biomarker (CRP > 5 mg/L or faecal calprotectin > 250 μ g/mg) or endoscopic signs of inflammation. All patients received a single IV re-induction with ustekinumab (≈ 6 mg/kg) and were then randomized 1:1 to blinded maintenance ustekinumab 90 mg SC Q4W (intervention) or 90 mg SC Q8W (control) for 48 weeks. Primary endpoint was proportion of patients with steroid-free clinical remission (definition: PRO2 (AP ≤ 1 AND SF ≤ 3) and FCP < 250 μ g/g and no steroids for 90 days prior to week 48) at week 48, missing data were handled using non-responder imputation.

Results: In total, 132 patients were screened, and 108 patients were included: 67% female, median [IQR] age 41 [32-54] year, median disease duration 14 [7-22] years. Prior anti-TNF exposure was reported in 92% of patients, while ustekinumab was the first-line advanced treatment in 7% of patients. The primary endpoint of steroid-free clinical remission at week 48 was achieved by 9/54 (17%) patients in the q4w regimen vs 8/54 (16%) in the q8w regimen ($p=0.96$). Endoscopic remission (SES-CD < 3) was achieved in 5/54 (10%) vs 3/54 (6%) ($p=0.52$), endoscopic response ($\geq 50\%$ decrease in SES-CD from baseline) was achieved in 11/54 (22%) vs 6/54 (12%) ($p=0.23$) and 0.52biomarker remission was achieved in 20/54 (38%) vs 13/54 (26%) ($p=0.19$) in the q4w regimen vs the q8w regimen, respectively. Time to first clinical remission was similar between groups. Association with ustekinumab serum levels will be reported. No new safety signals were observed.

Conclusions: In patients with CD experiencing secondary LOR to ustekinumab, dose optimization with a single IV re-induction followed by intensified maintenance dosing (90 mg SC q4W) was not superior to a single IV re-induction followed by conventional maintenance dosing (90 mg SC q8W) in achieving steroid-free clinical remission. The secondary endpoints were numerically higher but not significant in the intensified regimen.

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NATURAL HISTORY AND MRI PREDICTIVE FACTORS OF RADIOLOGICAL HEALING IN FISTULISING PERIANAL CRONH'S DISEASE. V. Delmotte (1), R. Gillard (2), E. Defraigne-Peigneur (2), E. Louis (1), P. Meunier

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Introduction: Fistulising perianal Crohn's disease (CD) is a disabling condition affecting up to 30 % of patients. While mucosal healing is associated with a better clinical outcome in luminal CD, the objective of the management of perianal CD is less clear. Radiological parameters are rarely considered as predictive factors of the disease evolution nor as an outcome. Some studies have suggested that a high degree of fibrosis of the fistula tract was associated with a better clinical outcome.

Aim: The aim of this study was to describe the natural history of perianal CD including MRI parameters and to identify clinical and radiological factors of perianal CD relapse and radiological healing.

Methods: All pelvic MRI performed for fistulizing perianal CD in the CHU of Liège, Belgium, between 2018 and 2023 were collected. MRI examinations were performed according to the protocol of the institution, using a 1.5-T [Siemens Aera or Sola] or 3-T [Siemens Vida] machine, including T2 turbospin-echo, T2 TSE fat-saturated, T1 TSE FS before contrast in the axial plane and T1 TSE FS after gadolinium. The MAGNIFI-CD index and the Van Assche (VA) index were evaluated for each patient. The degree of fibrosis of the fistula tract was evaluated by two radiologists, blinded for the clinical history. The first MRI was evaluated in all patients. Patients with perianal flare had only one MRI included in the analysis. The first and the last MRI performed during the study period were analysed, if available, in patients without perianal flare. Perianal flare was defined by the drainage of an abscess or a stoma for active perianal CD. Radiological healing was defined by a fibrosis of the fistula tract $\geq 80\%$ or a MAGNIFI CD score of 0.

Results: One-hundred and two pelvic MRI from 84 patients were included in the study. The median age of the patients was 39.0 (31-51) years old, 34 (40%) patients were female, the median duration of perianal CD was 52.00 (2-144) months, 22 (25.9%) had a seton at the time of the first MRI, 35 patients (41%) were on anti-TNF. Nineteen (22.4%) patients required at least one abscess drainage in the follow-up period. No clinical factors were associated with perianal flare. Several radiologic factors at MRI 1 were predictive of a flare in univariate analysis: % of fibrosis (OR=0.72, $p=0.033$), VA Hyperintensity T2 (OR=3.22, $p=0.028$), au VA rectal involvement (OR=1.75, $p=0.040$), VA inflammatory mass (OR=1.42, $p=0.022$), VA hyperintensity on T1 postC (OR=3.68, $p=0.045$), MAGNIFI CD score (OR=1.13, $p=0.022$), MAGNIFI hyperintensity on postcontrast T1 (OR=1.77, $p=0.031$), MAGNIFI inflammatory mass (OR=1.40, $p=0.033$). In multivariate analysis, only MAGNIFI hyperintensity on postcontrast T1 was significant (OR=1.77, $p=0.031$). Thirty % of the patients had radiological healing at MRI 1 (25/84) and 44% (8/18) at MRI 2. No clinical nor radiological factors at MRI 1 were predictive of radiological healing at MRI 2 but a trend was observed for hyperintensity on postcontrast T1 (OR=0.11 $p=0.071$) at the first MRI to predict the absence of radiological healing during the follow-up.

Conclusions: One fifth of the patients experienced perianal flare during the follow-up. Clinical and therapeutic factors were not predictive of clinical outcome. Only persistent signs of inflammation at pelvic MRI and low rates of fistula tract fibrosis were associated with future abscess drainage. Specific features at pelvic MRI should be evaluated as potential therapeutic goals in the management of perianal CD. These findings need validation in a prospective cohort.

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OPTIMIZING PATIENT-REPORTED OUTCOME MEASUREMENT IN AN IBD CARE PATHWAY: RESULTS OF THE PROMOTION STUDY. N. Lembrechts (1), S. Louis (1), K. Geerts (1), K. Van Brantegem (1), J. Derua (1), P. Bossuyt (1), L. Pouillon (1) / [1] Imelda Hospital, Bonheiden, Belgium, Gastroenterology.

Introduction: Patient-reported outcome measurements (PROMs) are essential for the clinical evaluation of patients and serve as a key quality indicator in IBD. Patient engagement is needed to collect PROMs but often remains suboptimal.

Aim: The PROMOTION (Patient Reported Outcome Measurement questiOnnaire intervenTION) study evaluated the response rate to PRO questionnaires before and after a patient empowerment intervention. Additionally, we assessed the number of patients with IBD in PRO-2 remission in an entire cohort.

Methods: PROMOTION was a single-centre, nurse-led prospective study, including all patients in follow-up within the designated IBD care pathway during the study period (January to September 2024). PRO questionnaires (PRO-2, IBD Disk, IBD Control) were sent before every (in-person or remote) ambulatory consultation, and bi-annual to patients in follow-up at the day clinic for IV therapy. The intervention was an information and empowerment campaign that took place in April 2024, aiming to improve patients' insights in the use and importance of PROMs. Response rates (percentage of questionnaires that were returned with partial or complete answers) were evaluated three months before (period 1) until six months after (period 2) the intervention. Secondary outcomes included the number of patients in PRO-2 remission during follow-up (CD: abdominal pain 0 or 1 and stool frequency max 3; UC: rectal bleeding =0 and stool frequency =0 or 1).

Results: A total of 1593 PRO questionnaires were sent to 811 individual patients during follow-up. Overall response rate was 58.6% (933/1593). Almost half (45%, 190/422) of the non-responders had low digital literacy. Responders and non-responders did not differ in mean (SD) age (47 (16) yrs for responders vs 51 (19) yrs for non-responders) nor in type of follow-up (consultation vs infusion unit). There was no difference in the overall response rate in the periods before

month after the intervention were, however, significantly higher than in the rest of the study period (71.8% (79/110) vs 57.6% (854/1483); $p=0.004$). PRO-2 remission was seen in 65.4% (323/494) of the total population who fully completed all questionnaires, with similar proportions seen in patients with CD (62.3%, 177/284) and UC (69.5%, 146/210; $p=0.1$). **Conclusions:** Improving patient participation in the assessment of PROMs by a single patient empowerment intervention leads to good short-term but poor long-term results. A more continuous motivational approach with direct feedback to the patients warrants further investigation. Clinical remission, as targeted by STRIDE-II, was achievable in the majority of patients.

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A RISK STRATIFICATION ALGORITHM TO PREDICT RELAPSE DURING INTRAVENOUS-TO-SUBCUTANEOUS SWITCHING OF INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Y. Hoffert (1), Z. Wang (1), M. Fumery (2), M. Nachury (3), M. Bazoge (4), A. Buisson (4), E. Dreesen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University Hospital of Amiens, France, Gastroenterology and Unité Peritox, [3] University of Lille, Inserm, CHU Lille, France, INFINITE Institute for Translational Research in Inflammation, [4] Université Clermont Auvergne, Clermont-Ferrand, France, Department Gastroenterology/Hepatology.

Introduction: A subcutaneous (SC) formulation of infliximab was recently approved for maintenance therapy of patients with inflammatory bowel disease (IBD). However, limited clinical experience, particularly with patients on escalated intravenous (IV) infliximab regimens, poses challenges for the transition to subcutaneous therapy, preventing the broad use of SC infliximab. We investigated the pharmacokinetics and pharmacodynamics of subcutaneous infliximab to identify early predictors of relapse upon switching.

Aim: We aim to inform the IV-to-SC switching to minimize the risk of relapse by identifying baseline characteristics to predict relapse.

Methods: We repurposed data from a prospective, multicentre trial (REMSWITCH trial) involving patients with IBD switching from IV to SC infliximab. We estimated each patient's infliximab clearance using Bayesian forecasting from a pre-switch sample and a population pharmacokinetics model. We performed logistic regression pharmacodynamics modelling to evaluate pre-switch predictors of post-switch relapse. To predict relapse, baseline phenotype and pharmacokinetic infliximab projections of individuals were tested. The best model was defined based on the corrected Akaike Information Criterion (AICc), a fitting parameter penalizing the number of parameters in a model, and low multicollinearity to prevent parameter correlation. Relapse was defined as clinical recurrence (partial Mayo score >2 or Harvey-Bradshaw Index >4) or an increase in faecal calprotectin ≥ 150 $\mu\text{g/g}$ upon switching. All modelling and simulation tasks were performed in R (v4.4.1).

Results: In total 98 patients (52% female) were included in the present analysis of which 14 experienced relapse after switching to a SC formulation. The majority of patients (45/98, 45.9%) patients received 5 mg/kg as a IV pre-switch dosing regimen, and 93/98 (94.9%) patients received 120 mg every other week after switching to SC formulation. At baseline, mean c-reactive protein was 2.5 mg/L (standard deviation 3.3 mg/L), and mean faecal calprotectin was 213.8 $\mu\text{g/g}$ (542.9 $\mu\text{g/g}$). The majority of the Crohn's disease patients were classified with a Harvey Bradshaw index of 0 (47/74, not available for two patients) and the majority of ulcerative colitis patients were classified with a partial Mayo score of 0 (17/21, not available for one patient). We identified infliximab clearance and faecal calprotectin as independent predictors of relapse. With increasing CL and faecal calprotectin, the risk of relapse increases. A model-based probability of relapse of 20%, derived from the Youden J index, discriminates best between patients with and without relapse. We developed a two-item risk score to stratify patients into low-risk ($<20\%$ probability of relapse; 79/98; 81%) and high-risk ($\geq 20\%$ probability of relapse; 19/98; 19%) groups (sensitivity 0.58 [95%CI 0.33–0.80], specificity 0.96 [95%CI 0.89–0.99], positive predictive value 79% [95%CI 49–95%], negative predictive value 90% [95%CI 82–96%]). The classification accuracy of our algorithm was 89% [81–94%]. Our pharmacokinetics-pharmacodynamics model successfully classified patients with and without relapse ($p < 0.0001$) with an area under the receiver operating characteristic curve of 0.83 (95%CI 0.68–0.95).

Conclusions: The present work introduces a pharmacokinetics-pharmacodynamics model of infliximab that can be used to predict individual patients' probability of relapse upon switching from intravenous to subcutaneous infliximab. Baseline infliximab clearance and faecal calprotectin are accurate and independent predictors of relapse after switching to SC infliximab therapy. Both, increased infliximab clearance and faecal calprotectin are alarm signals for relapse. An interactive risk stratification tool is provided to facilitate confirmation of a stratified medicine approach to improve infliximab therapy in IBD. The software tool is freely available and accessible at <https://lpmx.shinyapps.io/infliximab/>.

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DEVELOPMENT AND VALIDATION OF THE FR-QOL-29-DUTCH (FLEMISH) QUESTIONNAIRE SHOWS THAT FOOD-RELATED QUALITY OF LIFE IS DECREASED IN CROHN'S DISEASE, STRICTURING DISEASE

and after the intervention (period 1: 57.7% (335/581) vs period 2: 59.02% (598/1012); $p=0.6$). Response rates in the first AND THOSE WITH A SURGICAL HISTORY. J. Wellens (1), L. Guadagnoli (2), J. Vanderstappen (1), S. Hoekx (1), J. Vandaele (3), M. Ferrante (1), B. Verstockt (1), K. Whelan (4), S. Vermeire (1), J. Sabino (5) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Northwestern University Feinberg School of Medicine, IL, United States, Division of Gastroenterology and Hepatology, [3] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [4] King's College Hospital London, London, United Kingdom, Department of Nutritional Sciences, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: The food-related quality of life (FRQoL) questionnaire was developed in inflammatory bowel disease (IBD) to evaluate the psychosocial impact of diet, eating behaviours, and food-related anxiety on a person's quality of life. FRQoL has been shown to be reduced in IBD compared to controls and in active disease compared to remission and is associated with reduced intake of key nutrients, although there are no studies in a Belgian population. Since social construct affect dietary habits, proper translation and validation are necessary before implementing the English questionnaire in a different cultural and linguistic context.

Aim: The aim of this study was to translate and validate the FR-QoL-29 instrument into Dutch/Flemish and to investigate FRQoL and factors associated with it in a Belgian IBD population.

Methods: The original FR-QoL-29 was translated from English to Dutch and adapted to the Flemish setting using the forward-backward method. The translated instrument was then reviewed by an IBD patient focus group in collaboration with the Belgian 'Crohn & Colitis ulcerosa Vereniging vzw' to produce the final FR-QoL-29-Dutch (Flemish) questionnaire. All IBD patients attending the outpatient clinic and the infusion unit in one tertiary IBD centre were eligible and recruited from October 2023 to July 2024. Hospitalized patients and patients having an appointment to receive endoscopy were not included in the study. The FR-QoL-29 Dutch (Flemish) was completed alongside symptoms and disease-specific QoL questionnaires, and routine clinical and biochemical data were collected. Exploratory factor analysis (EFA) with promax rotation assessed the underlying factor structure. Reliability measures (internal consistency, test-retest reliability) were evaluated. Pearson correlations examined relationships between FR-QoL-29 scores and disease severity (PRO-2, Manitoba IBD Index) and IBD-related disability (IBD-disk). Correlation between FR-QoL-29 scores and clinical parameters were analysed using independent samples t-tests and Welch's ANOVA with Tukey post-hoc tests as appropriate.

Results: A total of 312 patients with IBD completed the FR-QoL-29-Dutch (Flemish), with 31 (9.9%) patients undertaking a retest within one to two weeks. Mean (SD) age was 45.2 (15.4) years, 46.5% of participants was female, median (SD) Body Mass Index was 25.7 (4.9) kg/m² and 64.4% of participants were diagnosed with Crohn's disease (CD). EFA revealed a one-factor structure explaining 55% of the variance. The FR-QoL-29-Dutch (Flemish) showed excellent internal consistency (Cronbach's $\alpha = 0.97$) and very good test-retest reliability (intraclass correlation = 0.94 [95% CI: 0.88-0.97]). Mean (SD) scores were 86.34 (24.6). Lower FR-QoL-29 scores were significantly correlated with increased disease activity (Manitoba: $r=-0.49$; PRO-2 for CD: $r=-0.48$; PRO-2 for UC: $r=-0.38$) and IBD-related disability ($r=-0.54$; all $p<0.001$). FR-QoL-29 scores were lower in CD ($p=0.01$) and those with a history of surgery ($p<0.0001$). Likewise, patients with stricturing CD (Montreal B2) had significantly lower FR-QoL-29 scores compared to B1 and B3 (all $p<0.01$). There were no differences when using advanced treatments or neuromodulators.

Conclusions: The FR-QoL-29-Dutch (Flemish) is a valid and reliable tool to assess FRQoL in IBD patients in the Flemish setting. FR-QoL-29 correlates with disease activity and IBD-related disability. CD patients, those with stricturing disease and those who underwent surgery have significantly lower FRQoL and should be targeted for dietetic and/or psychological support.

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REAL-LIFE HISTOLOGICAL REMISSION IN ULCERATIVE COLITIS PATIENTS TREATED WITH USTEKINUMAB: RESULTS FROM THE BELGIAN SULTAN TRIAL. T. Holvoet (1), M. Truyens (2), C. Reenaers (3), F. Baert (4), S. Vandenbranden (5), A. Cremer (6), L. Pouillon (7), P. Dewint (8), W. Van Moerkercke (9), J. Rahier (10), L. Vandermeulen (11), J. Van Dongen (12), H. Peeters (13), G. Lambrecht (14), A. Vijverman (15), A. Hoorens (16), A. Van Haecke (17), T. Lobaton (18) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology, [2] University Hospital of Ghent, , Belgium, Gastroenterology, [3] CHU de Liège, Liège, Belgium, Gastroenterology, [4] AZ Delta, , Belgium, Gastroenterology, [5] OLV Aalst, Aalst, Belgium, Gastroenterology, [6] Erasme Hospital, Brussels, Belgium, Gastroenterology, [7] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [8] AZ Maria Middelaars, Ghent, Belgium, Gastroenterology, [9] AZ Groeninge, Kortrijk, Belgium, Gastroenterology, [10] CHU UCL Namur, Yvoir, Belgium, Gastroenterology, [11] UZ Brussel, Brussels, Belgium, Gastroenterology, [12] AZ Sint Maarten, Mechelen, Belgium, Gastroenterology, [13] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology, [14] AZ Damiaan, Oostende, Belgium, Gastroenterology, [15] CHR Citadelle, Liège, Belgium, Gastroenterology, [16] University Hospital of Ghent, , Belgium, Pathology, [17] Ghent University Hospital, Ghent, Belgium, Pathology, [18] Ghent University Hospital, Ghent, Belgium, Gastroenterology.

Introduction: Histological remission is an aspirational therapeutic target in Ulcerative Colitis (UC) associated with lower relapse rates.¹ Ustekinumab (UST), a monoclonal antibody against the p40 subunit of interleukin (IL) 12 and 23 has shown in the UNIFI trials to be effective and safe in patients with moderate-to-severe UC. However, real-life data on histological remission rates are sparse.

Aim: To assess the real-life histological response and remission rates of UST in patients with UC across Belgian hospitals.

Methods: In this multicentric, retrospective observational study, patients with UC who initialised UST treatment between September 2020 and July 2023 were included. Histological remission was defined as Nancy score = 0, response as Nancy ≤ 1 and assessed at week 16 and 52 by the local pathologist. Other endpoints included steroid-free clinical remission (partial Mayo ≤ 2 with no subscore >1), endoscopic remission (endoscopic Mayo = 0), endoscopic response (Mayo score ≤ 1) and clinical response (decrease in partial Mayo score ≥ 3 points and $\geq 30\%$ plus a decrease in rectal bleeding score ≥ 1 or an absolute rectal bleeding score ≤ 1). UST drug persistence was analysed by Cox regression analysis, predictors of other endpoints by logistic regression.

Results: 120 patients with moderate to severe UC (86% patients with $\geq S2$ severity) were included across 16 participating centres. Median disease duration was 11 years (IQR 9) and 81 (68%) of patients had previously failed 2 or more biologicals. Histological remission was achieved in 3/37 (8%) and 5/45 (11%) at W16 and W52, while histological response was seen in 10.8% (4/37) and 26.7% (12/45) respectively. Steroid-free clinical remission rates were 41/120 (34%) and 38/85 (44%) while endoscopic remission was seen in 23/120 (19%) and 13/52 (25%) at W16 and 52 respectively. Two patients (40%) in histological remission at W52 had an endoscopic Mayo 0 score, while 3 had a Mayo 1 (60%) at the time of evaluation. Active smoking was a negative predictor for achieving steroid-free remission (OR 0.412, $p=0.011$). No significant predictors for histological remission or response could be identified. UST drug persistence by week 52 was 70.8%. Active smoking (OR 3.058, $p=0.02$), vedolizumab non-response (OR 2.592, $p=0.03$) and a high Nancy baseline score (OR 2.46, $p=0.04$) were associated with UST failure.

Conclusions: In this multi-centric, real-life cohort with highly refractory UC patients, UST shows acceptable clinical and endoscopic remission rates, but histological remission rates remain low after one year of treatment.

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COMPARATIVE STUDY OF SUBCUTANEOUS AND INTRAVENOUS INFLIXIMAB IN INFLAMMATORY BOWEL DISEASE: INTERIM ANALYSIS OF A PROSPECTIVE SINGLE CENTRE COHORT (THE SWITCH STUDY). C. Liefferinckx (1), C. Minsart (1), C. Husson (2), C. Helman (1), V. Wambacq (1), L. Amininejad (1), A. Cremer (1), D. Franchimont (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, [2] Université Libre de Bruxelles Faculté de Médecine, Brussels, Belgium, Centre for the study of IBD, Laboratory of Experimental Gastroenterology.

Introduction: Randomized control studies have demonstrated the efficacy of subcutaneous infliximab (IFX SC) compared to placebo, with pioneering studies confirming stable remission after switching partially optimized patients from intravenous (IV) to SC. However, real-life evidence remains scarce on the impact of this switch on effectiveness, safety, pharmacokinetics (PK), and quality of life in IBD management

Aim: This is a 1 year longitudinal prospective single centre cohort study (EC: P2021/570) comparing 2 groups: IBD patients remaining on IFX IV infusion (IV group) and patients switching from IFX IV to SC injection (SC group).

Methods: The study population included IBD patients in clinical, biological and endoscopic steroid -free remission on IFX IV maintenance. Decision to switch to SC or to remain on IV was based on patient preference. The primary outcome was the proportion of IBD patients with drug sustainability. Drug sustainability was defined as the absence of treatment interruption or modifications in the IFX regimen. The secondary endpoints were safety, PK over five timepoints and quality of life (via IBDQ). At each patient visit ($n=5$), IFX Trough Levels (TL) were measured using ELISA and expressed as $\mu\text{g/mL}$

Results: Sixty-eight IBD patients met the inclusion criteria with 42 patients switching to SC IFX At last IV infusion, all patients were treated at 5 mg/kg with regimen of every 8 ($n=49$), 6 ($n=9$) and 4 ($n=10$) weeks. Demographics and disease characteristics of SC and IV groups were comparable. The majority of patients in both groups had Crohn's disease (85.7% in SC vs. 73.1% in IV, $p=0.33$). Both groups had similar median BMI (SC =25 kg/m² [IQR 21.1–29] vs. IV = 24.2 kg/m² [IQR 22.4–27.4], $p=0.41$), and gender distribution was comparable, with approximately 59.5% and 57.7% females in the SC and IV groups, respectively. Disease duration was also similar between the two groups. Both groups had comparable history of previous biologic (64.3% SC vs. 80.8% IV, $p=0.23$) and immunosuppressor (66.7% SC vs. 69.2% IV, $p=1$) exposures. Median biomarker levels at baseline were also similar between groups, with C-reactive protein levels of 1.2 mg/L [IQR 0.6–2.3] for the SC group versus 1.1 mg/L [IQR 0.6–1.6] for the IV group ($p=0.36$) and faecal calprotectin levels of 22 $\mu\text{g/g}$ [IQR 5–58] in the SC group versus 48 $\mu\text{g/g}$ [IQR 21–75] in the IV group ($p=0.15$). At the time of this interim analysis, the mean follow-up is 37 weeks $\pm$ 20. Drug sustainability was not different in the 2 groups ($p=0.45$). The reasons for loss of drug sustainability were flare disease ($n=4$), neoplasia ($n=1$), pregnancy ($n=1$) or patient choice ($n=4$). At last, IV infusion, both IV and SC groups had similar TL distributions (6.64 $\mu\text{g/mL}$, IQR (3.8-7.7) (IV) vs 4.65 $\mu\text{g/mL}$, IQR (3.6-8.3) (SC), ($p=0.4$)), but as soon as patients were switched to SC (SC group),

IFX TL were significantly different from patients maintained in IV (IV group) at each timepoint. Week 8: (6.4 µg/mL, IQR (4.3-8.4) (IV) vs 24 µg/mL, IQR (14.4-41.4) (SC), ($p < 0.0001$)) Week 16: (7.14 µg/mL, IQR (4.8-7.9) (IV) vs 30 µg/mL, IQR (16.5-37.8) (SC), ($p < 0.0001$)) Week 52: (3.9 µg/mL IQR (2.9-5.1) (IV) vs 27.5 µg/mL, IQR (16.4-39.8) (SC), ($p < 0.001$)) Strikingly, in the SC group, median IFX TL at week 8 was significantly lower in patients failing drug sustainability (10.7 µg/mL, IQR (7.3-14.1) vs 27.5 µg/mL, IQR (25.8-45), ($p = 0.007$)). Neither the overall quality of life assessed via IBDQ nor the specific IBDQ domains (GI, systemic, social, or emotional) showed significant differences between the SC and IV groups. Although the incidence of IFX-related adverse events was higher in the SC group, the difference was not statistically significant (74% vs 41%; $p = 0.07$). Injection site reactions were the most common and specific adverse event in the SC group

Conclusions: This interim analysis of SWITCH study demonstrates comparable drug sustainability between IFX SC and IV in a remitter IBD population. Among patients switched to SC, week 8 IFX trough levels were predictive of drug sustainability. While SC treatment showed a trend toward higher adverse events, injection site reactions were the most common and specific to the SC group.

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THE IMMUNE CIS- REGULOME: WHOLE BLOOD CELL CULTURE - DERIVED RESPONSE EQTLS REVEALS POTENTIAL CAUSATIVE GENES IN RISK LOCI ASSOCIATED WITH INFLAMMATORY BOWEL DISEASES.

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Introduction: Genome-wide association studies (GWAS) have successfully identified many genetic regions linked to inflammatory bowel diseases (IBD), but since these often involve non-coding variants, the causative genes remain largely unknown. Matching cis-expression Quantitative Trait Loci (cis-eQTLs) in relevant tissues may help pinpoint candidate genes. Yet matching cis-eQTL can be found for ~50% of risk loci with the available eQTL data sets. One explanation is that these cis-eQTLs only appear under inflammatory conditions, known as response-QTLs (reQTLs).

Aim: The goal of our study is to investigate the risk loci associated with genetic IBD susceptibility in order to pinpoint the causative genes underlying the genetic associations revealed by GWAS

Methods: Toll-like receptor (TLR) and T cell receptor (TCR)- stimulated whole-blood cell cultures were carried out in a cohort of 406 healthy individuals (EC P2015/425). All individuals were genotyped using Illumina's OmniExpress BeadChips. RNA sequencing was performed using QuantSeq 3' mRNA-Seq Library Prep Kit FWD for a total of 1407 samples. The cis-regulome of the immune system was examined using QTL-tools and colocalization was performed with GWAS summary statistics from the last IBD meta-GWAS.

Results: The cohort included 248 females and 159 males with a median age (29 years, IQR 25-39) without any past medical history, use of medications or smoking habits. We identified 13.679 autosomal cis-eQTLs ($FDR \leq 0.05$) corresponding to 6.496 eGenes. Cis-eQTLs that influence the same gene across resting and stimulated conditions were merged into "cis-regulatory modules" (cRM) if they exhibited similar "eQTL association patterns" (EAPs). This yielded 8401 monogenic cRM with 4.695 of them not operating in resting condition, requiring immune stimulation to be detected (reQTLs). Next, we colocalized EAPs generated from our healthy cohort with disease associated pattern (DAP) identifying IBD risk loci. This comparative analysis assumes that if a risk locus influences disease risk by altering gene expression, the DAP for this locus and the EAP should show similar patterns of variant associations, as quantified by the θ metric. We found 187 significant correlations ($|\theta| > 0.6$) spanning 39 IBD risk loci and encompassing 68 genes. Significantly, 19.2 % of these correlations (36 out of 187) were associated with reQTLs, facilitating the colocalization of EAPs with 11 risk loci that would have been overlooked in the absence of stimulated conditions. The long non-coding gene AJ009632.2 is a remarkable example illustrating the relevance of immune stimulation. A positive correlation was observed by colocalizing eQTL captured in resting condition (Resting condition $\theta = 0.91$, $p\text{-val} = 0.0004$) which suggested that the eQTL linked to AJ009632.2 may increase disease risk. Contrarily, in stimulated conditions, EAP linked to AJ009632.2 displays an inverse trend (TLR 4 stim $\theta = -0.91$, $p\text{-val} = 0.0009$, TLR7/8 stim - $\theta = 0.66$, $p\text{-val} = 0.01$). This striking example stresses the need to have a deep knowledge about a regulatory variant (for instance through functional studies) before considering it as positively or negatively associated with disease. Another interesting example is illustrated by CTSS, a gene which encodes cathepsin S protein, a lysosomal enzyme expressed by immune and epithelial cells in response to inflammation, regulating antigen presentation and taking part in degradation of extracellular matrix. The reQTL linked to CTSS in our dataset matched the DAP related to the rs4845604 risk locus (Resting condition $\theta = -0.05$, $p\text{-val} = 0.1$, TLR 4 stim $\theta = -0.72$, $p\text{-val} = 0.004$, TLR7/8 stim - $\theta = -0.45$, $p\text{-val} = 0.03$). We observed other DAP-EAP correlations which highlight potentially relevant candidate genes: HORMAD1 (Resting condition $\theta = -0.02$, $p\text{-val} = 0.1$;

TLR 4 stim $\theta = -0.82$, p-val = 0.004; TLR7/8 stim - $\theta = -0.82$, p-val = 0.0009) , ZBTB38 (Resting condition $\theta = 0.39$, p-val = 0.03; TLR 4 stim $\theta = 0.73$, p-val = 0.0007, TLR7/8 stim - $\theta = 0.48$, p-val = 0.02)), TPPP (Resting condition $\theta = 0.01$, p-val = 0.1; TLR 4 stim $\theta = 0.8$, p-val = 0.0005; TLR7/8 stim - $\theta = 0.68$, p-val = 0.006).

Conclusions: In this unique cohort of healthy individuals, the identification of specifically stimulated whole- blood cell cultures derived cis-re QTLs expanded our ability to colocalize risk loci, and pinpoint relevant candidate genes in IBD

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DISTINCT INVOLVEMENT OF PLASMA CELLS AND MONOCYTES/MACROPHAGES IN ILEAL AND COLONIC ULCER FORMATION IN PATIENTS WITH CROHN'S DISEASE. N. Pierre (1), N. Jacobs (2), R. Fernández-Verdejo (3), E. Louis (1), S. Vieujean (1) / [1] GIGA Institute, University of Liège, Liège, Belgium, Laboratory of Translational Gastroenterology, [2] GIGA Institute, University of Liège, Liège, Belgium, Cellular and Molecular Immunology, [3] Universidad Finis Terrae, Santiago, Chile, Laboratorio de Fisiología del Ejercicio y Metabolismo (LABFEM).

Introduction: Despite its interest for the development of personalised medicine, the pathophysiological distinctions between ileal and colonic Crohn's disease (CD) have been poorly characterised.

Aim: To search for immunological differences between ileal and colonic CD.

Methods: We reanalysed our proteomic dataset (Pierre N. et al., Journal of Crohn's and Colitis, 2020, doi: 10.1093/ecco-jcc/jjz130) to extract non-exploited immunological information. Using mass spectrometry-based proteomics, we previously compared the proteome of ulcer edges and adjacent normal mucosa (paired design) in the ileum (n=16 biopsies) and colon (n=16 biopsies) of 16 CD patients. A total of 4,428 and 5,204 proteins were screened in the ileum and colon, respectively. To identify proteins specific to particular immune cell populations, we searched in the Human Proteome Atlas and literature.

Results: We identified markers specific to plasma cells (IgA1, IgM, IgG1, IgG2, IgG3, IgG4, immunoglobulin J chain [IGJ], and immunoglobulin lambda-like polypeptide 5 [IGLL5]), monocytes/macrophages (cluster of differentiation 14 [CD14]), and mast cells (chymase [CMA1], mast cell carboxypeptidase A [CPA3], and tryptase alpha/beta-1 [TPSAB1]). No specific markers were identified for the other immune cells. The number of increased plasma cell markers (ulcer edges vs adjacent normal mucosa) was higher in the ileum (IgA1, IgM, IgG1, IgG2, IgG3, IGLL5, and IGJ) than in the colon (IgG3). Of note, immune exclusion markers (IgM, IgA1, IGJ) were increased in the ileum, but not the colon (ulcer edges vs adjacent normal mucosa). The marker of monocytes/macrophages CD14 was increased in the colon, but not in the ileum (ulcer edges vs adjacent normal mucosa). Mast cells markers (CMA1, CPA3, and TPSAB1) showed no significant change in the ileum or colon (ulcer edges vs adjacent normal mucosa).

Conclusions: Plasma cells and monocytes/macrophages may play distinct roles in the formation of ileal and colonic ulcers in patients with CD, suggesting further investigations.

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IMPACT OF ASSAY ON THE PREDICTIVE PERFORMANCE OF MODEL-INFORMED PRECISION DOSING OF USTEKINUMAB IN PATIENTS WITH CROHN'S DISEASE. W. Zhang (1), T. Dervieux (2), D. Thomas (1), M. Ferrante (3), S. Vermeire (3), E. Dreesen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] Prometheus Laboratories, United States, Prometheus Laboratories, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Therapeutic drug monitoring (TDM) concentrations of ustekinumab measured by homogeneous mobility shift assay (HMSA) are significantly higher than those measured by enzyme-linked immunosorbent assay (ELISA). However, the impact of assay format on the predictive performance of model-informed precision dosing (MIPD) remains unknown.

Aim: To evaluate the impact of assay variation on the predictive performance of MIPD.

Methods: Data from 83 patients with Crohn's disease were repurposed. Patients received intravenous ustekinumab induction and subcutaneous maintenance injections every eight weeks. Serum samples were collected at week (w)4, w8, w16, and w24. Concentrations were measured using HMSA (Data_HMSA) and ELISA (Data_ELISA). Two corresponding population pharmacokinetics (popPK) models were developed: Model_HMSA and Model_ELISA. Bayesian forecasting was performed under four scenarios: (1) w8 predicting w16, (2) w8 predicting w24, (3) w16 predicting w24, and (4) w8 and w16 predicting w24. Predictive performance was assessed using relative bias (rBias) and relative root mean square error (rRMSE). Clinically acceptable rBias was $\pm 20\%$ with a 95% confidence interval (CI) including zero, and rRMSE thresholds were 30%. Regression and Bland-Altman plots were used to examine correlation and agreement between forecasted ustekinumab clearance estimates.

Results: When datasets and models were matched (Data_HMSA-Model_HMSA, Data_ELISA-Model_ELISA), rBias met clinical standards across all scenarios. However, mismatched combinations yielded poorer accuracy. Model_HMSA

overestimated Data_ELISA concentrations, with rBias 8.54% [95% CI 0.149%–16.9%], 18.5% [6.81%–30.1%], 27.4% [16.9%–37.8%], and 19.7% [8.88%–30.6%] for scenarios 1, 2, 3, and 4, respectively. Conversely, Model_ELISA underestimated Data_HMSA in scenarios 3 and 4, with rBias -11.2% [-17.2%– -5.13%] and -10.8% [-17.2%– -4.45%], but met clinical standards in scenarios 1 and 2. Precision was highest using Data_HMSA. All rRMSE values met clinical thresholds with Model_HMSA, while three scenarios (1, 2, and 4) met thresholds with Model_ELISA. Data_ELISA failed to achieve precision under any scenario, regardless of the model used. Clearance estimates were systematically lower using Model_HMSA than Model_ELISA, with high determination coefficients (R^2 range 0.94–1.00). Bland–Altman plots indicated poor agreement between clearance estimates from the two models.

Conclusions: This study is the first to assess the impact of the assay format on the performance of MIPD. Our findings highlight the importance of matching the TDM assay format with the assay format used to build the popPK model.

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UNRAVELLING GENETIC VERSUS ENVIRONMENTAL FACTORS DETERMINING DISEASE COURSE IN IBD: A POPULATION-BASED COHORT STUDY IN FIRST- AND SECOND-GENERATION IMMIGRANTS A. D'Hooghe (1), G. Juul Poulsen (1), C. Nikolai Sørensen (1), P. Tandon (2), N. Nyboe Andersen (3), S. Vermeire (4), B. Verstockt (4), T. Jess (1) / [1] Aalborg University, Denmark, Centre for Molecular Prediction of Inflammatory Bowel Disease, PREDICT, Department of Clinical Medicine, [2] University of Toronto, Canada, Division of Gastroenterology and Hepatology, University Health Network, [3] Zealand University Hospital, Koge, Denmark, Department of Gastroenterology and Hepatology, [4] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Inflammatory bowel diseases (IBD) incidence in immigrants approximates that of the host country in progressive generations.

Aim: We investigate how immigrant generation affects IBD outcomes.

Methods: In this population-based cohort study, IBD-related hospitalizations, major and minor surgery, targeted therapies, and perianal disease were compared between first- and second-generation immigrants (stratified into Western/non-Western) and native Danes. Their sex, age at diagnosis and time of diagnosis were used to estimate adjusted hazard ratios (aHRs) using Cox proportional hazard regression.

Results: First-generation immigrants had lower risk of major surgery (aHR_{Western} 0.89; 95% confidence interval [CI] 0.75–1.05, aHR_{non-Western} 0.79; 95% CI 0.67–0.92) and targeted therapy (aHR_{Western} 0.87; 95% CI 0.76–0.99, aHR_{non-Western} 0.83; 95% CI 0.74–0.93) than native Danes, whereas second-generation immigrants resembled native Danes. However, second-generation immigrants had higher risk of hospitalization than native Danes (aHR_{Western} 1.28; 95% CI 1.05–1.55, aHR_{non-Western} 1.40; 95% CI 1.28–1.54), whereas in first-generation immigrants this was only observed in non-Western ulcerative colitis (UC) patients (aHR 1.19; 95% CI 1.08–1.32). Across both generations, non-Western immigrants had higher risk of minor surgery (Crohn's disease [CD]: aHR_{first-generation} 1.39; 95% CI 1.10–1.75, aHR_{second-generation} 1.53; 95% CI 1.18–1.97), mainly due to increased incidence of perianal disease (CD: aHR_{first-generation} 1.55; 95% CI 1.25–1.92; aHR_{second-generation} 1.58; 95% CI 1.25–2.01).

Conclusions: Disease outcomes change across immigrant generations, pointing to environmental factors possibly impacting disease course, which needs further investigation. In contrast, non-Western immigrants have more perianal disease in both generations, suggesting a possible role of genetics for this debilitating phenotype.

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OPTIMIZING THE SWITCH FROM ESCALATED INTRAVENOUS TO SUBCUTANEOUS INFliximab: A POPULATION PHARMACOKINETICS–PHARMACODYNAMICS STUDY. Z. Wang (1), M. Ferrante (2), S. Vermeire (2), E. Dreesen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: The standard subcutaneous (SC) infliximab (IFX) of 120 mg bi-weekly (Q2W) has shown non-inferior pharmacokinetics (PK) and comparable efficacy to the intravenous (IV) IFX of 5 mg/kg Q8W in clinical trials. However, it remains unclear whether patients on escalated IV dosing regimens can transition to standard SC dosing without losing therapeutic response.

Aim: This study aims to elucidate the dose–exposure–response relationship during IV-to-SC switching of IFX in patients with Crohn's disease (CD) and ulcerative colitis (UC) through population pharmacokinetics–pharmacodynamics (popPK–PD) modelling and simulation.

Methods: Data were collected from healthy volunteers in two single-dose Phase I studies ([1]; NCT03446976) and patients with IBD in a two-part Phase I study (NCT02883452). In patients with IBD, frequent PK sampling was conducted during switching from 5 mg/kg IV IFX to Q2W SC IFX injections of 120/180/240 mg in Part 1 and 120/240

mg in Part 2. Faecal calprotectin was measured in patients at baseline, week (w)2, w6, and Q8W thereafter until w54. Endoscopic remission was assessed at screening, w22/30, and w54. We performed popPK–PD modelling and simulation (n=1000) using NONMEM to evaluate post-switch FC time courses and probabilities of endoscopic remission.

Results: A total of 253 healthy volunteers and 179 patients (101 CD, 78 UC) contributed 7351 serum infliximab and 1201 faecal calprotectin concentrations. Three models were sequentially developed: a popPK model linking infliximab dosing to infliximab concentrations, a calprotectin model describing the inhibitory effect of infliximab exposure on faecal calprotectin release, and an endoscopic remission model linking faecal calprotectin concentrations at w14 to the probability of endoscopic remission at w22/30. Infliximab clearance increased with decreasing serum albumin, increasing body weight, and the presence of neutralizing antibodies. Faecal calprotectin levels decreased when overall infliximab exposure (not just trough concentrations) increased. Lower faecal calprotectin at w14 was associated with increased probabilities of endoscopic remission in patients with UC, but not CD. Simulations showed that the IV-to-SC switch at w6 of infliximab therapy (as per the CT-P13 1.6 study) further decreases calprotectin levels in both patients with CD and UC. For example, in patients with UC making the standard IV-to-SC switch, the predicted pre-dose calprotectin level dropped from 263 µg/g (90% prediction interval [PI], 21–1695) at w6 to 111 µg/g (90% PI, 13–757) at w54 ($p<0.0001$). Furthermore, the predicted probability of achieving endoscopic remission at w22/30 increased from 54% (90% PI, 16–88) to 63% (90% PI, 18–94) in patients with UC when switching to label-recommended 120 mg Q2W SC maintenance dosing instead of continuing standard IV maintenance therapy ($p<0.0001$). A similar trend was observed in the CT-P13 1.6 study, where patients who switched to standard SC 120 mg Q2W at w6 had a numerically higher rate of endoscopic remission at w22/30 compared to those who continued standard IV 5 mg/kg Q8W (59% [n=23/39] vs 50% [n=21/42]). However, a sample size calculation indicated that 480 patients per arm would be necessary to confirm biochemical superiority of standard SC infliximab maintenance therapy over standard IV infliximab maintenance therapy. Simulations also showed that patients on escalated Q6W/Q8W IV maintenance regimens could switch to 120 mg Q2W SC infliximab without faecal calprotectin levels increasing. Patients on Q4W IV infliximab require SC dose escalation to either 120 mg QW or 240 mg Q2W to avoid an increase in faecal calprotectin.

Conclusions: Infliximab trough concentrations are only a surrogate for therapeutic outcomes, with overall infliximab exposure being the true driver. Therefore, the higher trough concentrations on standard SC dosing are needed to compensate for the lower SC peak concentrations. Standard SC dosing is superior to standard IV infliximab dosing as evidenced by lower faecal calprotectin and higher endoscopic remission rates (in patients with UC). Patients on Q6W and Q8W IV regimens can switch to standard SC infliximab without an increase in faecal calprotectin.

Reference: [1] Westhovens R et al., [P0387] Poster presented at UEGW 2017.

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MODEL-INFORMED DOSAGE DE-ESCALATION OF INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES. Z. Wang (1), I. De Greef (2), W. Kantasiripitak (1), S. Wicha (3), S. Tops (1), M. Nigro (2), A. Outtier (2), B. Verstockt (2), J. Sabino (2), D. Thomas (1), S. Vermeire (2), M. Ferrante (2), E. Dreesen (4) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University of Hamburg, , Germany, Department of Clinical Pharmacy, [4] KUL - University of Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Extending the infliximab (IFX) infusion interval has been attempted in patients with Crohn's disease (CD) and ulcerative colitis (UC) who maintained response following an earlier interval shortening.

Aim: We aimed to compare therapeutic drug monitoring (TDM) and model-informed precision dosing (MIPD) for successful de-escalation of infliximab dosage in patients with CD and UC.

Methods: MODIFI is a monocentric, open-label, historically controlled Phase 4 trial (NCT04982172). Eligible patients with steroid-free clinical (two-item patient-reported outcome [PRO2] ≤ 1 for UC and ≤ 8 for CD) and biological remission (C-reactive protein <5 mg/L and faecal calprotectin <250 mg/kg) on accelerated IFX dosing underwent interval extension to every eight week. The extension was guided by either TDM (historical control) or MIPD targeting an infliximab trough concentration (C_{trough}) of 5 mg/L (prospective intervention). Bayesian forecasting was performed using the TDMx Infliximab module (www.TDMx.eu). Steroid-free clinical and biological remission and IFX concentrations were measured at each study visit over 52 weeks. The primary endpoint was sustained steroid-free clinical and biological remission over one year.

Results: The study enrolled 52 patients: 21 patients (11 CD, 10 UC) in the TDM arm and 31 patients (19 CD, 12 UC) in the MIPD arm. Although the proportion of patients achieving the primary endpoint was numerically higher in the MIPD arm (52%, n=16/31) compared to the TDM arm (29%, n=6/21), this was not significantly different ($p=0.17$). However, the proportion achieving sustained steroid-free clinical remission over one year was significantly higher in the MIPD arm compared to the TDM arm (81%, n=25/31, vs. 38%, n=8/21, $p<0.01$), particularly in the UC subpopulation (100% in the MIPD arm, n=12/12, vs. 30% in the MIPD arm, n=3/10, $p<0.01$). The proportion of patients achieving sustained steroid-free biological remission over one year did not statistically differ between the MIPD and TDM arms, both in

the total population and in the subpopulation analyses ($p > 0.50$). The infliximab Ctrough at baseline was significantly higher in the MIPD arm (median 9.2 [interquartile range, IQR 6.5–14.0] mg/L) than in the TDM arm (5.7 [4.3–9.1] mg/L) ($p < 0.01$). Following a single model-informed dose at baseline, the infliximab Ctrough immediately decreased to 5.9 mg/L [4.4–7.5 mg/L] with 65% of patients having an infliximab Ctrough > 5 mg/L. Furthermore, MIPD resulted in reduced variability in infliximab Ctrough among patients at nearly all study visits. The infliximab dose per infusion over the course of one one-year period was comparable between the TDM arm (7.5 [IQR 7.4–8.2] mg/kg) and the MIPD arm (8.8 [IQR 6.6–10.9] mg/kg). None of the patients in the MIPD arm required co-medication with immunomodulators or corticosteroids during the trial. In the TDM arm, one patient required immunomodulators.

Conclusions: This is the first study to prospectively evaluate and compare MIPD and TDM in guiding infliximab dosage de-escalation in patients who regained response on escalated infliximab maintenance therapy. MIPD-guided dosage de-escalation of infliximab resulted in numerically higher rates of sustained steroid-free clinical and biological remission compared to TDM. Future randomized studies with sufficient sample size are needed to validate our findings. A sample size calculation based on observed rates – which are considered clinically relevant – suggests that 70 patients with IBD per arm would be necessary to detect a statistically significant difference in the primary endpoint between the TDM and MIPD in a future, confirmatory trial. For UC patients, the required sample size could be reduced to 16 per arm to observe a statistical difference.

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SUBCUTANEOUS INFLIXIMAB IN IBD PATIENTS PREVIOUSLY TREATED WITH AN OPTIMIZED INTRAVENOUS INFLIXIMAB DOSING SCHEDULE: PRELIMINARY RESULTS ON EXPECTATIONS AND SATISFACTION OF SWITCHING FROM INTRAVENOUS TO SUBCUTANEOUS INFLIXIMAB. T. Holvoet (1), A. Moens (2), P. Bossuyt (3), T. Lobaton (4), A. Posen (5), A. Cremer (6), L. Capirchio (7), C. Caenepeel (8), G. Lambrecht (9), A. Amezaga (10), C. Reenaers (11), H. Peeters (12), B. Willandt (13), N. Deprez (14), J. De Rechter (15), I. Arijs (15), N. Straetmans (5), E. Dreesen (16), Belgian Research and Development (15), M. Ferrante (17) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology, [2] Heilig Hartziekenhuis Lier, Lier, Belgium, Gastroenterology, [3] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [4] Ghent University Hospital, Ghent, Belgium, Gastroenterology, [5] AZ Vesalius Tongeren, Tongeren, Belgium, Gastroenterology, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [7] Chwapi, Tournai, Belgium, Gastroenterology, [8] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology, [9] AZ Damiaan, Oostende, Belgium, Gastroenterology, [10] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [11] CHU de Liège, Liège, Belgium, Gastroenterology, [12] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology, [13] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology, [14] AZ Maria Middelaers, Ghent, Belgium, Gastroenterology, [15] BIRD vzw - Belgian IBD Research and Development, Zaventem, Belgium, BIRD, [16] KUL - University of Leuven, Leuven, Belgium, Pharmaceutical and Pharmacological Sciences, [17] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology.

Introduction: The anti-TNF agent infliximab (IFX) CT-P13 has been approved in a subcutaneous (SC) formulation. Unanswered questions persist regarding the use of SC IFX in patients previously on optimized intravenous (IV) dosing regimens.

Aim: The AMARETTO study aims to investigate whether switching to weekly SC administrations of IFX 120 mg is associated with better outcomes compared to bi-weekly administrations in patients previously treated with an optimized IV dosing schedule. In this preliminary analysis, we explored patients' expectations and satisfaction with switching to the SC formulation.

Methods: This Belgian multicentre, randomized, open-label prospective superiority trial includes adult patients with IBD treated with optimized IV IFX in steroid-free clinical and biological remission, defined as 1/ no need for any type of steroids in previous eight weeks, 2/ PRO-2 based on last 3 days before study visit with rectal bleeding score of 0 and stool frequency score of ≤ 1 (UC/IBD unclassified [IBDU]), or average daily abdominal pain score of ≤ 1 and a liquid stool frequency score of ≤ 2.8 (CD), and 3/ CRP < 10 mg/L, faecal calprotectin < 250 μ g/g (ClinicalTrials.gov ID: NCT06113913). Eligible patients may either continue their optimized IV treatment (IV comparison group) or switch to SC treatment. Patients opting for SC treatment are randomized to one of two open-label groups: the SC intervention group, receiving 120 mg SC IFX weekly, or the SC comparison group, receiving 120 mg SC IFX bi-weekly. The primary endpoint is the proportion of patients maintaining steroid-free clinical and biological remission at week 52 without treatment optimization after switching to SC IFX. Secondary endpoints include quality of life, treatment optimization, and patient expectation at baseline and satisfaction with SC treatment at different timepoints (week 8, week 24 and week 52). Here we focus on the patient expectation at baseline and satisfaction at week 8 scoring, using a 11-point Likert scale with 0 = lowest score and 10 = highest score.

Results: Between May 2024 and October 2024, 163 patients were screened, and 120 were included, with 66 (55%) patients in the SC group and 54 (45%) in the IV group: 66/54 M/F, median (interquartile range [IQR]) age 43 (31-54) years, 78 (65%) CD, 41 (34%) UC and 1 (1%) IBDU, median (IQR) disease duration 12 (5-20) years, IFX first line

in 73% of patients. Of the 66 patients willing to switch, 57 (37 CD, 20 UC/IBDU) already had the baseline visit with first administration of SC IFX and completed their treatment expectations questionnaire, and 29 of these patients have already been treated with SC IFX for at least 8 weeks and completed a satisfaction questionnaire. The autoinjector was preferred by 42 (74%), the syringe by 4 (7%) and 11 patients (19%) had no preference. The main reasons for choosing the autoinjector are 'visibility of needle' (16/42, 38%) and 'control of injection' (20/42, 48%). Training for SC injection was provided mainly by an IBD-nurse (N=43, 78%). Satisfaction of training, confidence level and ease of use received median (IQR) scores of 10 (9-10), 9 (8-10) and 9 (8-10), respectively. By week 8, the median (IQR) score of confidence level remained stable 9 (9-10) and increased for the ease of use 10 (8-10). At week 8, median (IQR) scores for pain and fear during injection were 2 (0-4) and 0 (0-1), respectively. The median (IQR) satisfaction score and score for recommending SC treatment at week 8 were both 9 (8-10). No significant differences at week 8 were observed between both SC groups.

Conclusions: Preliminary results indicate a highly positive patient experience with SC IFX in patients previously treated with an optimized IV dosing schedule, highlighting strong preferences for the autoinjector and good satisfaction rates regarding training, ease of use, confidence and injection pain. The AMARETTO trial will further clarify whether optimized weekly SC dosing offers superior outcomes compared to the standard bi-weekly SC IFX regimen.

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TREATMENT PERSISTENCE, CLINICAL, AND BIOLOGICAL OUTCOMES FOLLOWING AN ELECTIVE SWITCH FROM INTRAVENOUS TO SUBCUTANEOUS INFLIXIMAB AND VEDOLIZUMAB. A. Outtier (1), Y. Hoffert (2), E. De Dycker (1), P. Geens (1), T. Lambrechts (1), E. Loddeewijckx (1), A. Paps (1), B. Verstockt (1), J. Sabino (1), S. Vermeire (1), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences

Introduction: Subcutaneous (SC) formulations of infliximab (IFX) and vedolizumab (VDZ) are approved for treating ulcerative colitis (UC) and Crohn's disease (CD).

Aim: This study reports on treatment persistence, as well as clinical, biological and pharmacological outcomes following an elective switch from maintenance intravenous (IV) to SC IFX and VDZ.

Methods: We conducted a single-centre, prospective, observational study from November 2021 through June 2024, enrolling stable inflammatory bowel disease (IBD) patients (based on physician global assessment) willing to switch from maintenance IV IFX or VDZ to SC treatment, and with a minimum follow-up of 34 weeks. Data were collected on patient characteristics, prior and current medications, clinical and biological activity, and pharmacokinetics. Assessments were made at time of last IV infusion, baseline (first SC injection, 4 weeks after last IV), week 8, week 34, and last follow-up. The primary objective was SC treatment persistence. Secondary objectives included change in the two-component patient reported outcome (PRO2), C-reactive protein (CRP), faecal calprotectin and serum levels (SL).

Results: In this study, 140 IBD patients (median age 44.2 years, 78 female, 64 UC, 76 CD) switched from IV IFX (n=59) or VDZ (n=81) to SC treatment. Standard IV dosing was given in 115 and optimized dosing in 25 patients (19 IFX, 6 VDZ). No patient received concomitant immunosuppressants. Over a median follow-up of 20.2 (IQR 13.6-26.4) months, 83.6% of patients remained on the SC formulation, with more patients continuing on SC IFX compared to VDZ (odds ratio 2.56 [95% CI 1.12-5.88], p=0.025). No other baseline factors were linked to treatment persistence. The reasons for discontinuation were disease flare (n=9), injection site reaction (n=5), side effects (n=2), increased symptoms (n=2), patient preference (n=2), inadequate response (n=1), non-compliance (n=1), and unknown (n=1). Seventeen patients returned to IV treatment, while six patients switched to another biologic. Median (IQR) PRO2 (for UC: 0 [0-0] at baseline, 0 [0-1] at week 8, and 0 [0-0] at week 34; for CD: 2 [0-7] at baseline, 2 [0-7] at week 8, and 0 [0-6] at week 34), CRP (1.6 [0.7-3.8] mg/L at baseline, 1.4 [0.6-3.7] mg/L at week 8, and 1.9 [0.7-5.1] mg/L at week 34), and faecal calprotectin (30 [30-112] µg/g at baseline, 37 [30-139] µg/g at week 8, and 54 [30-86] µg/g at week 34) remained stable over time. However, median (IQR) IFX SL rose from 5.5 (3.5-7.9) µg/mL at last IV infusion to 15.0 (12.7-19.3) µg/mL at baseline, 17.1 (13.3-20.9) µg/mL at week 8, and 14.7 (11.1-20.7) µg/mL at week 34. Similarly, VDZ SL increased from 11.3 (7.98-15.5) µg/mL at last IV infusion to 26.8 (21.4-35.1) µg/mL at baseline, 27.5 (22.6-33.1) µg/mL at week 8, and 29.1 (23.6-38.7) µg/mL at week 34 (all p<0.0001).

Conclusions: Switching from maintenance IV to SC IFX or VDZ is a viable option for stable IBD patients, though 16% experienced flare-ups or side effects after switch. Treatment discontinuation was more common with SC VDZ than IFX.

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COMPREHENSIVE IBD CARE: INTRODUCTION OF AN IBD-SPECIALIZED PSYCHOLOGIST IN A MULTIDISCIPLINARY IBD TEAM. B. Keersmaekers (1), K. Vanderbist (2), S. Vermeire (3), B. Verstockt (3), J. Sabino (3), M. Ferrante (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Inflammatory bowel diseases (IBD) can have a substantial impact on patients' quality of life and increase the risk of psychological comorbidities. The integration of an IBD-specialized psychologist into the multidisciplinary care team is recommended by the ECCO Quality of Care Standards (Fiorino, JCC 2020). A specialized psychologist can provide targeted interventions for IBD-related challenges, such as disease acceptance, coping strategies, stress, and symptom management.

Aim: In October 2021, a clinical psychologist with expertise in IBD joined our multidisciplinary team. We assessed the characteristics of referred patients, the reasons for referral, treatments provided, and patient satisfaction.

Methods: This retrospective study gathered demographic and psychological data on all IBD patients referred to the IBD psychologist between September 2021 and June 2024. In addition, a satisfaction survey with 10 questions was distributed to all patients who had at least one consultation with the IBD psychologist since her appointment.

Results: Over the 34-month study period, 1,214 patient contacts with the IBD psychologist were recorded, showing a steady increase from an average of 44 to 152 contacts per quarter. A total of 274 unique IBD patients (57.8% female, median [IQR] age 36 [28-50] years, 67.5% with Crohn's disease, 78.8% outpatients) were referred for an initial consultation. Patients had a median [IQR] of 3 [1-6] contacts, with 15.2% requiring ≥ 10 follow-up visits. Approximately one third of patients (29.9%) had a single consultation, primarily during hospitalization (62.3%). Reasons for inpatient referral included disease acceptance and grief counselling (loss of health, 68.2%), need for crisis support (21.4%) and anxiety concerning upcoming surgery (9.1%). Reasons for outpatient referral included disease acceptance and grief counselling (35.1%), symptom management (abdominal pain, urgency, fatigue) (18.7%), depression and anxiety due to disease related avoidance behaviour (17.3%), stress management (15.2%), disease mediated eating disorders (5.3%), health behaviour counselling and lifestyle change support (medication compliance, smoking cessation, sleep & physical exercise) (5.2%) and disease related relational and sexual problems (3.2%). Psychological interventions provided were tailored to the patients' needs, including Cognitive Behavioural Therapy (CBT) for anxiety and depression (35.1%), CBT for symptom management and fatigue (28.4%), mindfulness for IBD (10.1%), CBT for eating disorders (5.3%), motivational interviewing (5.8%), relaxation and diaphragmatic breathing (5.2%), and couples counselling (3.0%). For 67.2% of patients, the psychologist considered treatment to be completed. While 7.2% remained in follow-up, 25.6% were referred to other specialized mental health professionals. The satisfaction survey results (n=70, response rate 27.2%) indicated high levels of satisfaction. Nearly 87% rated the quality of care as excellent or good, and over 91% felt their needs were mostly met. Additionally, 80% reported that psychological support helped improve their coping abilities, and 90% expressed overall satisfaction with their experience.

Conclusions: The integration of an IBD psychologist within the multidisciplinary care team has significantly enhanced psychological support for IBD patients. The rising frequency of consultations highlights the increasing recognition of the need to address the psychological aspects of IBD. Overall, this integration has contributed to more comprehensive and effective patient care.

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VALIDATION OF AN ACUTE MURINE MODEL OF INFLAMMATION TO STUDY THE INTEREST OF BIO-ACTIVE PEPTIDE HYDROLYSATES. C. Cauwelier (1), A. Neyrinck (1), G. Thirion (2), P. Stordeur (2), P. Filée (3), N. Delzenne (1), D. Torres (3) / [1] Université catholique de Louvain (UCLouvain), Belgium, LDRI, [2] CERgroupe, Marche-en-Famenne, Belgium, Preclinical and pharming, [3] CERgroupe, Marche-en-Famenne, Belgium, Immunobiology Laboratory

Introduction: Physiologically, the intestinal immune system is in a continuous balance between, effective pathogen defence and immune tolerance to dietary components and beneficial microbial antigens. In patients suffering from inflammatory bowel disease (IBD) this balance is disrupted due to an inappropriate activation of immune cells leading to chronic inflammation and destruction of the mucosal wall of the intestine. Growing evidence suggest a role of the innate immune system including toll-like receptor 4 (TLR4) in promoting IBD. TLR4 is an important innate immunity sensor that recognizes lipopolysaccharide (LPS) and induces cytokine release triggering an inflammatory response. Several bioactive peptides targeting TLR4 present a promising therapeutic avenue for IBD.

Aim: This project aims to compare the effect of a TLR4-antagonistic peptide (C-L peptide) and Naticol®, a fish collagen hydrolysate, in an acute murine model of LPS-induced inflammation.

Methods: C57BL/6J mice received either the C-L peptide intraperitoneally or Naticol via the intragastric route one day and one hour prior to the intraperitoneal LPS injection. The mice were euthanized three hours post LPS injection. Inflammatory parameters were assessed by measuring the gene expression of TNF- α , IL-1 β , IL-6, TLR4 and of genes involved in the integrity of the intestinal barrier (ZO-1, Occludin and Mucin-2) in colonic tissue as well as the levels of the pro-inflammatory cytokine TNF- α in both the plasma and colonic tissue.

Results: Mice administered with the C-L peptide showed a significant reduction of TNF- α levels in the plasma and colonic tissues. This reduction was not observed in the gene expression of pro-inflammatory cytokines. Curiously, the C-L peptide led to a significant increase in the gene expression of IL-1 β . When Naticol® was administered orally to

control mice, it increased the gene expression of Occludin and Mucin-2 in the colon, suggesting a beneficial impact on the intestinal barrier. However, this effect was cancelled when administered to LPS-treated mice. Additionally, Naticol® did not reduce any marker of LPS-induced inflammation.

Conclusions: Altogether, these findings partly confirm the anti-inflammatory effects of peptide C-L, but not those of Naticol® in an acute model of LPS-induced inflammation. However, our results suggest that Naticol® given orally might have a protective function on the integrity of the intestinal wall in healthy mice, that could be of interest in the context of mild inflammation. The perspective of this work (Peptiboost project - <https://www.foodwal.be/en/peptiboost-2/>) is to develop, produce and test new protein hydrolysates containing peptides targeting intestinal TLR4 and the gut barrier that could be administrated orally for the management of intestinal inflammation.

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PROTEOMIC PROFILES ASSOCIATED WITH RESIDUAL ULTRASTRUCTURAL ANOMALIES IN THE EPITHELIUM OF IBD PATIENTS IN ENDOSCOPIC REMISSION. M. Meuwis (1), J. Loly (2), C. Salée (3), C. Massot (3), D. Baiwir (4), M. Fléron (5), G. Mazzucchelli (6), S. Vieujean (7), J. Somja (8), E. Louis (9) / [1] CHU of Liège and GIGA institute ULiège, Liege, Belgium, Hepato-Gastroenterology and Digestive Oncology Department, Translational gastroenterology laboratory, [2] CHU de Liège, Liège, Belgium, Hepato-gastroenterology and digestive oncology, [3] GIGA Institute, University of Liège, Liège, Belgium, Translational gastroenterology laboratory, [4] University of Liege, Liege, Belgium, GIGA Proteomics Facility, [5] University of Liege, Liège, Belgium, GIGA Proteomics Facility, [6] University of Liege, Liège, Belgium, Laboratory of mass spectrometry, [7] CHU of Liege, GIGA institute Uliege, CHRU Nancy, Liege, Belgium, Hepato-gastroenterology and digestive oncology, Translational gastroenterology laboratory, Gastroentreology dep INSERM, [8] CHU de Liège, Liège, Belgium, Department of Pathology, [9] CHU of Liège and GIGA institute ULiège, Liege, Belgium, Hepato-gastroenterology and digestive oncology, Translational gastroenterology laboratory.

Introduction: Increased permeability, mucosal barrier and epithelial anomalies (crypt distortion, wider crypt lumen, epithelial gaps) as well as altered tight junctions have been described in active ulcerative colitis (UC) and Crohn's Disease (CD). Probe based Confocal laser endomicroscopy (pCLE) is able to monitor epithelial anomalies in vivo.

Aim: This study aimed at comparing the proteomic profiles of the colonic epithelium associated with pCLE anomalies in UC, CD and non-IBD subjects.

Methods: Biopsies were collected in IBDs in endoscopic remission (n=37) and non-IBD control (CT)

(n=10) undergoing colonoscopy with pCLE as previously described (Loly J-P et al. IBD 2023). Biopsy sampled in the right colon and the rectum were analysed by mass spectrometry label free proteomics, with enrichment of epithelial cells using laser capture microdissection (Merli et al, JCC2021).. Comparisons of epithelial protein profiles, in presence (1) or absence (0) of fluorescein leaks were obtained in the colon and rectum, in CD, UC and non-IBD-CT. Significant proteins obtained were confronted and the entire protein profiles were evaluated using Gene Ontology (GO) functional annotations.

Results: Colon and rectum samples analyses provided 3227 and 3303 protein identifications ($\geq 50\%$ occurrence in minimum 1 group). Unique proteins ($\geq 50\%$ occurrence in only 1 group) were identified in the colon (n=40) and rectum (n=18). Differential analyses (0vs1) in the colon highlighted 165 and 152 significant proteins in CD and UC respectively, from which 13 were in common. In non-IBD CT (0vs1) 88 proteins were discriminant, with 9 and 6 being shared with CD and UC respectively. In the rectum, 74 and 172 discriminant proteins were obtained in CD and UC, from which 16 were also found significant in colon CD and UC protein lists(0vs1). DAZAP, STK4, LAMC1 and PDCD10 showed similar distribution tendencies in both segments in CD0vs1. While HNRPH1 and 2, VASP, TMX1 and PREP distributions were akin in UC0vs1 in both segments. GO analyses highlighted more numerous proteins with a decrease when leaks were observed in IBDs than in non-IBD-CT. These proteins are associated with junction proteins, matrix and cytoskeleton, proteasome, protease, peptidase functions, or are involved in apoptosis and innate immune controls and morphogenesis. STK4 product, a key regulator of the HIPPO and MAPK pathways, showed a drop (0>1) in IBDs and non-IBD CT with leaks.

Conclusions: This proteomic study reveals proteins with perturbed epithelial distributions associated with pCLE fluorescein leaks. Functional analyses are required to disclose and understand our findings and might confirm very early epithelial key players involved in IBD epithelial homeostasis loss.

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DEVELOPMENT OF NOVEL INFLAMMATORY AND ER STRESS MIXES TO SIMULATE IBD PHENOTYPES IN DIFFERENTIATED INTESTINAL ORGANOID. L. Giorio (1), K. Arnauts (1), J. Sabino (2), M. Ferrante (2), S. Vermeire (2), B. Verstockt (2) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Centre for Gastrointestinal Disorders TARGID, CHROMETA, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Differentiated intestinal organoids (ORG), which retain patient- and disease-specific features, offer a powerful model to study inflammatory bowel disease (IBD) mechanisms. While ORG preserve IBD characteristics, acute inflammation fades in culture. To address this, we developed two mixes: one to induce a predominantly inflammatory (INF) response and another to combine endoplasmic reticulum (ER) stress with inflammation, reflecting key pathways involved in IBD pathogenesis and potential therapeutic targets.

Aim: This study aimed to optimize two specific mixes: one to induce a purely INF response and another to simulate ER stress-driven inflammation in differentiated intestinal ORG.

Methods: Biobanked intestinal ORG cultures, derived from non-inflamed endoscopy biopsies from UC patients (n=9), were expanded, mechanically split, and exposed to human expansion media (HM) for two days (1). Next, ORG cultures were exposed to differentiation media (DM) for four days. From day 6 onwards, ORG were maintained in DM only or supplemented with an INF mix (50 ng/ml TNF- α , 20 ng/ml IL1 β , 1 μ g/ml Flagellin) or an ER stress mix (10 ng/ml TNF α , 20 ng/ml IL1 β , 1 μ g/ml Flagellin, Tunicamycin (TM) 25ng/ml) for 48 hours. As TM can induce both inflammatory and ER stress pathways, a concentration range of TM (25 ng/ml – 1 μ g/ml) and TNF- α (10 ng/ml – 100 ng/ml) has been evaluated by cell morphology to determine the threshold without comprising cell viability. RNA was sequenced by TruSeq mRNA on Illumina (HiSeq4000). Differential gene expression was studied through R packages like DESeq2 and PCAtools (removing the lower 10% of variables based on variance). Pathway Analysis was also performed ($|\log_2FC| > 1$, FDR < 0.05).

Results: Principal component analysis (PCA) was performed and captured respectively 24.05 %, 21.04 % and 16.1 % of the total variance for PC1, PC2, PC3 and demonstrated distinct clustering by treatment condition, with clear separation observed across all groups - NO-MIX, INF and ER mix. PCA plots showed consistency with the directionality of key genes driving the PC. For instance, the upregulation of PLA2 (2) in the ER and INF-mix groups contributes to the separation along PC1, PSAT1 (3), drives the separation along PC2, aligning with the ER mix group, and CCL20(4) is instead driving PC3. In ORG treated with the ER stress mix, multiple ER stress markers like HSP90B1, HSPA5, and XBP1 showed strong upregulation compared to those exposed to the INF mix, with a more pronounced effect in terms of significance and fold change. Pathway analysis of the contrast of the NO-mix versus the ER mix further confirmed the activation of ER stress-related pathways: • UPR (-log(p-value)=9.18, Ratio=2.87X10⁻¹, z-score= 3.638), • XBP1(S) activates chaperone genes (-log(p-value)=7.1, Ratio=3.33X10⁻¹, z-score= 4.000), • ATF4 activates genes in response to endoplasmic reticulum stress (-log(p-value)=4.24, Ratio=3.33X10⁻¹, z-score= 2.333), • ATF6 (ATF6-alpha) activates chaperone genes (-log(p-value)=3.51, Ratio=5.00X10⁻¹, z-score= 2.236).

Conclusions: We developed two mixes to model INF and ER stress in differentiated intestinal ORG. PCA analysis confirmed distinct clustering by condition, with key genes driving group separations. In addition, a stronger upregulation of ER stress markers and pathways was observed in the ORG treated with the ER-mix. These newly designed mixes will facilitate preclinical compound evaluation in a disease representative IBD model.

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PERIANAL FISTULA CLOSURE AFTER HETEROLOGOUS MESENCHYMAL STEM CELL INJECTIONS IS ASSOCIATED WITH PROTEIN LEVELS INDICATING LOWER TISSUE IMMUNE INFILTRATE, SPECIFIC PROTEINS INVOLVED IN THE CONTROL OF APOPTOSIS, AND PROBABLE HIGHER TISSUES REMODELLING AND PROTEASOME ACTIVITY. M. Meuwis (1), D. Baiwir (2), M. Fléron (2), G. Mazzucchelli (3), L. Boutaffala (4), C. Reenaers (4), C. Van Kemseke (4), S. Vieujean (5), V. Bettonville (6), A. Briquet (6), C. Lechanteur (6), C. Coimbra Marques (7), E. Louis (8) / [1] CHU of Liège and GIGA institute ULiège, Liege, Belgium, Hepato-Gastroenterology and Digestive Oncology Department and Translational Gastroenterology, [2] University of Liege, Liege, Belgium, GIGA Proteomics Facility, [3] University of Liege, Liege, Belgium, Laboratory of mass spectrometry, [4] CHU Liege, Liège, Belgium, Hepato-gastroenterology and digestive oncology, [5] CHU of Liege, GIGA institute Uliège, CHRU Nancy, Liege, Belgium, Hepato-gastroenterology and digestive oncology, Translational gastroenterology laboratory, Gastroenterology Department INSERM, [6] CHU Liege, Liège, Belgium, LTCG Division of Haematology, [7] CHU Liege, Liège, Belgium, Abdominal, Senology, Endocrine surgery and Transplantation, [8] CHU of Liège and GIGA institute ULiège, Liege, Belgium, Hepato-gastroenterology and digestive oncology Department and Translational gastroenterology laboratory.

Introduction: Perianal fistulae affect 30-34% of patients with Crohn's Disease (CD) (C. G. C. McGregor et al. CMGH 2022). Scarce evidences are available on the perianal fistula pathophysiology. Bone marrow-derived Mesenchymal Stem Cells (bmMSCs) local injections have been found safe and efficient for 50% of CD patients included in a previous prospective monocentric study (Reenaers et al, JCC2023).

Aim: The present study aims at identifying potential protein markers associated with fistulae closure following bmMSCs local injection, using the biological material collected during fistula tract curettage.

Methods: In the prospective interventional uncontrolled study carried out at CHU of Liège (2019 - 2021), 16 CD have been treated and 10 curettage samples have been analysed by label free proteomics using mass spectrometry technology as in (Merli et al. JCC 2021). Differential analysis comparing responders (R) with perianal fistula closure at W48 (n=5) with non-responders (NR), with absence of closure at any visit including W48, (n=5), identified specific proteomic profile changes, which were also evaluated by Gene Ontology analyses to identify biological processes, cell types and pathways associated with fistula closure.

Results: A total of 1883 proteins were identified and the differential analysis revealed 48 proteins differentially distributed in R versus NR profiles. Only 18 were more abundant in R, among which the product of the STK4, PLP2, CYB5B and FLG genes, showing the strongest significant increases in R and therefore potential associations with fistula closure after bmMSCs injections. The fistula tract material of patients showing no closure (NR) reveal higher number of proteins, together with NR>R relative abundances, associated with inflammatory and immune infiltrates, with chemokines, bacterial invasion. NR profiles show as well lower numbers and relative levels of proteins involved in wound healing and in matrix remodelling than in R. Among the proteins differentially distributed in R versus NR, specific pro-apoptotic (R>NR) and anti-apoptotic proteins (NR>R) could be highlighted, in addition to specific proteins acting upstream pathways involved in morphogenesis, carcinogenesis and fibrosis (HIPPO, MAPK, JAK-STAT pathways and TGF signalling).

Conclusions: Our data provide the first descriptive picture of proteins and likely process/pathways associated with fistula closure after bmMSCs treatment. While independent confirmations are required these preliminary results suggest that the apoptotic process, cell infiltrate degree and proteins involved in tissue remodelling and wound healing, already impacted in fistulae tracts before the bmMSCs injections might be important factors associated with fistula closure outcome in this trial.

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IS IT POSSIBLE TO HAVE INFLAMMATORY BOWEL DISEASE AND FATTY LIVER? THE RESULTS OF A SINGLE-CENTRE STUDY IN A BELGIAN SECONDARY HOSPITAL M. Maisin (1), B. De Vroey (2), O. Descamps (3), J. Ghilain (2), O. Dewit (1), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroentérologie, [2] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Gastroentérologie, [3] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Médecine interne.

Introduction: The therapeutic management of inflammatory bowel diseases (IBD) has been greatly expanded and improved in recent years, leading to better patients' nutritional status. Inflammatory gut factors are also suspected as a possible cause of liver steatosis (gut-liver axis).

Aim: To assess the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) in IBD patients and identify risk factors.

Methods: This retrospective cohort study includes consecutive adult patients followed up in consultation in a Belgian secondary hospital (Hôpital de Jolimont-Helora) to monitor their IBD between November 2023 and May 2024. MASLD was defined by the evidence of fatty liver meeting the following criteria: presence of at least one cardiometabolic risk factor together with a fatty liver index > 60 or fatty liver index 30-60 with hyperechoic liver on imaging. Other causes of chronic liver disease were excluded. Clinical and biological data, the presence of a metabolic syndrome and detailed IBD data were recorded. In the case of MASLD, patients were offered transient elastography as part of their routine liver work-up.

Results: Of the 110 IBD patients who were screened, 7 were excluded (6 with primary sclerosing cholangitis and 1 with mixed ALD-sclerosing cholangitis). Of the 103 patients, 34 had an FLI score > 60 (33 %), 27 a score between 30 and 60 (26%), and 42 an FLI score < 30 (40%). Of the patients with a FLI score between 30 and 60, 7 had steatosis on imaging, 6 had no imaging available and 14 had no evidence of steatosis. Collectively, out of 97 patients with available data (69% with Crohn's disease et 31% with ulcerative colitis), 41 (42%) were considered MASLD and 56 (58%) non-MASLD. For the whole population, the mean age was 49.7 years, the mean BMI was 27 kg/m², obesity was present in 26% of patients, and type 2 diabetes in 24%. The mean age at diagnosis of IBD was 34.6 years. 60% had the disease for more than 10 years. Compared with non-MASLD patients, MASLD patients were older (55 years vs. 46 years, p=0.007), had a metabolic syndrome (61% vs. 14%, p=0.0001), were obese (56% vs. 4%, p=0.0001; mean BMI 31 vs 24 kg/m², p=0.001) and had a larger abdominal circumference (112 cm vs. 85 cm, p=0.0001), with more IBD diagnosed after age 40 (51% vs. 23%, p=0.017), stricturing phenotype (B2 Montréal classification) (62% vs. 37%, p=0.046) and less use of JAK-2 inhibitors (0% vs. 11%, p=0.027). There were no other differences in terms of disease manifestations, location or activity. Only twenty-four patients with MASLD (56%) agreed to undergo transient elastography during their follow-up. Of these, twenty-three (96%) had confirmed hepatic steatosis, most often severe. Liver elasticity ranged from 4.3 kPa to 22.3 kPa.

Conclusions: Forty-two percent of IBD patients have MASLD. The risk factors are the same as in the general population (obesity, metabolic syndrome, older age). Importantly, 39% of the IBD-MASLD patients do not present metabolic syndrome. Other risk factors specific to IBD include diagnosis of IBD at a later age, stricturing phenotype, as well as the

absence of certain treatments. This high prevalence justifies screening these patients, as severe fibrosing MASLD has been diagnosed. Analysis of larger cohorts would be useful to confirm the specific risks associated with IBD and possibly propose more specific screening in this population.

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INTESTINAL ULTRASOUND CORRELATES WITH PATIENT-REPORTED IBD DISABILITY IN ULCERATIVE COLITIS: A STEP TOWARDS INTEGRATED MONITORING. E. Eggermont (1), M. Lenfant (1), L. Fierens (2), S. Vermeire (1), M. Ferrante (1), J. Sabino (1), B. Verstockt (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA).

Introduction: Non-invasive imaging methods, particularly intestinal ultrasound (IUS), are increasingly pivotal in guiding management in ulcerative colitis (UC). While long-term treatment goals focus on reducing IBD-related disability, the link between ultrasonographic findings and patient-reported outcome measures (PROMs), such as IBD-related disability, remains unclear.

Aim: In this study, we aimed to investigate the link between patient-reported outcome measures (PROMs) and intestinal ultrasound findings in patients with ulcerative colitis.

Methods: Data on IBD-related disability (using the IBD disk) were prospectively gathered through a digital questionnaire from patients with UC undergoing routine IUS and performed within maximal one week of each other. Patients with isolated proctitis were excluded. Bowel wall thickness (BWT) was averaged from two independent measurements >1 cm apart, alongside colour Doppler assessments, all blinded to IBD disk data. The Milan Ultrasound Criteria (MUC) score was calculated, with relevant ultrasound activity defined as MUC >6.2 (worst affected segment). A high IBD-related burden was defined as an IBD disk score >40.

Results: Thirty-one paired assessments (median interval: 0.0 [IQR 0.0–3.0] days) were conducted on unique UC patients (38.7% female, median age 32.6 [28.0–45.9] years, median disease duration 1.3 [0.3–6.6] years, 71.0% left-sided colitis). Ultrasound activity (MUC >6.2) was present in 51.6% of patients, while 29.0% reported a high IBD-related disability. Total IBD disk scores correlated significantly with maximal BWT ($r=0.41$, $p=0.02$), modified Limberg Doppler signal ($r=0.35$, $p=0.05$), and MUC scores ($r=0.44$, $p=0.01$). Patients without MUC-defined inflammation showed significantly lower IBD-related disability (median IBD disk score: 41.0 [26.0–52.0]) compared to those with inflammation (72.0 [58.0–78.0], $p=0.001$). Individual IBD disk components—abdominal pain, body image, education/work impact, emotions, energy, interpersonal interactions, defecation regulation, sexual function, and sleep—differed significantly between patients with and without ultrasonographic inflammation. Quartile analysis revealed that normal ultrasonographic findings were most likely in patients with the lowest IBD disk scores (Q1 vs Q2–Q4: 87.5% vs 53.3%, $p=0.02$). Receiver Operating Characteristic (ROC) analysis suggested a stricter MUC cutoff of 5.3, achieving 71.0% [48.1–93.8%] accuracy in estimating IBD-related disability with a negative predictive value of 88.2%.

Conclusions: In patients with UC, IUS findings correlate with IBD-related disability and warrant further exploration as potential endpoint and/or treatment target. However, these metrics seem complementary rather than fully interchangeable.

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DEVELOPMENT OF A PATIENT-CENTRED DASHBOARD FOR ROUTINE IBD MONITORING. L. Fierens (1), C. Hedin (2), G. Novacek (3), M. Julsgaard (4), E. Gross (5), I. Arijs (6), C. Sander (7), V. Vakouftsi (8), J. Koenders (9), M. Vanhaverbeke (1), T. Stamm (10), M. Ferrante (11) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Diseases and Metabolism (CHROMETA), [2] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Medicine Solna, [3] Medical University of Vienna, Vienna, Austria, Department of Internal Medicine III, [4] Aarhus University Hospital, Aarhus, Denmark, Aarhus, Denmark, Department of Hepatology and Gastroenterology, [5] Österreichische Morbus Crohn / Colitis ulcerosa Vereinigung (ÖMCCV), Austria, Österreichische Morbus Crohn / Colitis ulcerosa Vereinigung (ÖMCCV), [6] Belgian IBD Research and Development (BIRD), Belgium, Belgian IBD Research and Development (BIRD), [7] Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung (DCCV e.V.), Germany, Referat Wissenschaft, [8] Hellenic Society of Crohn's disease and ulcerative colitis patients (HELLESCC), , Greece, Hellenic Society of Crohn's disease and ulcerative colitis patients (HELLESCC), [9] Takeda Pharmaceuticals International AG, The Netherlands, Health Data partnerships / New Product Planning Centraal & Oost Europa, [10] Medical University of Vienna, Vienna, Austria, Institute for Outcomes Research, Centre for Medical Data Science, [11] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: A core outcome set (COS) for patients with inflammatory bowel disease (IBD) was recently developed through a multi-stakeholder consensus in the Health Outcomes Observatory (H2O) project.(1) Recognising the importance of data visualisation in enhancing disease management, the H2O website now provides a population-level

dashboard to track quality and key performance indicators.(2) Patient-level dashboards are designed to support both healthcare providers (HCPs) and patients by facilitating individual health monitoring, encouraging patient-clinician dialogue, and supporting shared decision-making.

Aim: This work aimed to develop a patient-level dashboard for HCPs to routinely monitor IBD patients, visualising data collected in the H2O IBD COS.

Methods: In November 2023, a core team comprising three public and four private sector researchers, was formed to coordinate the project. To guide discussions with target users, the lead academic centre developed a static dashboard template including all IBD COS variables. On- and offline feedback was gathered from target users and incorporated iteratively to refine the dashboard until consensus was achieved. Six patients from six countries reviewed the template, identifying unclear or missing outcomes essential for discussion during an outpatient clinic.

Results: A total of 15 HCPs and 7 academic researchers from 8 countries reviewed dashboard templates, providing feedback over two improvement rounds. Key improvements included integrating medication tracking with graphical displays of biomarkers and patient-reported outcomes (PROs) related to disease activity, adding pop-up information on hover, and introducing graph customisation options. In March 2024, consensus among target users was reached on the third version of the static dashboard, which was later also approved by all consulted patients without requiring additional adjustments. In a one-screen overview, this final static dashboard presents basic demographic information; treatment information with related adverse events, adherence and satisfaction; and baseline condition factors (extraintestinal manifestations, disease location and behaviour). Furthermore, faecal calprotectin, C-reactive protein, haemoglobin, BMI and several patient-reported outcomes related to disease activity symptoms, quality of life or health management are visualised in a graphical way. An additional alert box was incorporated to flag unexpected hospitalisations, emergency room visits, malnutrition and active smoking, as well as vaccination reminders.

Conclusions: We developed a patient-level dashboard for HCPs to support routine monitoring of IBD patients. The static template offers flexibility, allowing implementation teams to add customised information. The template is currently being transformed into a dynamic version for integration into the electronic health records of four academic hospitals. Additionally, the patient-level dashboard is currently being adjusted in close collaboration with patients to integrate into existing PRO collection tools, enabling patients to actively track their health progress themselves, and ensuring that patients and HCPs speak a common language to drive shared decision making.

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CHARACTERIZATION OF A EUROPEAN POPULATION WITH RECENTLY DIAGNOSED CROHN'S DISEASE: RESULTS FROM THE PROSPECTIVE CROHN'S DISEASE COHORT (CROCO) STUDY. S. Vieujean (1), L. Monin (1), J. Revés (2), N. Arebi (3), A. Fadra (4), J. Burisch (5), Gorm Roager (5), B. Anthony (6), M. Dodel (7), M. Cravo (8), D. Duricova (9), P. Ellul (10), I. Kaimakliotis (11), S. Shaji (12), I. Ordas (13), I. Rodríguez-Lago (14), I. Mocanu (15), V. Hernandez (16), M. Nachury (17), M. Fumery (18), A. Goldis (19), N. Pedersen (20), D. Conceição (21), B. Barberio (22), A. Guedes (23), R. Ribeiro (24), R. Ungaro (25), J. Mary (26), N. Bigot (27), J. Lambert (28), . Colombel (29), J. Torres (30) / [1] CHU Liege, Liège, Belgium, Department of Gastroenterology, [2] Hospital Beatriz Ângelo, Loures, Portugal, Division of Gastroenterology, [3] St Mark's National Bowel Hospital, United Kingdom, Department of IBD, [4] St Mark's National Bowel Hospital, United Kingdom, Department of IBD, [5] Copenhagen University Hospital - Amager and Hvidovre, Denmark, Gastrounit Medical Division, [6] CHU Clermont - Ferrand, France, IBD Unit, [7] CHU Clermont - Ferrand, , France, IBD Unit, [8] Hospital da Luz- Luz Saúde, Portugal, Division of Gastroenterology, [9] ISCARE a.s., Czech Republic, IBD Clinical and Research Clinic, [10] Mater dei hospital, Malta, Department of Gastroenterology, [11] American Gastroenterology Center, Cyprus, American Gastroenterology Center, Gastroenterologie and Hepatologist, Strovolos- Cyprus, Cyprus, [12] Hull University Teaching Hospitals, BD Research Unit, United Kingdom, Department of Gastroenterology, Hull, United Kingdom., [13] Hospital Clinic Barcelona- IDIBAPS- CIBER-EHD, Spain, IBD Unit- Department of Gastroenterology, [14] Hospital Universitario de Galdakao- Biobizkaia Health Research Institute, , Spain, Department of Gastroenterology, Galdakao, Spain, [15] Hospital Garcia de Orta, Portugal, Department of Gastroenterology, Almada, Portugal, [16] Hospital Alvaro Cunqueiro, , Spain, Gastroenterologie, [17] Univ. Lille- Inserm- CHU Lille- U1286 - INFINITE, France, Institute for Translational Research in Inflammation, Lille, France, [18] CHU Amiens-Picardie Hôpital Sud, France, Department of Hepato - Gastroenterology, [19] Algomed Policlinic, Romania, Algomed Policlinic, Gastroenterology, Timisoara, Romania, [20] Slagelse Hospital, Denmark, Slagelse Hospital, Gastroenterologie, Slagelse, Denmark, [21] Instituto Português de Oncologia de Lisboa, Lisbon, Portugal, Division of Gastroenterology, [22] University of Padua, Padua, Italy, Division

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Introduction: Crohn's disease (CD) is a chronic and progressive condition with a growing global prevalence, leading to potential bowel damage and disability. Data on the clinical presentation, outcomes, and treatment options in newly diagnosed CD patients in Europe in the current era are essential to guide physicians.

Aim: The aim is to describe the clinical characteristics of a contemporary European cohort of recently diagnosed CD patients.

Methods: The Crohn's Disease Cohort (CROCO) is an ongoing, multicentre, European prospective study of CD patients diagnosed within the last 12 months, aimed at tracking bowel damage progression and disability. This report presents the baseline characteristics at study inclusion.

Results: From August 2021 to October 2024, 399 patients (56% male, 46% current or former smokers) with a median age at diagnosis of 33.7 years (IQR 24.6; 49.2) were recruited across 18 centres. The median delay between symptom onset and diagnosis was 6.2 months (IQR 2; 15.4), and the median disease duration at inclusion was 3.8 months (IQR 1.6; 7.4). Ileal involvement (L1/L3) was reported in 85% of patients. Overall, 15% had perianal disease and 28% had extraintestinal manifestations, predominantly arthritis/arthralgia. Complicated disease behaviour was observed in 32% of patients at diagnosis (stricturing: 17%; penetrating: 15%); 6% had undergone intestinal surgery, and 3% perianal surgery from diagnosis to inclusion. CD-related hospitalizations were reported by 22% of patients. Regarding treatments, 51% received steroids (28% systemic steroids), 17% 5-ASA, 1% immunosuppressants monotherapy, and 44% initiated biological therapy (168 anti-TNF, 8 anti-IL 12/23, and 6 anti-integrin, representing 42%, 2% and 2% of the cohort, respectively). A total of 31% were managed with a combination of biologic and immunosuppressant therapies. Disability assessment showed that 48% of patients reported no disability, 24% mild disability, and 28% moderate to severe disability.

Conclusions: In this prospective European cohort of newly diagnosed CD patients, nearly one-third had a complicated disease phenotype and moderate to severe disability, despite a relatively short diagnostic delay. While steroid use remains common, early initiation of biological therapy in 44% of patients reflects a shift in CD management strategies.

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EVOLUTION OF THE IBD-DISABILITY INDEX IN A COHORT OF RECENTLY DIAGNOSED CD PATIENTS: RESULTS FROM THE PROSPECTIVE CROCO (CROHN'S DISEASE COHORT) STUDY. A. Buisson (1), M. Dodel (1), J. Revés (2), J. Burisch (3), G. Madsen (4), N. Arebi (5), A. Fadra (5), S. Vieujeau (6), L. Monin (6), M. Cravo (7), D. Duricova (8), P. Ellul (9), I. Kaimakliotis (10), S. Shaji (11), I. Ordás (12), I. Rodríguez-Lago (13), I. Mocanu (14), V. Hernandez (15), M. Nachury (16), M. Fumery (17), A. Goldis (18), N. Pedersen (19), D. Conceição (20), B. Barberio (21), A. Guedes (22), R. Ribeiro (23), R. Ungaro (24), J. Mary (25), N. Bigot (25), J. Lambert (25), J. Colombel (26), J. Torres (2) / [1] CHU Clermont - Ferrand, France, IBD Unit, [2] Hospital Beatriz Ângelo, Loures, Portugal, Division of Gastroenterology, [3] Copenhagen University Hospital - Amager and Hvidovre, Denmark, Copenhagen University Hospital - Amager and Hvidovre, Gastrounit Medical Division, Hvidovre, Denmark., [4] Copenhagen University Hospital - Amager and Hvidovre, Denmark, Gastrounit Medical Division, [5] St Mark's National Bowel Hospital, United Kingdom, Department of IBD, [6] CHU Liege, Liège, Belgium, Department of Gastroenterology, [7] Hospital da Luz- Luz Saúde, Portugal, Division of Gastroenterology, [8] ISCARE a.s., Czech Republic, IBD Clinical and Research Clinic, [9] Mater dei hospital, Malta, Department of Gastroenterology, [10] American Gastroenterology Centre, Cyprus, Gastroenterologie and Hepatologist, [11] Hull University Teaching Hospitals, BD Research Unit, United Kingdom, IBD Research Unit- Department of Gastroenterology, [12] Hospital Clinic Barcelona- IDIBAPS- CIBER-EHD, Spain, IBD Unit- Department of Gastroenterology, [13] Hospital Universitario de Galdakao- Biobizkaia Health Research Institute, Spain, Department of Gastroenterology, [14] Hospital Garcia de Orta, Portugal, Department of Gastroenterology, [15] Hospital Alvaro Cunqueiro, Spain, Gastroenterology, [16] Univ. Lille- Inserm- CHU Lille- U1286 - INFINITE, France, Institute for Translational Research in Inflammation, [17] CHU Amiens-Picardie Hôpital Sud, France, Department of Hepato - Gastroenterology, [18] Algomed Policlinic, Romania, Gastroenterologie, [19] Slagelse Hospital, Denmark, Gastroenterology, [20] Instituto Português de Oncologia de Lisboa, Lisbon, Portugal, Division of Gastroenterology, [21] University of Padua, Padua, Italy, Division of Gastroenterology- Department of Surgery- Oncology and Gastroenterology, [22] Hospital da Luz Learning Health- Luz Saúde- Lisboa- Portugal, Portugal, Research Department, [23] Hospital da Luz Learning Health- Luz Saúde, Portugal, Research Department, [24] Icahn School of Medicine at Mount Sinai, United States, Department of Gastroenterology, [25] Centre of Research in Epidemiology and Statistics- UMR 1153- Inserm, France, ECSTRRA Unit, [26] Mount Sinai Hospital, United States, Department of Gastroenterology.

Introduction: Crohn's disease (CD) often results in progressive bowel damage and disability. Disability has been proposed as an endpoint for disease-modification trials by the SPIRIT-IOIBD consensus (Le Berre C, et al. Gastroenterology, 2021), though data on the evolution of the IBD-Disability Index (IBD-DI) over time remain limited.

Aim: The Crohn's Disease Cohort (CROCO) is a prospective, ongoing study of newly diagnosed CD patients (within 12 months of diagnosis), assessing changes in bowel damage and disability.

Methods: Disability was measured using the validated IBD-Disability Index (IBD-DI), which includes 14 questions scoring from 0-100 across domains of health, sleep and energy, emotional well-being, body image, pain, defecation, interpersonal activities, and work/education. The IBD-DI was categorized as no disability (0-20), mild disability (21-35), moderate disability (36-50) and severe disability (51-100). We examined changes in the IBD-DI from baseline to the second year of follow-up.

Results: Among 394 patients recruited, 105 had complete IBD-DI data at inclusion and at 24 months. The cohort was 54% male, with a median age at diagnosis of 35.5 years (IQR 24.9-47.9). Median time from symptom onset to diagnosis was 6.1 months (IQR 2-20), with a disease duration of 8.2 months (IQR 4.6-10.3) at study entry. Between baseline and year 2, disability decreased in 30% of patients, remained stable in 48%, and increased in 23% (Figure 1). Changes in IBD-DI were significantly associated with gender ($p=0.004$) and symptoms (Harvey-Bradshaw index) at baseline ($p=0.002$), but not with extra-intestinal manifestations (EIM), therapies, or surgical history. Among patients with bowel resection within the 1st year of diagnosis, IBD-DI decreased in 50%, remained unchanged in 43%, and increased in only 7% between baseline and year 2 ($p=0.15$). Starting an advanced therapy within the 1st year after diagnosis did not impact IBD-DI evolution between baseline and year 2 ($p=0.92$).

Conclusions: Our findings show the evolution of disability in newly diagnosed CD patients highlighting that IBD-DI is able to change in more than half of the patients within the first two years after diagnosis. While disability improved in almost 1/3 of patients, 1/4 of patients still experience moderate-to-severe disability after 24 months.

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THE PREVALENCE AND CAUSES OF CHRONIC LIVER BIOCHEMISTRY ABNORMALITIES AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE. F. Harduin (1), W. Kwanten (2), M. Somers (3), E. Macken (3), L. Vonghia (2), J. Derdeyn (2), T. Steinhauser (2), T. Vanwolleghem (2), S. Francque (4), A. Jauregui Amezcaga (3) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, hepatology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, gastroenterology, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology.

Introduction: Up to one third of patients with inflammatory bowel disease (IBD) has altered biochemical liver tests ranging from a transient liver test abnormality (LTA) to liver failure. Based on clinical guidelines a basic panel of liver biochemistry (i.e. ALT, AST, ALP, γ -GT) should be performed at IBD diagnosis and repeated regularly. Chronic LTA is defined by LTA present for more than 6 months. In case of LTA further assessment is required with additional blood tests and radiological examinations. Exceptionally, if the examinations are negative or inconclusive, a liver biopsy might be considered.

Aim: The primary aim of this study was to establish the current overall prevalence of chronic LTA in a large monocentric cohort of patients with IBD. The secondary aim was to identify the different types of liver disease and their respective prevalence among these patients, both de novo as well as already previously established liver disease.

Methods: Patients aged 18 years or older with a diagnosis of IBD who visited the IBD unit at the Antwerp University Hospital between the 1st of January and 31st of December 2023 were included in this retrospective analysis. To be eligible, patients needed to have at least 2 blood tests, one conducted during this period and the other one at least six months after the first. Liver biochemistry (ALT, AST, ALP and γ -GT) was assessed and scored deviant if higher than the ULN as indicated by the lab. Chronic LTA was defined if abnormalities were found at both occasions (not necessarily for the same liver test). In patients with chronic LTA, additional extended blood test for causes of chronic LTA, additional medical imaging and, if necessary, a liver biopsy, were assessed to see whether they were performed, and which was the underlying aetiology.

Results: A total of 622 patients were screened, 324 patients met the inclusion criteria and were analysed in our study: 65.7 % (213) of patients with Crohn's disease, 32.7 % (106) with ulcerative colitis, and 1.6% (5) with unclassified disease. We identified 46 individuals with chronic LTA, resulting in a prevalence of 14%. Among the patients with chronic LTA, 67.4% (31) had Crohn's disease, 28.3% (13) ulcerative colitis and 4.3% (2) unclassified colitis. In case of chronic LTA, an elevation in AST was found in 58.7% (27) of the patients, ALT in 60.9% (28), GGT in 56.5% (26) and ALP in 32.6% (15). Eighty percent (37) of the LTA were considered mild ($<5\times$ ULN) and 20% (9) were considered moderate ($5-15\times$ ULN). Of the 46 patients with chronic LTA, 32 (70%) were already known to have a liver disease, with MASLD being the most frequent (44%). Notably, 9 out of 324 (2.7%) patients had a previously established liver disease without any LTA. The most common cause of chronic LTA was MASLD, found in 44% of the patients (22). Other causes included PSC (12%, 6 patients), AIH (4%, 2 patients), alcohol-related liver disease (4%, 2 patients), viral hepatitis (2%, 1 patient), DILI (2%, 1 patient), IgG4-related liver disease (2%, 1 patient), and ABCB4-related liver disease (2%, 1 patient). Four patients had a combination of diagnoses. In 28% (14) of the cases no clear diagnosis was found.

Conclusions: Chronic LTA are frequent among patients with IBD, some of which are moderately elevated. Conversely, only a few patients known to have a concomitant liver disease did not exhibit chronic LTA. The most frequent cause of chronic LTA in IBD is MASLD, followed by PSC, AIH and alcohol-related liver disease.

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SPEED OF DISEASE PROGRESSION AS HALLMARK OF CROHN'S DISEASE SEVERITY: THE RAPID AND SLOW PROGRESSORS. C. Vuckovic (1), A. Cremer (1), L. Amininejad (1), C. Minsart (1), J. Bottieau (2), D. Franchimont (1), C. Liefferinckx (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology, [2] Laboratoire de Gastro-Entérologie Expérimentale (LGE), Université Libre de Bruxelles, Anderlecht, Belgium, Gastroenterology.

Introduction: The natural course of Crohn's Disease (CD) can involve the development of intra-abdominal strictures and fistulae (Montreal B2 and B3 phenotypes, respectively) which often require complex, multidisciplinary treatments. Yet, the speed of disease progression to these phenotypes may differ among patients. To date, identifying those patients, who may require early and intensive treatment strategies, remains a challenge.

Aim: This study retrospectively analyses a large cohort of CD patients with luminal phenotype at diagnosis (Montreal B1) and evaluates the speed of disease progression to B2/B3 phenotypes, in a Belgian tertiary centre.

Methods: A total of 1,262 patients diagnosed with Inflammatory Bowel Diseases (IBD) were screened from the 3000+ IBD patient's clinics. Patients with unconfirmed CD diagnosis, missing data, and patients diagnosed before 1990 were excluded. Among the 516 CD patients meeting the inclusion criteria, 372 presented with a luminal B1 phenotype at diagnosis. Of these, 108 patients progressed to B2/B3 phenotypes during follow-up (FU) and were retrospectively analysed. All events were recorded from date of diagnosis to maximum follow-up (FU), to achieve high granularity, from demographics (sex, tobacco use) and disease characteristics (CD phenotype based on Montreal Classification, presence of extra-intestinal manifestations, associated IMIDs, first degree familial history of IMIDs or IBD) to treatment adaptations (immunomodulators, biologics, surgeries for B2/B3 phenotypes). Patients were then stratified into rapid progressors (within 5 years after CD diagnosis) and slow progressors (beyond 5 years after CD diagnosis), based on the median progression time to B2/B3 phenotypes in our cohort of 108 patients (median 5 years [1.8-9.9]). Continuous variables were presented as medians (IQR25-75). Categorical data were expressed as absolute numbers and percentages. Subpopulation comparisons were conducted using Fisher's exact test and Mann-Whitney test, as appropriate. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using Prism.

Results: Of the 108 patients progressing to B2/B3 phenotypes through FU, 56 (52%) were rapid progressors (median time of progression from B1 to B2/B3 phenotypes: 1.8 years [0.8–3.5]) and 52 (48%) were slow progressors (median time of progression from B1 to B2/B3 phenotypes: 10 years [7.0–12.6]; p<0.0001). Rapid progressors were older at CD diagnosis (median age 25 years [21–38] vs 19 years [15–24], p<0.0001), as paediatric CD was more prevalent among slow progressors (33% vs 5%, p=0.0003). Although both groups required biologics and surgeries in similar proportions, rapid progressors required biologics earlier (median time between CD diagnosis and first biologic initiation: 1.3 years [0.3–3.1] vs 5.6 years [2.7–8.9], p<0.0001) and underwent surgery for disease progression earlier compared to slow progressors (median time between CD diagnosis and first surgery: 2 years [1.1–4.3] vs 10 years [6.9–13.4], p<0.0001). All surgeries occurred after disease progression to B2/B3 phenotypes. Slow progressors underwent surgery later after initiating biologics compared to rapid progressors (median between first biologic initiation and first surgery: 6.7 year [2–9.5] vs 1.2 year [0.3–2.7], p<0.0001). Interestingly, although the proportion of anoperineal disease at diagnosis was similar in both groups, rapid progressors exhibited less anoperineal disease at maximum FU compared to slow progressors (16% vs. 46%, p=0.002). While this difference may reflect the longer disease duration among slow progressors (Median FU: 15 years [11–20] vs. 9 years [7–13], p<0.0001), the potential impact of earlier initiation of multimodal treatments in rapid progressors cannot be ruled out.

Conclusions: CD patients with initial B1 phenotype progressing to B2/B3 phenotypes can be classified as rapid and slow progressors, based on their speed of progression to these phenotypes. Rapid progressors demonstrate a more aggressive disease course, with earlier biologics initiation and need for surgery. The description of disease progression may uncover a new dynamic phenotype of disease severity that is often overlooked or lacking in the current reported cohort and population-based studies. Stratification by the speed of progression may better define patients with severe disease, potentially guiding tailored therapeutic strategies.

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A CLUSTERING APPROACH TO DISCRIMINATE SLOW AND RAPID BIOLOGICS SWITCHERS IN DIFFICULT-TO-TREAT CROHN'S DISEASE PATIENTS. C. Vuckovic (1), A. Cremer (1), L. Amininejad (1), C. Minsart (1), J. Bottieau (2), D. Franchimont (1), C. Liefferinckx (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology, [2] Laboratoire de Gastro-Entérologie Expérimentale (LGE), Université Libre de Bruxelles, Anderlecht, Belgium, Gastroenterology.

Introduction: CD patients exhibit highly variable responses to biologics. While some patients achieve sustained remission with only one biologic over the course of their disease, other will require the sequencing of multiple biologics (“difficult-to-treat” patients) for optimal disease control.

Aim: The aim of this study was to delineate the treatment regimen profile of CD patients with luminal disease, in a Belgian tertiary centre.

Methods: Among 323 CD patients diagnosed between 1999 and 2019 with a luminal B1 phenotype at diagnosis, 203 patients who maintained this phenotype at maximum follow-up (FU) were selected (median FU 11 years [8–15]), based on inclusion criteria. All events were recorded from CD diagnosis to maximum FU, from disease characteristics to any treatment adaptations. Only biologics initiated for refractory disease (primary non-response or loss of response to the previous biologic) were documented, with exclusion of biologics prescribed after serum sickness-like reactions, other secondary effects, pregnancy. Combined with the selection of patients maintaining a B1 phenotype throughout FU, this approach minimized confounding factors related to heterogeneity in disease phenotypes and treatment modalities within the cohort. A temporal clustering approach using k-means was then applied to the 203 patients to determine the different biologic treatment regimen profiles. Patient profiles were compared using the Dynamic Time Warping (DTW) similarity measure, considering the three successive cumulative biologics exposures over the first 10 years of FU after CD diagnosis. Missing values for right-censored patients were padded accordingly. The number of clusters was chosen to balance maximizing the silhouette score while ensuring sufficient individuals per cluster. For each cluster, cumulative biologic exposures were summarized as ‘cluster profiles,’ represented by barycentres computed with soft-DTW distance. The clustering approach was implemented using the Python package tslearn.

Results: The 203 patients were clustered in 5 distinct profiles, based on their cumulative biologics’ exposures within the 10 first years after CD diagnosis. - Cluster 1 (n=55 patients): no biological exposure - Cluster 2 (n=51 patients): single biologic, late onset. Patients were exposed to a single biologic, initiated with a median of 5.7 years after CD diagnosis [3.7-7]. - Cluster 3 (n=53 patients): single biologic, early onset. Patients were exposed to a single biologic, initiated with a median of 0.5 years after CD diagnosis [0.13-1.3]. - Cluster 4 (n=23): multiple biologics, early onset. Patients were exposed to multiple biologics, with the first one initiated with a median of 1.6 years after CD diagnosis [0.41-4.1]. They were then exposed to a second biologic (median time between CD diagnosis and 2nd biologic: 7.1 years [6.1-8.2]) and a third biologic (median time between CD diagnosis and 3rd biologic: 9.3 years [8.5-11.4]). - Cluster 5 (n=21 patients): multiple biologics, early onset. Patients were exposed to multiple biologics, with the first one initiated with a median of 0.5 years after CD diagnosis [0.13-1.9]. They were then exposed to a second biologic (median time between CD diagnosis and 2nd biologic: 3.1 years [2.11-4.3]) and a third biologic (median time between CD diagnosis and 3rd biologic: 6.9 years [5.6-8.9]). Patients from Cluster 2 were exposed to biologics later than patients from Clusters 3 to 5 ($p<0.0001$), as also shown by their lower biological exposure compared to those of Clusters 3 to 5 (median proportion of their FU exposed to biologics: 48% [37-58] vs 80% [60-89], $p<0.0001$). Within patients requiring multiple biologics during the first 10 years of FU, patients from Cluster 5 required faster biologics changes compared to patients from Cluster 4. In Cluster 5 (or “Rapid biologic Switchers”) patients were exposed earlier, compared to patients in Cluster 4 (or “Slow biologic Switchers”), to the first ($p<0.005$), the second ($P<0.005$) and the third biologic ($p=0.01$).

Conclusions: This clustering approach highlights the highly variable pattern of response to biologics in luminal CD patients. Furthermore, this study discriminates single and multiple biologics-exposed patients within the first 10 years of disease course and introduces the concept of rapid and slow biologic switchers among CD patients with luminal B1 phenotype.

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LONG-TERM EFFECTIVENESS AND TREATMENT PERSISTENCE OF USTEKINUMAB BASED ON ITS POSITIONING IN THE TREATMENT LINE FOR CROHN’S DISEASE. M. Brognet (1), C. Liefferinckx (1), R. Maréchal (2), D. Franchimont (1), A. Cremer (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2] CHU Tivoli, La Louvière, Belgium, Gastroenterology.

Introduction: Ustekinumab (UST), an anti-IL-12/23 monoclonal antibody, is widely used for the treatment of moderate-to-severe Crohn’s disease (CD). Its effectiveness and treatment persistence may vary based on prior exposure to other biologics.

Aim: This study aimed to evaluate the long-term effectiveness and treatment persistence of UST based on its position in the treatment line and to identify predictive factors for achieving steroid-free clinical remission. These findings are particularly relevant as UST is now reinstated as a first-line option for CD in Belgium, while anti-IL-23 therapy is now available as second-line treatment and may offer superior outcomes.

Methods: This retrospective monocentric study included 122 patients with active moderate-to-severe CD treated with UST at a single tertiary referral centre from December 2016 to September 2023. Patients were classified into three groups based on their treatment line: first-line (biologic-naïve), second-line (exposed to one prior biologic), or $\geq$ third-line (exposed to two or more prior biologics). Outcomes assessed included steroid-free clinical remission

and biological remission at weeks 16 and 52, and endoscopic remission after one year. Treatment persistence was evaluated using Kaplan-Meier curves, and predictive factors for steroid-free clinical remission at week 52 were identified via univariate and multivariate analyses.

Results: Of the 122 patients (44% male; median age 38.5 years; median disease duration 9.5 years), 17 (14%) were biologic-naïve, 51 (42%) had been exposed to one prior biologic, and 54 (44%) to two or more biologics. Most patients (82%) had prior exposure to anti-TNF α agents, and 23% to vedolizumab. At UST initiation, 28% of patients were on corticosteroids, and 19% were taking concomitant immunomodulators. Steroid-free clinical remission rates at weeks 16 and 52 were 36% and 60%, respectively, in the first-line group, compared to 37% and 30% in the $\geq$ third-line group. Biological remission rates followed a similar pattern, with 67% and 50% in the first-line group versus 36% and 22% in the $\geq$ third-line group at weeks 16 and 52, respectively. Endoscopic remission after one year was achieved in 78% of the first-line group, compared to 50% of the $\geq$ third-line group. Despite these trends, none of the differences in remission rates across treatment lines reached statistical significance. In terms of treatment persistence, the probability of remaining on UST at one year was 82% for the first-line group versus 69% for the $\geq$ third-line group. Median treatment persistence was 4.1 years for first-line therapy compared to 2.9 years for third-line therapy. However, these differences were not statistically significant ($p=0.319$). Multivariate analysis identified prior exposure to vedolizumab (OR=0.17; 95% CI: 0.04–0.63) and longer disease duration (OR=0.94; 95% CI: 0.86–0.99) as significant negative predictors of steroid-free clinical remission at week 52.

Conclusions: This study highlights that UST may be more effective when used as first-line therapy for CD, with higher trends in clinical, biological, and endoscopic remission rates, and better treatment persistence, though these differences were not statistically significant. Prior vedolizumab exposure and longer disease duration were identified as significant negative predictors of steroid-free clinical remission. These findings are crucial in the evolving treatment landscape. This underscores the importance of carefully tailoring treatment strategies to optimize patient outcomes.

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BILE ACID PROFILING OF ILEAL FLUID IN CROHN'S DISEASE USING METABOLOMICS. I. De Greef (1), S. Loopmans (2), G. Bislenghi (3), A. D'Hoore (3), I. Terrasson (3), B. Verstockt (4), J. Sabino (4), M. Ferrante (4), B. Ghesquière (2), S. Vermeire (4), S. Verstockt (5) / [1] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases and Metabolism (CHROMETA), [2] KUL - University of Leuven, Leuven, Belgium, Department of Cellular and Molecular Medicine, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal surgery, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism.

Introduction: An ileal resection is known to cause bile acid malabsorption in Crohn's disease (CD), but its impact on the bile acid landscape remains understudied.

Aim: Therefore, we studied bile acid composition in ileal fluid of CD and control patients using targeted metabolomics and assessed the impact of sample preparation.

Methods: Ileal fluid was collected from CD patients ($n=10$) and non-IBD controls ($n=10$) having an ileostomy. Targeted metabolomics (LC-MS/MS) was applied on full ileal fluid samples as well as on their supernatants (ie. after centrifugation of a full fluid sample aliquot). Bile acid raw abundances were normalised to sample weight (g), and only bile acids detected in at least 40% of all samples (per sample type) were included for further analysis. A comparative analysis between full ileal fluid and its supernatants across all samples was assessed by Spearman correlations, while the bile acid abundances between CD and controls was compared using Mann-Whitney U tests. A nominal p value < 0.05 was considered significant.

Results: For the CD group, the median [min-max] length of resected ileum was 15.0 [0.0-33.5] cm and 0.0 [0.0-15.0] cm for the control group. Ten primary, 6 secondary and 2 modified bile acids were present in full ileal fluid as well as in the corresponding supernatants. While bile acid abundances were 1.2 to 6.0 times higher in full ileal fluid compared to paired supernatants, the overall bile acid profiles remained highly consistent. In particular, 13 out of 18 bile acids showed a strong correlation between both sample types ($r>0.8$, $p<0.05$), and the remaining 5 showed moderate but significant correlations ($r=0.5-0.7$, $p<0.05$). Lastly, while the abundances between the full CD and control groups were similar, a subanalysis comparing CD patients with an ileal resection ($n=5$) to controls with a total mesorectal excision ($n=6$), revealed an increase in primary bile acids glycocholic acid (GCA) ($p=0.052$) and glycochenodeoxycholic acid (GCDCA) ($p=0.056$) in the CD subgroup.

Conclusions: In this pilot metabolomics study, we detected both primary and secondary bile acids in the ileal fluid of CD patients and controls. Bile acid composition in full ileal fluid aligns well with its derived supernatant, suggesting supernatant as a viable alternative for measurements, simplifying sample preparation. GCA and GCDCA, both primary bile acids typically reabsorbed in the ileum, tended to be increased after ileal resection in CD patients. A broader screening of bile acid and microbiota metabolites in ileal fluid on a larger scale may unravel novel targets contributing to disease recurrence after resection.

OPTIMIZING CARE FOR WOMEN OF CHILDBEARING AGE WITH INFLAMMATORY BOWEL DISEASE: DEVELOPING A SPECIFIC PATHWAY UTILIZING EUROPEAN CROHN'S AND COLITIS ORGANISATION GUIDELINES AND THE AMERICAN GASTROENTEROLOGY ASSOCIATION RECOMMENDATIONS. E. De Dycker (1), P. Geens (1), T. Lambrechts (1), E. Loddewijckx (1), A. Paps (1), J. Degry (2), C. D'Hondt (3), A. Matthijs (3), S. Vermeire (1), J. Sabino (1), B. Verstockt (1), L. Lannoo (3), K. Van Calsteren (3), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases and Metabolism, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Obstetrics and Gynaecology.

Introduction: Recent advances have greatly improved our understanding of the interaction between Inflammatory bowel disease (IBD) and reproductive health. The European Crohn's and Colitis Organisation (ECCO) and the American Gastroenterology Association (AGA) have both provided valuable guidelines to support best practices in this area. Translating these guidelines into a practical care pathway is useful for patients with a pregnancy wish or for those who are already pregnant, ensuring effective implementation in daily practice.

Aim: Our goal was to develop the IBD multidisciplinary Family planning uz leuven care pathway (IBD INFANT Wish) and to improve preconception counselling for IBD patients with a pregnancy wish.

Methods: To develop, implement and evaluate this pathway, we applied a 7-phase model. Our structured approach aims to provide comprehensive, multidisciplinary care tailored to the unique challenges and needs of IBD patients during preconception, pregnancy and postpartum.

Results: After completing the first three phases of the 7-phase methodology, we developed the IBD INFANT Wish care pathway. It adapts to patient type, risks, and comorbidities ensuring personalized care throughout their journey from pregnancy planning to postpartum. Structured as a time-task matrix, it outlines key actions at each stage. Preconception phase: Tailored information for IBD patients is crucial, covering fertility, heredity, and the impact of IBD and its treatments on conception and pregnancy. While patients may fear passing IBD to their children, the risk is only 3-5% if one parent is affected, rising to 30% with both parents. Women with IBD in remission and without previous lower abdominal surgery have similar fertility rates to healthy women. However, active disease can reduce fertility. Preconception counselling should focus on achieving remission, reviewing medications, and replacing contraindicated drugs (e.g. methotrexate, small molecules) with safer alternatives. Lifestyle changes, including a healthy diet, exercise, smoking cessation, and avoiding alcohol or drugs, are essential. Vaccination updates and higher-dose folic acid supplementation (especially for those on sulphasalazine) are key to optimize maternal and foetal health. Pregnancy phase: Pregnant IBD patients require intensified monitoring, including IBD clinic visits once per trimester and regular obstetric appointments. Disease activity is assessed using faecal calprotectin, as pregnancy can affect the reliability of blood markers. A thorough review of medication is necessary, as certain IBD-related drugs, including methotrexate, JAK inhibitors and S1P receptor modulators, are contraindicated during conception and pregnancy. Personalized counselling addresses patient concerns and provides tailored advice, helping reduce anxiety. Emphasizing the importance of achieving and maintaining remission during conception and pregnancy is crucial for both pregnancy and infant outcomes. Remission should ideally be confirmed by endoscopy and/or faecal calprotectin to ensure disease control. Adequate weight gain is crucial for foetal health, and dietary advice should be provided if needed. Vaginal delivery is preferred unless complications (e.g. active perianal disease or IPAA warrant a caesarean section). During pregnancy, patients should also be informed about vaccination restrictions for children exposed to biologics in utero. Live attenuated vaccines (e.g. Rota) should be withheld during the first year of life or until the biologic is no longer detectable in the infant's blood. In case of flares, a multidisciplinary approach is required, considering disease severity, prior medications, and gestational age. Due to the heightened risk of venous thromboembolism during pregnancy and postpartum, prophylactic anticoagulation may be necessary for high-risk patients. Postpartum phase: Postpartum care includes follow-ups for both gynaecological and IBD management. If biologics were paused during pregnancy, they should be resumed to maintain remission and prevent flares. Medications safe during pregnancy are safe for breastfeeding and can be restarted. Counselling on family planning and future pregnancies is essential, addressing timing, risks, and strategies for disease control. Mothers should also be reminded of vaccination restrictions for children exposed to biologics during pregnancy.

Conclusions: The development of the IBD INFANT Wish marks a significant advancement in guiding IBD patients of childbearing age, providing multidisciplinary and evidence-based care tailored to improve both maternal and infant outcomes while setting a new standard for future practice.

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- K01 -

THE IMPROVECARENOW REGISTRY: PREDICTION OF DIFFERENT REMISSION RATES IN PAEDIATRIC ULCERATIVE COLITIS. J. Van Hecke (1), G. Veereman (2), K. Huysentruyt (1), L. Wauters (3), J. Adler (4), E. De Greef (1) / [1] UZ Brussel, Brussels, Belgium, Paediatric Gastroenterology and Nutrition, [2] UZ Brussel, Brussels, Belgium, Paediatric Gastroenterology, [3] KUL - University of Leuven, Leuven, Belgium, Gastroenterology, [4] Michigan Medicine, Michigan, United States, Paediatric Gastroenterology and Nutrition.

Introduction: Identifying clinical predictors of remission in paediatric ulcerative colitis (UC) will impact therapeutic approach.

Aim: We aimed to define and to predict time to first remission (TFR), time to corticosteroid-free remission (TCSFR, ≥ 3 months corticosteroid withdrawal) and time to sustained remission (TSR, ≥ 6 months) in paediatric UC.

Methods: We retrospectively analysed prospectively collected data on 2383 patients provided by the ImproveCareNow Registry (2007–2023). We included UC patients under 18 years at diagnosis with enrolment and first visit within 3 months of diagnosis. Remission was defined as a Paediatric UC Activity Index (PUCAI) less than 10 points. IBM SPSS v.29 was used for statistical analysis with multiple imputation to handle missing data. Cox regression was used to identify predictors at diagnosis/enrolment (T0) or first visit (T1) on the outcomes (n=1785).

Results: Mean TFR was 177,7 days, predicted by disease extent ($p>0,05$) at T0 and the presence of acute severe UC (ASUC, HR=1,142, $p=0,05$) before T0. A subgroup (n=964) showed prediction of TFR by PUCAI (moderate HR=0,867 or severe disease HR=0,697, $p<0,1$) at T1 and the presence of ASUC (HR=1,292, $p=0,007$) before T1. Mean TCSFR was 569,6 days, predicted by PUCAI (only mild HR=0,728 and moderate HR=0,559, $p<0,001$) and use of corticosteroids (HR=0,668, $p<0,001$) at T1. Mean TSR was 631,0 days, predicted by PUCAI (only mild HR=0,721 and moderate HR=0,541, $p<0,001$) and the use of oral aminosalicylates (HR=0,793, $p=0,003$) at T1.

Conclusions: Several clinical parameters in early disease course predict the outcomes with increasing PUCAI as useful negative predictor to influence therapeutic strategy.

- K02 -

CLINICAL BENEFITS OF MARALIXIBAT FOR PATIENTS WITH ALAGILLE SYNDROME ARE DURABLE THROUGH 7 YEARS OF TREATMENT: DATA FROM THE MERGE STUDY. E. Sokal (1), B. Kamath (2), E. Gonzales (3), D. Kelly (4), K. Murray (5), D. Leung (6), D. Mogul (7), W. Garner (8), P. Vig (7), E. Jacquemin (9) / [1] UCLouvain, Cliniques Universitaires St Luc, Belgium, Paediatric Hepatology, [2] The Children's Hospital, United States, of Philadelphia, [3] Service d'Hépatologie et de Transplantation Hépatique Pédiatriques, Centre de Référence de l'Atrésie des Voies Biliaires et des Cholestases Génétiques (AVB-CG), France, FSMR FILFOIE, ERN RARE LIVER, Hôpital Bicêtre, AP-HP, Faculté de Médecine Paris-Saclay, Le Kremlin-Bicêtre, and Inserm U1193, Hépatinov, Université Paris-Saclay, [4] Birmingham Women's & Children's Hospital NHS Trust and University of Birmingham, United Kingdom, Liver Unit, [5] Cleveland Clinic Children's Hospital, United States and Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, [6] Texas Children's, United States, Hospital, [7] Mirum Pharmaceuticals, Inc, United States, Scientific Affairs, [8] Mirum Pharmaceuticals, Inc, United States, Biostats, [9] Service d'Hépatologie et de Transplantation Hépatique Pédiatriques, Centre de Référence de l'Atrésie des Voies Biliaires et des Cholestases Génétiques (AVB-CG), France, FSMR FILFOIE, ERN RARE LIVER, Hôpital Bicêtre, AP-HP, Faculté de Médecine Paris-Saclay, Le Kremlin-Bicêtre, and Inserm U1193, Hépatinov, Université Paris-Saclay.

Introduction: Maralixibat (MRX), an ileal bile acid transport inhibitor (IBATi), is approved for the treatment of cholestatic pruritus in patients with Alagille Syndrome (ALGS) ≥ 2 months of age in Europe. Improvements in pruritus, serum bile acids (sBA), and height have been demonstrated from prior clinical trials including ICONIC, which followed participants up to 4 years, as well as IMAGO/IMAGINE and ITCH/IMAGINE-II, which reported outcomes to approximately 1.5 years. Participants from ICONIC, IMAGINE, and IMAGINE-II trials were invited to enrol in MERGE for additional long-term follow-up (LTFU); prior long-term survival outcomes (e.g., liver transplant, death) for this group have been previously reported.

Aim: Here we report on efficacy in participants with additional LTFU from MERGE, including some participants that have received treatment for 7 years.

Methods: All participants from ICONIC, IMAGINE and IMAGINE-II were included in the analysis. Impact of MRX was assessed for pruritus [ItchRO(Obs) 0-4 scale, with a ≥ 1 -point reduction considered clinically meaningful], sBA, height and weight z-scores, ALT, total bilirubin (TB) and direct bilirubin (DB). Change from Baseline (CFB) was determined by comparing median (Q1, Q3) values from enrolment in the initial trial (i.e., ICONIC, IMAGO, or ITCH) to data from the visit in MERGE that best aligned with an annual visit.

Results: Data were analysed for 86 participants at Baseline, with follow-up to 1 year for 76 participants, 4 years for 42 participants, and 7 years for 23 participants. Of the 86 participants, 84 had a genetic diagnosis of ALGS via the JAG1 mutation, 2 participants had a genetic diagnosis of ALGS via the NOTCH2 mutation, and 1 participant had an unidentified mutation. Baseline mean (SD) ItchRO(Obs) was 2.65 (0.75) and clinically meaningful reductions over time with CFB of -1.57 (-0.83, -2.14), -2.00 (-1.43, -2.56), and -2.14 (-1.43, -3.00) at 1 year, 4 years and 7 years, respectively. Likewise, Baseline sBA was 254 (207) $\mu\text{mol/L}$ and decreased with CFB of -57 (8, -150) $\mu\text{mol/L}$, -62 (-32, -152) $\mu\text{mol/L}$, and -105 (-41, -266) $\mu\text{mol/L}$ at 1 year, 4 years and 7 years. Improvement was observed in height, with Baseline z-score of -1.7 (1.27) and CFB of 0.1 (-0.1, 0.3), 0.3 (0.0, 1.0), and 0.7 (0.0, 1.2) at 1 year, 4 years and 7 years while weight z-scores were largely unchanged. Reductions in TB and DB were observed after treatment with MRX. No clinically meaningful changes in ALT or AST were observed with MRX treatment. There were no new safety signals.

Conclusions: In this unmatched cohort, the benefit of MRX in ALGS patients, including both improvements in clinical outcomes and sBA, persist through 7 years of treatment. No new safety concerns were identified in the long-term.

- K03 -

ANTIBIOTICS POST-APPENDECTOMY IN PAEDIATRIC PATIENTS – A LITERATURE REVIEW LEADING TO PROPOSITION FOR A NEW TREATMENT PROTOCOL. C. Goovaerts (1), M. Miserez (2), K. van Hoeve (1), I. Hoffman (1)/[1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Paediatric Gastroenterology, Hepatology & Nutrition, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery.

Introduction: Despite acute appendicitis being very common in the paediatric population, a lot of controversy remains considering the postoperative antibiotic treatment. A clear, evidence-based protocol for postoperative treatment is still lacking. The aim of this review is to develop a protocol for postoperative antibiotic treatment in children with acute appendicitis. By introducing this protocol, we hope to achieve a more straightforward policy and avoid overtreatment with antibiotics. Acute appendicitis (AA) is a common surgical presentation with a lifetime incidence of 9% (1). Despite being among the most common reasons for abdominal surgery in paediatric patients a great variation in treatment exists. Generally, AA is managed with an appendectomy, followed by antibiotics in case of complicated appendicitis. The indication and the optimal duration of postoperative antibiotics for AA still poses significant ambiguity, as described in the consensus document by the European Association of Endoscopic Surgery (EAES) in 2015 where the duration of antibiotic treatment varied between 3, 5, 7, and 10 days. They also stated that the evidence on the duration of postoperative antibiotic treatment is limited (2). The World Society of Emergency Surgery (WSES) recommends transitioning to oral administration of postoperative antibiotics after 48 hours, advocating for a total treatment duration of less than 7 days (3). However, they do not provide specific guidance on duration based on classification or define parameters for discontinuation. The experience is that treatment is often based on the preference of the treating physician. We therefore aimed to create a protocol concerning antibiotic use post appendectomy in the paediatric population, based on the most recent literature.

Aim: Antibiotics post-appendectomy in paediatric patients – a literature review leading to proposition for a new treatment protocol.

Methods: Exclusion and inclusion criteria Only studies reporting on postoperative antibiotic treatment of acute appendicitis in children (< 18 years) written in Dutch or English were included. Randomized controlled trials, pro- and retrospective studies, (systematic) reviews and international guidelines were included. Articles describing planned postoperative treatment were included whereas studies describing prolonged treatment due to postoperative complications (such as surgical site infections) were excluded. We excluded letters to the editor, comments on articles, surveys or research letters. Studies describing a conservative antibiotic treatment approach without appendectomy were not included. Also, patients who had an appendicular mass at first presentation were excluded, since in these cases different approaches are possible depending on disease duration and clinical signs (appendectomy, conservative treatment with antibiotics, percutaneous drainage) and this was beyond the scope of this review.

Results: Literature research To identify potential studies and guidelines, a literature search was performed according to the PRISMA guidelines in Pubmed (Figure 1) using the Medical Subject Heading (MeSH) terms ‘acute appendicitis AND (paediatric OR children OR child) AND (antibiotics OR antibiotic) AND (postoperative OR appendectomy OR surgery)’. For including the most recent literature, we decided to review publications from the last 11 years from 01/08/2012 until 01/03/2024. Duplicates were removed using Covidence.

Conclusions: Based on an extensive literature search, we made a proposition of a treatment protocol for planned postoperative antibiotic treatment after appendectomy in the paediatric population. An overview of the treatment protocol can be seen in in Figure 2. Our aim is primarily to implement a straightforward policy and to avoid further treatments based on a physician’s preference. We opted for a transparent and evidence based yet safe protocol taking into account the clinical evolution of the patient and implemented the use of WBC counts to guide antibiotic duration trying to avoid unnecessary overtreatment based on the physician’s preference. We plan to prospectively evaluate our treatment protocol by evaluating surgical site infections in the first month postoperatively. Also, a prospective analysis of peritoneal cultures will be done to re-evaluate if a switch in type of antibiotic use is necessary.

EVALUATION OF TRANSCUTANEOUS INTERFERENTIAL ELECTRICAL STIMULATION IN THE TREATMENT OF CHRONIC CONSTIPATION IN CHILDREN: A PILOT STUDY. H. Van Gool (1), E. Baert (2), I. Geraerts (2), M. Miserez (3), K. Van Hoeve (4), I. Hoffman (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Paediatric gastro-enterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Physiotherapy, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Paediatric Gastroenterology.

Introduction: Despite the availability of numerous treatment options for managing pelvic floor dyssynergia-type constipation, many children continue to experience therapy-resistant constipation. Neuromodulation, particularly in the form of interferential therapy (IFT), is a well-established treatment modality primarily recognized for addressing slow transit constipation.

Aim: The aim of this study was to evaluate the effectiveness of IFT in the treatment of therapy-resistant pelvic floor dyssynergia-type constipation in children.

Methods: Children with chronic treatment-resistant constipation received baseline investigations to select patients with pelvic floor dyssynergia-type constipation. Defecation frequency, soiling frequency, stool consistency and laxative use were recorded at baseline using a stool diary. First sensation and urge to defecate was recorded at baseline using anal manometry. Quality of life scores of parents and children were recorded. All children received IFT at home (3 times a week, 20 minutes, for three months). IFT was administered through an interferential stimulator, with four adhesive electrodes (two on the lower abdomen, two on the back), so currents cross within the lower abdomen. IFT is easy to use, non-invasive and can be administered at home. After three months, therapy was increased or decreased depending on the results. Primary outcome measures were achieving a defecation frequency between three times a week to three times a day, 50% reduction in soiling episodes and improvement in stool consistency to a consistency of 3 – 4 – 5 on the Bristol Stool Chart for 50% of the bowel movements. Secondary outcome measures were reduced use of laxatives, improvement in rectal sensation and improvement in quality-of-life scores. The follow-up period was one year.

Results: This pilot study, conducted at a tertiary care centre, included 15 children (6 girls, 9 boys) aged 8 to 15 years (mean 11,4 years), with chronic treatment-resistant pelvic floor dyssynergia-type constipation. After one year of follow-up we observed a trend towards increased defecation frequency (mean 6,1/week to mean 8,8/week, $p = 0,06$), a significant improvement in stool consistency (75% of patients to 100% of patients achieving normal consistency in at least 50% of bowel movements, $p = 0,01$) and a trend towards reduced soiling episodes (mean 2,4/week to mean 0,5/week, $p = 0,22$). There was a significant reduction in laxative use (from 75% to 45% of patients using laxatives, $p = 0,05$) with 45% of patients no longer requiring any therapy at the one-year follow-up. Quality of Life (QoL) scores demonstrated significant improvements: gastrointestinal QoL scores increased from a mean of 69/100 to 82/100 for patients ($p = 0,01$) and from a mean of 65/100 to 82/100 for parents ($p = 0,01$). General QoL scores rose from a mean of 64/100 to 78/100 for patients ($p = 0,00$) and from a mean of 58/100 to 76/100 for parents ($p = 0,00$). Additionally, there was a significant improvement in rectal sensation and the urge to defecate as assessed by anal manometry. No adverse events were reported during the study period.

Conclusions: IFT improves stool consistency in children with pelvic floor dyssynergia-type constipation. We observed a significant reduction in the use of laxatives and water enemas and a significant improvement in patient and parental quality of life scores. We observed a significant improvement in rectal sensation and urge to defecate. IFT is a safe therapy, and no adverse events were reported. Adding IFT to the standard medical treatment for patients with dyssynergia-type constipation could possibly prevent the need for water enemas and could significantly improve the quality of life of the patient and their families.

THE IMPROVECARENOW REGISTRY: PREDICTION OF TWO-YEAR NON-REMISSION IN PAEDIATRIC ULCERATIVE COLITIS. J. Van Hecke (1), G. Veerman (2), K. Huysentruyt (1), L. Wauters (3), J. Adler (4), E. De Greef (1) / [1] UZ Brussel, Brussels, Belgium, Paediatric Gastroenterology and Nutrition, [2] UZ Brussel, Brussels, Belgium, Paediatric Gastroenterology, [3] KUL - University of Leuven, Leuven, Belgium, Gastroenterology, [4] Michigan Medicine, Michigan, United States, Paediatric Gastroenterology and Nutrition.

Introduction: Identifying predictors of unfavourable disease course in paediatric ulcerative colitis (UC) could impact therapeutic strategy.

Aim: We aimed to define predictors of paediatric UC patients unable to reach remission two years after diagnosis.

Methods: We performed a retrospective analysis of prospectively collected information of 2383 patients from 2007 till 2023 using de-identified data provided by ImproveCareNow (ICN). We included UC patients under 18 years at diagnosis with enrolment and first visit within three months of diagnosis. Remission was defined as a Paediatric UC Activity Index (PUCAI) less than 10 points. Statistical analysis was performed using IBM SPSS v.29. Multiple imputation was used

for missing data. Demographic information at diagnosis/enrolment (T0), first visit (T1) and follow-up (T2, closest to 24 months) were calculated between relevant groups. Binary logistic regression was used for identification of predictors on the outcome (n=1290).

Results: Two years after diagnosis, 900 patients reached remission and 390 patients did not. Differences in disease severity and treatment were observed at T1 and T2. PUCAI (mild OR=1,946, moderate OR=1,735 or severe disease OR=3,183, $p<0,01$), the use of immunomodulators (IM) (OR= 0,631, $p=0,053$) and Body Mass Index (BMI) z-score (OR= 1,149, $p=0,022$) at T1 (mean 30 days) predicted non-remission at T2 with poor discriminating ability (AUC 0,599 to 0,621).

Conclusions: Predictors for unfavourable disease course were increasing disease severity according to PUCAI, increasing BMI z-score and non-use of IM at T1. These predictors should impact therapeutic strategy shortly after diagnosis.

- K06 -

EFFICACY AND SAFETY OF MULTIPLE SWITCHING FROM INFLIXIMAB ORIGINATOR TO DIFFERENT BIOSIMILARS IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. S. De Groote (1), K. van Hoeve (2), I. Hoffman (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Paediatric Department, University Hospitals Leuven, KU Leuven, Leuven, Belgium, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition.

Introduction: While infliximab (IFX) is highly effective, its high cost poses a significant economic burden, leading to the development of biosimilars. However, limited data exist on double switching from originator IFX to biosimilars in patients with inflammatory bowel disease (IBD), particularly in children with restricted pharmacokinetic information.

Aim: This study evaluated the safety and efficacy of sequential switching from originator IFX to two different IFX biosimilars (CT-P13) in IBD patients.

Methods: In this single-centre study, all children with Crohn's disease (CD) and ulcerative colitis (UC) receiving maintenance IFX therapy were subsequently switched from originator (Remicade®) to two biosimilars. The first switch was to CT-P13 (Inflectra®, cohort A) in January 2018, and the second switch was to another CT-P13 (Remsima®, cohort B) in February 2022. Patients who underwent both switches were classified as cohort C. Demographics, disease activity indices and IFX drug levels were collected from six months before till six months after each switch. Baseline refers to data collected six months before the first switch on the IFX originator. Data are reported as median [interquartile range].

Results: A total of 42 children (26 CD and 16 UC; cohort A) and 44 children (31 CD and 13 UC; cohort B) underwent a single switch to CT-P13, with a median duration on IFX of 13.5 [6.8-35.5] and 21.53 [11.2-39.4] months, respectively, before switching. Among them, 14 children (11 CD and 3 UC; cohort C) underwent multiple switches. Patient characteristics were comparable across cohorts, except cohort C patients were younger at diagnosis and had more severe UC phenotypes. No significant changes in IFX trough levels were observed after single switching. The median IFX trough level was 7.9 µg/mL [5.3-10.6] at baseline versus 8.2 µg/mL [6.7-10.0] six months after the second switch ($p=0.792$). Antibodies to IFX appeared in one patient (cohort A) post-switch. The proportion of patients in clinical and/or biological remission did not significantly change after switching (all $p>0.05$), except for a higher clinical remission rate six months after the second switch compared to baseline in a sub-analysis of cohort C (McNemar $p=0.039$). No clinically significant changes were noted in C-reactive protein, erythrocyte sedimentation rate, or albumin after the switch. The safety profile was similar, with fewer adverse events reported in cohort B post-switch, attributed to seasonal variation with more upper respiratory infections pre-switch. After adjustment, this difference was not significant ($p=0.465$). No serious adverse events were reported.

Conclusions: Switching to biosimilar CT-P13 maintains clinical and biological remission without significant changes in disease activity or adverse events. These findings confirm the safety and efficacy of single and multiple switches in paediatric IBD patients.

SUCCESS RATE AND ITS PREDICTORS WHEN DEPRESCRIBING PROTON PUMP INHIBITORS IN PRIMARY CARE. J. Scheepers (1), F. Carbone (2), K. Van den Houde (1), J. Tack (2) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Centre in Gastro-intestinal Disorders, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department for Gastroenterology and Hepatology.

Introduction: Inappropriate proton pump inhibitor (PPI) use is a growing concern, with up to 70% (1,2) of long-term use lacking a valid medical indication. However, success rates of PPI deprescription in primary care remain poorly defined.

Aim: This study evaluates the success rate of PPI deprescription and identifies predictors for successful deprescription in primary care PPI users who lack a strict medical indication.

Methods: Sixty-one general practitioners enrolled long-term, chronic PPI users without a strict medical indication. Baseline data on demographics, duration and dosage of PPI use, gastrin levels, and medical history were collected (Visit 0). Patients on a high dose PPI at baseline, were instructed to down-titrate to a maintenance dose for 1 month before starting deprescription at Visit 1. At Visit 1, all patients were instructed to deprescribe their PPI within one month. After this period, patients returned for Visit 2, where the PPI was stopped completely if feasible. One month later, during Visit 3, patients entered a one-year follow-up period. Patients returned after 6 and 12 months for Visit 4 and 5, respectively, with online check questionnaires at 3 and 9 months. Gastrointestinal symptoms (nausea, fullness, bloating, upper abdominal pain, lower abdominal pain, heartburn, using PAGI-SYM) and psychosocial co-morbidities (depression, somatization, anxiety using PHQ-9, PHQ-15, GAD-7, respectively) were assessed at all visits and online checks. Successful deprescription was defined as ≤ 3 PPI doses/month. Results are shown as mean $\pm$ SD or median (IQR).

Results: Of 645 enrolled patients (60 $\pm$ 14 years, 59% female, BMI 28 $\pm$ 5 kg/m²), 44% reported previous attempts to stop their PPI use. Patients took their PPI for a median of 9(15-5) years before starting the trial. High-dose PPI use was documented in 19.5% (n=121) of patients, of which 7% (n=8) were unable to lower to a maintenance dose. At the end of the intervention period (Visit 3, 1 month after intended PPI stop, n=514), the overall success rate was 76%. Success rates were similar across patient subgroups according to initial indication, with 75% success in patients using PPI for functional dyspepsia (n=145), 76% in those with an indication of low-grade GERD (n=264), and 83% in patients with non-gastric indications (e.g. polypharmacy, n=48). During a 6-month follow-up period (Visit 4), 83% of patients who reduced their PPI use successfully at Visit 3 maintained PPI cessation, resulting in an overall sustained success rate of 64% (n=235/365). No significant differences in success rate were observed based on age, sex, BMI, PPI dose, initial indication, gastrointestinal symptoms or psychosocial factors. Patients with successful PPI reduction at Visit 3, had lower baseline gastrin levels (93 (233-42) vs. 119 (260-63) pg/ml, p=0.032, n=359), a shorter duration of PPI therapy (9 (15-5) vs. 11 (17-6) years, p=0.037), and more concomitant antacid use during the intervention period (48% vs. 38%, p=0.0491). Transient increases in nausea (0 (0.67-0) vs. 0 (1-0), p=0.008), upper abdominal pain (0.5 (2-0) vs. 1 (2-0), p=0.040), and heartburn (0.43 (1.6-0) vs. 1 (2-0.4), p<0.0001) scores were observed during deprescribing (Visit 2) but returned to baseline values in the follow-up period.

Conclusions: PPI deprescription is feasible in primary care, with 76% achieving success and 64% maintaining cessation at 6 months. Predictors of successful PPI discontinuation include shorter duration of PPI therapy, concomitant antacid use, and lower baseline gastrin levels. Transient symptom increases were common during deprescribing.

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ONE PILL A DAY KEEPS EOSINOPHILIC OESOPHAGITIS AWAY? MAINTENANCE TREATMENT WITH BUDESONIDE ORODISPERSIBLE TABLETS OR VISCOUS SOLUTION. J. Defrancq (1), K. Raymenants (2), J. Tack (2), T. Vanuytsel (2), L. Wauters (2) / [1] KUL - University of Leuven, Leuven, Belgium, Biomedical Sciences, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Swallowed topical steroids are a highly effective treatment for patients with eosinophilic oesophagitis (EoE). Budesonide Orodispersible Tablet (BOT) is the first on-label drug developed for EoE, whereas Budesonide Viscous Solution (BVS) has been used off-label. We previously showed favourable outcomes with Budesonide once daily in EoE (1). While once daily maintenance therapy is now included in the reimbursement criteria for BOT in Belgium, this is only possible after twice daily induction therapy.

Aim: To evaluate the feasibility and real-world efficacy of maintenance therapy with BOT after induction therapy with BVS for EoE.

Methods: We performed a retrospective analysis of a prospectively collected database of confirmed EoE patients at a tertiary care centre (UZ Leuven). Patients using BVS 1mg once or twice daily with adequate follow-up (endoscopy and histology) were switched to BOT 1mg once or twice daily. Dysphagia Symptom Questionnaire (DSQ), Eosinophilic Esophagitis symptom Activity Index (EEsAI), Adult Eosinophilic Esophagitis Quality of Life Questionnaire (EoE-QOL-A) were completed at baseline and after switch. The primary endpoint was histological remission, defined as <15 eosinophils per high-power field (HPF). Secondary endpoints included changes in peak eosinophil counts (PEC), total endoscopic reference scores (EREFS) and clinical symptoms, as well as the clinical presence of oropharyngeal or oesophageal candidiasis. Data are presented as proportions or medians with interquartile ranges, with paired tests for proportions (McNemar) or other variables (Wilcoxon).

Results: Thirty patients (20 male, age 33.5 (28-38.8) years and BMI 23.6 (20.9-27.1) kg/m²) were included, with a follow-up of 205.5 days (113-341). Symptom severity scores were low and disease-related quality of life was high in all groups, before and after switching. After switching from BVS once daily to BOT once daily (n= 18), histological remission remained very high (87.5% after switch vs. 83.33% at baseline, P= 0.5). There was no significant difference in PEC (0/HPF (0-0) after switch vs. 0/HPF (0-9.25) at baseline, P= 0.72). The EREFS score remained low (0 (0-1) after switch vs. 1 (0.25-2) at baseline, P= 0.05) with a similar proportion of Candida (17.65% after switch vs. 16.67% at baseline, P= 0.5). After switching from BVS twice daily to BOT once daily (n= 3), one patient achieved and two patients remained in histological remission. EREFS score improved in one patient and remained zero in the others, with identification of candidiasis in one patient after switching to BOT. Finally, after switching from BVS twice daily to BOT twice daily (n= 9), histological remission numerically increased (100% after switch vs. 55.6% at baseline, P= 0.12). PEC numerically decreased (0/HPF (0-0) after switch vs. 6/HPF (0-49) at baseline, P= 0.1). The EREFS score improved significantly (1 (0-1) after switch vs. 3 (0-3) at baseline, P< 0.05) with a clinical suspicion of Candida in 33.3% after switch vs. 11.1% at baseline (P= 0.24).

Conclusions: Once daily therapy with BOT after switching from BVS is feasible and highly effective in EoE patients. Outcomes may even improve after twice daily therapy of BOT compared to BVS in patients with longer disease duration or more extensive disease. While candidiasis may increase with BOT, this has been linked to treatment response and adherence in EoE (2). A longer follow-up of maintenance therapy with BOT is ongoing.

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- N03 -

EFFECT OF A STANDARDIZED FODMAP OR GLUCOSE MEAL ON FUNCTIONAL DYSPEPSIA SYMPTOMS: A RANDOMIZED DOUBLE-BLIND TRIAL. L. Van Lieshout (1), B. Broeders (2), F. Carbone (2), K. Van den Houte (2), K. Routhiaux (2), T. Vanuytsel (2), J. Tack (2) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, TARGID.

Introduction: Functional dyspepsia (FD) is a disorder of gut-brain interaction affecting approximately 7.2% of the population. The exact etiology remains unknown, but proposed aspects of its pathophysiology include alterations in visceral sensitivity and motility. Research has shown that individuals with FD often experience symptoms triggered by specific food items, particularly those high in Fermentable Oligo-, Di-, Monosaccharides and Polyols (FODMAPs). This may be due to their structure, FODMAPs increase the osmotic pressure and gas production in the bowel, leading to the activation of chemo- and mechanoreceptors. Moreover, a study showed improvement of gastrointestinal symptoms in FD patients after following a low-FODMAP diet.

Aim: The aim of the current study is to identify differences in symptoms after intake of mannitol and glucose.

Methods: Patients with FD and healthy volunteers (HV) were recruited to consume a meal containing either mannitol or glucose on two separate days, following a double blind, randomized cross-over design. Previous research identified mannitol as a personal FODMAP trigger for the patients. In fasted state, participants were administered the study meal, which consisted of porridge made from 40 g of oatmeal and 270 mL of water, together with a glass of tapwater (200 mL). The same meal was administered during two separate study visits: once with 7.5 g of mannitol (total: 167 kcal) and once with 15 g of glucose (total: 209 kcal). Participants filled out questionnaires for 5 gastrointestinal symptoms (nausea, fullness, satiety, epigastric pain and epigastric burning) rated on a Likert scale from 0 to 4 over a period of 4 hours postprandially. Statistical tests were done using a paired T-test for continuous variables and Fisher's exact test for categorical variables. Symptom data were evaluated as Area Under the Curve (AUC). Data are shown as mean ± standard deviation.

Results: Nine HV and 8 patients were recruited with a similar sex (60% vs 100% female) and body mass index (23.4 vs 24.1 kg/m²). HV were significantly younger than patients (30 ± 12 years vs 42 ± 13 years, p=0.04). All participants finished the whole meal. Patients reported more severe gastrointestinal symptoms compared to HV after consuming the glucose (52 ± 31 vs 26 ± 21, p=0.03) and mannitol containing meal (68 ± 54 vs 26 ± 20, p=0.02). However, among the patients, there was no significant difference in FD symptoms between both meals (52 ± 31 vs 68 ± 54, respectively

glucose and mannitol, $p=0.26$). After analysing the gastrointestinal symptoms separately, there was no significant difference in the severity of nausea, fullness, satiety, epigastric pain and burning when comparing after the glucose and mannitol meals.

Conclusions: In this double-blind study, FD patients experienced more severe gastrointestinal symptoms after a standardized oat porridge meal than healthy subjects. Although this study has a limited sample size, these data suggest that glucose is an equal symptom trigger when compared with a FODMAP like mannitol. This is in contrast with IBS where glucose only triggers symptoms in a minority of patients. The underlying mechanism needs to be further evaluated.

- N04 -

EFFICACY OF THE DOMINO DIET IN MANAGING IRRITABLE BOWEL SYNDROME: SYMPTOM AND PSYCHOSOCIAL OUTCOMES IN TERTIARY CARE. L. Schaar (1), K. Routhiaux (1), L. Waegemans (1), K. Van den Houte (1), J. Tack (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (ChroMeta).

Introduction: Irritable Bowel Syndrome (IBS) is a disorder of gut–brain interaction, characterized by abdominal pain and altered bowel habits, including diarrhoea, constipation, or a combination of both. IBS has a significant impact on quality of life and daily functioning, often accompanied by psychological comorbidities such as anxiety and depression. Dietary interventions play a central role in the management of IBS. The low FODMAP diet, which systematically reduces the intake of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), is a widely used approach to relieve symptoms. Although effective, the low FODMAP diet requires strict compliance and recurring supervision by a dietitian to limit risks such as nutritional deficiencies and psychological burden. Given these challenges, the DOMINO diet, designed as a simplified approach, combining NICE dietary guidelines with moderate FODMAP restrictions in a self-management smartphone application, showed beneficial effects on gastrointestinal symptoms in a large primary care IBS cohort. The efficacy of the DOMINO diet app in specialist care patients, where the symptom pattern may be more severe, has not been evaluated.

Aim: We aim to investigate the effectiveness of the DOMINO diet as a less restrictive alternative to the low FODMAP diet in tertiary care IBS. Therefore, we assessed the efficacy of the diet based on IBS symptoms, and evaluated the long-term effect on gastrointestinal symptoms, treatment outcome, and its impact on psychosocial comorbidities.

Methods: After a 2-week baseline period, the intervention phase consisted of an 8-week DOMINO diet, using a mobile application, with participants filling out daily symptom diaries. IBS symptom severity scores (IBS-SSS) were collected before and after the diet to measure changes in symptom severity. Additional assessments included IBS symptoms registered in a daily diary, treatment outcomes using the overall treatment effect (OTE) scale, and psychosocial comorbidities evaluated with PHQ-9 (depression), PHQ-15 (somatic symptoms), and GAD-7 (anxiety) questionnaires. Analyses for psychosocial comorbidities examined baseline differences between responders (≥ 50 point reduction on IBS-SSS) and non-responders, as well as pre-and post-diet changes in responders. Data were reported as mean $\pm$ SEM or median [IQR], and continuous variables were analysed using t-tests or Wilcoxon tests, with statistical significance set at $p \leq 0.05$.

Results: In 40 tertiary care IBS patients (80% female, age 35 ± 12 years, BMI 25.4 ± 5.4 kg/m²) treated with the DOMINO diet, the overall response rate was 80%, with a significant reduction in IBS-SSS compared to baseline (182 ± 95 vs. 289 ± 75 , $p < 0.0001$). In addition, all individual symptoms reduced significantly (duration of abdominal pain (41 [30–56] vs. 18 [10–41], $p < 0.0001$), severity of abdominal pain (38 [26–52] vs. 18 [7–34], $p < 0.0001$), bloating (47 [27–55] vs. 22 [10–38], $p < 0.0001$), and flatulence (50 [30–59] vs. 20 [11–34], $p < 0.0001$). The majority of patients reported their symptoms as much improved (65%), or slightly improved (27.5%). Psychosocial outcomes showed significant improvement at the end of the diet period compared to baseline in somatization (11 [7–14] vs. 7.5 [5–13], $p < 0.0001$), depression (5 [3–9] vs. 4 [2–6], $p = 0.0002$), and anxiety (5 [2–9] vs. 3.5 [1–6], $p = 0.002$).

Conclusions: We demonstrated that the DOMINO diet effectively reduces tertiary care IBS symptom severity and improves individual symptoms, including abdominal pain, bloating, and flatulence. The response rate to the diet was high, with the majority of patients reporting meaningful improvements of symptoms. This was associated with significant improvements in psychosocial factors, such as somatization, depression, and anxiety. These results underscore the potential of the DOMINO diet as an effective, less restrictive dietary approach for managing IBS in tertiary care.

- N05 -

AMISULPRIDE FOR THE TREATMENT OF IDIOPATHIC GASTROPARESIS: RESULTS OF A DOUBLE-BLINDED PLACEBO-CONTROLLED STUDY. H. Soliman (1), I. Huang (2), C. van de Bruaene (2), K. Van den Houte (2), L. Holvoet (1), J. Arts (3), P. Caenepeel (1), F. De Clerck (1), T. Vanuytsel (1), F. Carbone (2), J. Tack (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastro-enterology, [2] KUL - University of Leuven, Leuven, Belgium, TARGID, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, TARGID.

Introduction: Drug treatment options for patients with delayed gastric emptying are scarce, with metoclopramide being the only FDA-approved drug. A recent meta-analysis reported that antipsychotics, such as sulpiride could have clinical efficacy in functional dyspepsia (1). These drugs were only tested in patients with diabetic gastroparesis, but not in patients with idiopathic gastroparesis (2).

Aim: Thus, we aimed to assess the efficacy of amisulpride on symptoms and gastric emptying function.

Methods: A randomized double-blinded placebo-controlled trial was performed in UZ Leuven from 2013 to 2024. Non-diabetic patients with gastroparesis symptoms and delayed gastric emptying were included. After a 2-week screening period, patients were randomized either to amisulpride 25mg TID, or placebo TID for 6 weeks, followed by a 6-week open-label period with amisulpride with a dose increase to 50mg TID. The primary endpoint was an improvement of the Gastroparesis Cardinal Symptom Index (GCSI) at week 6. Symptomatic scores, including anxiety, depression, and somatization scores were also collected. Gastric emptying tests were performed at randomization and week 6.

Results: Among 49 patients screened, 42 were randomized in the trial. Three patients stopped the treatment prematurely or were lost to follow-up. Thus, 39 patients had available data, 21 in the amisulpride group, and 18 in the placebo group (32 female patients (82%), mean age 38 years). Baseline characteristics were similar in the two groups, with a mean GCSI score of 2.64 ± 0.89 . After 6 weeks, the GCSI score significantly decreased in the amisulpride group (2.72 ± 0.94 to 2.17 ± 1.17 ; $p=0.02$), but not in the placebo group (2.54 ± 0.85 to 2.11 ± 1.24 ; $p=0.11$). However, the total GCSI score at 6 weeks and the Δ GCSI compared to baseline were not different between the 2 groups (Table 1). None of the GCSI subscales differed between amisulpride and placebo groups, and the same was true for epigastric pain and anxiety, depression, and somatization scores (Table 1). Patients in the amisulpride group reported more weeks with overall improvement (16.6% vs 1.4%; $p=0.007$). Finally, the acceleration of gastric emptying time was not different at week 6 (Table 1). Two patients stopped amisulpride for somnolence, while no side effect was reported with placebo. After 12 weeks, the Δ GCSI score as compared to baseline was higher in the amisulpride group, suggesting that a longer treatment period could improve the treatment efficacy (1.14 ± 1.00 vs 0.52 ± 1.03 ; $p<0.05$). The decrease was significant on the fullness subscale but not on the nausea/vomiting or bloating subscales. Table 1. Comparison of scores at 6 weeks between amisulpride and placebo groups

	Amisulpride (n=21)	Placebo (n=18)	p-value
Total GCSI score	2.16 ± 1.17	2.11 ± 1.24	0.93
Δ Total GCSI	0.56 ± 0.91	0.43 ± 1.10	0.69
GCSI Nausea subscale	1.25 ± 1.06	1.04 ± 1.12	0.45
Δ Nausea GCSI subscale	0.51 ± 0.89	0.51 ± 1.09	0.81
Fullness GCSI subscale	2.36 ± 1.40	2.69 ± 1.53	0.49
Δ Fullness GCSI subscale	0.57 ± 1.35	0.21 ± 1.01	0.35
Bloating GCSI subscale	2.88 ± 1.54	2.59 ± 1.52	0.63
Δ bloating GCSI	0.60 ± 1.11	0.59 ± 1.72	0.95
Epigastric pain (0-100)	41.3 ± 33	45.9 ± 35.6	0.17
SF-NDI	101 ± 55	101 ± 56	0.79
VSI	65.2 ± 18.6	53.8 ± 18.7	0.02
HAD	10.4 ± 8.0	11.4 ± 5.7	0.33
PHQ-15	11.8 ± 6.3	9.6 ± 5.9	0.40
Gastric emptying (min)	78.2 ± 39	93.2 ± 41.4	0.29
Δ Gastric emptying	40.5 ± 84.1	42.2 ± 83.9	0.96

Δ were calculated from W0 to W6. GCSI: Gastroparesis Cardinal Symptom Index SF-NDI: Short Form – Nepean Dyspepsia Index; VSI: Visceral Sensitivity Index; HAD: Hospital Anxiety and Depression Scale; PHQ-15: Patient Health Questionnaire.

Conclusions: Amisulpride is not superior to placebo in patients with idiopathic gastroparesis at 6 weeks. A longer treatment period could be necessary to reach a higher treatment efficacy.

BELGIAN GROUP FOR DIGESTIVE ONCOLOGY (BGDO)

- O01 -

PREVALENCE OF CLAUDIN 18.2 POSITIVITY IN A BELGIAN COHORT OF PATIENTS WITH GASTRO-OESOPHAGEAL CANCER. F. Van Herpe (1), F. Deman (2), G. Rasschaert (1), M. De Wit (1), K. Dumon (1), R. Govaerts (1), S. Romanus (1), S. Cappuyns (1), J. Dekervel (1) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology - GI Oncology, [2] Ziekenhuis aan de Stroom Antwerpen, Antwerpen, Belgium, Pathology.

Introduction: Gastro-oesophageal adenocarcinoma (GEA) is the fifth most lethal cancer worldwide. Currently HER2, dMMR and PD-L1 CPS score are standard of care biomarkers and predictors of response to biomarker-directed therapies for GEA. Recently, zolbetuximab, a claudin 18.2 (CLDN18.2) directed monoclonal antibody, was approved by the FDA and EMA for the first-line treatment of patients with CLDN18.2 positive metastatic GEA in combination with chemotherapy based on the results of the GLOW and SPOTLIGHT phase 3 trials. The prevalence of CLDN18.2 positivity in GEA has been reported to be around 40%. However, these studies included mostly Asian patients, and we lack data on the relation between CLDN18.2 expression levels and other established biomarkers. An overview of cross positivity could aid the development of biomarker-tailored treatment algorithms in the future.

Aim: We aimed to determine the prevalence of CLDN18.2 positivity by immunohistochemistry (IHC) in a Western cohort of patients with both localized and metastatic GEA and put this into context of the established biomarkers (HER2 overexpression, PD-L1 CPS and MMR status). The secondary objective was to explore the prognostic impact of CLDN18.2 positivity on relapse-free and overall survival.

Methods: This retrospective, single-centre study evaluated all patients treated at the University Hospitals of Leuven for GEA from January 2019 until December 2023 for either localized or metastatic disease of which archival tissue was available. Demographics, MSI status, HER2 IHC, HER2 SISH and PDL1 CPS score was extracted from the patients' records. If missing, MMR status, HER2 IHC and PDL1 CPS was additionally determined. CLDN18.2-positivity, defined as $\geq 75\%$ of tumour cells showing moderate-to-strong membranous CLDN18 staining, was assessed by immunohistochemistry using the VENTANA CLDN18 [43-14A] RxDx Assay. Staining was interpreted by trained pathologists of the ZAS pathology team led by Dr. F. Deman. A Fisher's exact test compared categorical variables between subgroups and Kaplan-Meier curves were constructed for OS and RFS/PFS of different subpopulations. A research grant was obtained from Astellas and AMGEN. Roche provided research support by supplying the kits for CLDN18.2 assessment.

Results: A total of 409 patients with gastro-oesophageal adenocarcinoma were included in this study. Here, we share the preliminary results of the first 199 patients (146 patients with localized disease and 53 patients with metastatic disease). The cohort consisted of mostly men ($n = 143$, 71%) with a median age of 65 years (range 24-90 years). 52% of tumours were localized at the gastro-oesophageal junction and 48% of tumours were gastric cancers. CLDN18.2 positivity of $\geq 75\%$ with moderate to strong staining was seen in 42% of patients, which was in line with the prevalence in the phase 3 randomized controlled trials SPOTLIGHT/GLOW (40% positivity). MMR deficiency was detected in 6% of patients. HER2 overexpression (2+ or 3+) was present in 32% of cases while amplification was detected by SISH in 13%. PDL1 CPS score was <1 , 1-4, 5-9 and ≥ 10 in 48%, 18%, 12% and 22% of cases, respectively. The prevalence of PDL1 CPS score ≥ 1 (52%) was slightly lower than other real-world data (60-80% positivity). For the 146 patients with localized GEA, there was no significant difference in RFS ($p=0,2$) nor OS ($p=0,46$) between CLDN18.2 positive or negative disease ($p=0,2$) with a median follow-up (FU) of 28 months. In patients with primary metastatic disease, no difference in terms of PFS ($p=0,58$) or OS ($p=0,32$) was seen between CLDN18.2 positive or negative disease with a median FU time of 54 months.

Conclusions: In this first interim analysis of a large Belgian cohort of patients with GEA, the rate of CLDN18.2 positivity was 42%, in a context of 6% dMMR disease, 13% HER-2 amplification and 52% PD-L1 CPS ≥ 1 . CLDN18.2 positivity did not affect survival or recurrence in locoregional nor metastatic disease.

- O02 -

PERIOPERATIVE FLOT CHEMOTHERAPY FOR LOCALLY ADVANCED OESOPHAGEAL ADENOCARCINOMA: FROM ESOPHAGUS TO DAILY PRACTICE. A. Bouckaert (1), F. Van Herpe (2), J. Moons (1), S. Vanstraelen (1), J. Dekervel (2), L. Depypere (1), K. Haustermans (3), T. Lerut (1), Y. Mandeville (4), H. Van Veer (1), P. Naftaux (1) / [1] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Thoracic Surgery, [2] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Gastroenterology and Digestive Oncology, [3] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Radiation Oncology, [4] AZ Delta, Belgium, General, Abdominal and Thoracic Surgery.

Introduction: Neoadjuvant treatment strategies have been conflicting for localized oesophageal and gastro-oesophageal junction (GEJ) adenocarcinoma with 2 potential strategies: either chemoradiation according to the CROSS trial or

peri-operative chemotherapy according to the FLOT-4 trial. The ESOPEC trial recently showed a significant improved overall survival in favour of FLOT towards CROSS. Here we provide a single centre experience of perioperative FLOT for oesophageal and GEJ adenocarcinoma.

Aim: This study aimed to validate the results of both the FLOT-4 and ESOPEC-trials in real life setting and to assess overall survival of patients with locally advanced oesophageal and gastro-oesophageal adenocarcinoma treated with perioperative FLOT and surgery.

Methods: This retrospective cohort study included all consecutive patients with locally advanced oesophageal adenocarcinoma (cT1/2 N+ or cT3/4 N0/+) treated with perioperative FLOT +/- surgery in our institution between 2017 and 2023. A 2-week cycle of FLOT consisted of docetaxel 50 mg/m² on day 1, oxaliplatin 85 mg/m² on day 1, leucovorin 200 mg/m² on day 1, and 5-FU 2600 mg/m² as 24-h infusion on day 1. Surgical resection consisted of transthoracic esophagectomy and gastrectomy (partial or complete) with either intrathoracic or cervical anastomosis depending on the clinical situation. An extensive 2-field lymphadenectomy was performed. Complications were graded according to ECGG definitions. The primary endpoint was overall survival.

Results: A total of 145 consecutive patients were included. The majority of tumours (n=117, 81%) were located at the gastro-oesophageal junction and were clinically staged as locally advanced (cT3 (n=120, 82%), cT4 (n=14, 10%)) and node positive (cN1 (n= 37, 26%), cN2 (n=60, 41%), cN3 (n=17, 13%)). Most frequent tumour differentiation grade was moderate (n=41, 28%) to poor (n=73, 50%). Twenty patients (13.8%) started FLOT but were not referred for surgery (PRE). One-hundred twenty-five patients (86.2%) underwent surgery of whom 67.6% (n=98) started postoperative FLOT (PRE-SURG-POST) and 18.6% (n=27) did not receive any FLOT in the postoperative setting (PRE-SURG). The vast majority of patients (n=118, 94.4%) underwent an open transthoracic esophagectomy and all patients had an extensive lymph node dissection performed (median number of 32 resected lymph nodes). Major postoperative complications (Clavien-Dindo grade $\geq$ 3B) occurred in 18 patients (14.4%). There was no in-hospital mortality, and 90-day mortality was 2.4% (n=3). Complete pathologic response (pCR) was achieved in 8.8% of tumours. After a median follow-up time of 24.8 months, for the whole group, median overall survival was 53.3 months. Median overall survival for PRE patients was 13.6 months (95% CI 9.8-17.4) and 23.7 months (95% CI 19.5-27.9) for PRE-SURG patients. Median survival for PRE-SURG-POST patients was not yet reached (NR) but was significantly higher than in both other groups (p<0.001). Similarly, median disease-free survival was 43.1 months (NR) for PRE-SURG-POST patients, significantly higher than 14.0 months (95% CI 9.3-18.7) for PRE-SURG patients (p=0.004) and 6.8 months (95% CI 2.4-11.3) for PRE patients (p<0.001) respectively.

Conclusions: Our results, achieved in a real-life practice setting with predominantly clinically advanced bulky tumours with multiple positive lymph nodes at clinical staging, confirm that perioperative FLOT with surgery offers overall and disease-free survival, consistent with the FLOT-4 and ESOPEC trials. Completion of the treatment schedule including preoperative FLOT, surgery and at least 1 cycle of postoperative FLOT was associated with improved disease-free and overall survival. These results emphasize the importance of patient selection, high quality surgery and adequate supportive care during chemotherapy with the goal to offer the patients a maximal chance of completing the full perioperative FLOT scheme and as such increasing survival.

- O03 -

THE PROGNOSTIC VALUE OF CIRCULATING TUMOUR DNA IN CURATIVELY TREATED GASTRO-OESOPHAGEAL CANCER TREATED: A SYSTEMATIC REVIEW AND META-ANALYSIS. F. Van Herpe (1), Q. Van Caenegem (2), G. Rasschaert (1), S. Cappuyns (3), J. Dekervel (1) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology - GI Oncology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology - GI oncology.

Introduction: Gastro-oesophageal cancer (GEC) is an aggressive disease characterized by high mortality and a poor prognosis due to limited treatment options. Most patients are being treated with a heavy triplet chemotherapy followed by surgery that has a high impact on post-operative morbidity and carries a mortality risk of 2-3%. Currently no good biomarkers can predict relapse in the post-surgical setting and all patients are offered post-operative chemotherapy. Circulating tumour DNA (ctDNA) is increasingly being investigated to detect detecting minimal residual disease (MRD) post-surgery. The current literature is very heterogeneous, and case numbers are low. Hence, we conducted a systematic review with meta-analysis to evaluate the added value of ctDNA MRD testing in curatively treated GEC.

Aim: Our aim is to investigate the prognostic value of circulatory tumour DNA based on the different clinical trials, different types of ctDNA testing that have been published until June 2023.

Methods: We searched Pubmed, Embase, and Cochrane Library between May and June 2023. Articles that investigated the relation between ctDNA detection and clinical outcome (including progression-free survival (PFS), overall survival (OS), and time to recurrence) following treatment with curative intent for patients with GEC, were eligible for inclusion. Our primary endpoint was to assess the validity of ctDNA value at baseline and after surgery in the context of MRD in curatively treated GEC. The secondary endpoint was to examine the risk of recurrence based on ctDNA status.

We extracted hazard ratios (HRs) for death and progression with corresponding 95% confidence intervals (CIs) and calculated the relative risk (RR) for recurrence using data from the included trials. Outcome data from individual studies were pooled using an inverse variance random-effects meta-analysis.

Results: Our search identified 257 records of which 14 studies reporting on 788 patients were eligible for inclusion in this meta-analysis. Post-surgical ctDNA positivity was associated with worse PFS (HR 8.95, 95% CI: 5.09-15.73) and OS (HR 8.30, 95% CI: 3.99-17.28). In contrast, no significant association was found between baseline ctDNA positivity and PFS (HR 1.37, 95% CI: 0.78-2.42). After calculating the RRs, our meta-analysis shows that the risk of recurrence was higher in ctDNA-positive patients at baseline and after surgery compared to ctDNA-negative patients (RR 1.54, 95% CI: 1.16-2.05 and RR 3.18, 95% CI: 2.44 - 4.13, respectively).

Conclusions: Detection of ctDNA after surgery is associated with shorter PFS and OS, making it a promising biomarker in GEC as it could guide the clinical decision-making process after surgery. Additionally, ctDNA positivity at baseline predicts a higher risk of recurrence, enabling it to optimize staging at diagnosis of locally advanced GEC. However, further validation in larger prospective cohorts with time-to-event analysis is needed to confirm baseline ctDNA as a prognostic feature.

- O04 -

RESULTS OF THE EORTC SURVEY ON THE MANAGEMENT OF NON-METASTATIC PANCREATIC ADENOCARCINOMA: A FOCUS ON RADIOTHERAPY. C. Bouchart (1), M. Delaye (2), I. Garajova (3), F. Huguet (4), C. Neuzillet (2) / [1] Institut Jules Bordet, Brussels, Belgium, Radiotherapy-Oncology, [2] Institut Curie, Saint Cloud, France, Medical Oncology, [3] University Hospital of Parma, Parma, Italy, Medical Oncology Unit, [4] Hôpital Tenon, Paris, France, Radiation Oncology.

Introduction: Although representing relatively common clinical situations, the optimal management of pancreatic adenocarcinoma (PDAC) remains debated due to the lack of high-level evidence and conflicting clinical trial results.

Aim: The aim of this survey was to explore current clinical practices for the management of non-metastatic PDAC at European level with a particular focus on radiotherapy (RT).

Methods: The survey was developed by a multidisciplinary team (radiation oncologists [RO], medical oncologists and gastroenterologists) under the aegis of the EORTC digestive group. Survey consisted of 75 items, including 23 on RT and the Google Form platform was used (Google, Mountain View, USA). The questionnaire was distributed between March and June 2024 through the EORTC and several national societies of digestive cancer. It was addressed to gastroenterologists, medical oncologists, RO and digestive surgeons practicing in Europe.

Results: A total of 83 practitioners from 16 European countries responded to the survey, 23 of them were RO. A majority of participants had a very experienced profile, managing PDAC for more than 10 years. In case of resectable PDAC, 74% of respondents opted for surgery first while 22% proposed neoadjuvant chemotherapy (mainly FOLFIRINOX). For borderline resectable PDAC, respondents opted for an induction chemotherapy followed by RT as preferred strategy in 25% (57% with SBRT and 43% with chemoRT) and in 70% for induction chemotherapy alone. In this case, RT was proposed to be added in a second time after chemotherapy by 37% of the panel, mostly in case of poor response or persistence of vascular contact (particularly arterial). After the end of RT, the minimal and maximal waiting time allowed before surgical exploration were a median of 4 and 8 weeks, respectively. For locally advanced PDAC, the panel's preferred choice was induction chemotherapy followed by chemoRT in 42% followed by chemotherapy alone in 35%, and chemotherapy followed by SBRT in 23%. Induction chemotherapy was most often performed for 6 (43%) or 4 months (30%). Respondents proposed a cancellation of RT after chemotherapy and immediate surgical exploration in case of very good response without remaining vascular contact in 77% and following a normalization of CA19-9 in 42%.

Conclusions: This survey highlighted the great heterogeneity in PDAC current clinical practices, particularly for RT. Many questions persist regarding the management of these patients, especially on the reconsideration of the planned therapeutic strategy often proposed according to the evolution under chemotherapy, a question not explored in clinical trials. This study demonstrates the need to establish work to harmonize practices in Europe and could serve as a basis for the design of future European clinical trials.

- O05 -

EFFICACY AND SAFETY OF CHEMOEMBOLIZATION IN VERY EARLY AND EARLY-STAGE HEPATOCELLULAR CARCINOMA. A. De Buck Van Overstraeten (1), M. Pezzullo (2), A. Bucalau (1), M. Van Wette (2), I. Tancredi (3), F. Tannoury (2), A. Demols (1), G. Verset (4) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology, [2] HUB Hôpital Erasme, Brussels, Belgium, Radiology, [3] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Radiology, [4] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and the fourth leading cause of cancer-related deaths. It accounts for approximately 90% of primary liver cancers, with its incidence continuing

to rise, particularly in regions with a high prevalence of chronic liver diseases. Among various therapeutic algorithms, the Barcelona Clinic Liver Cancer (BCLC) staging system is the most widely used in Europe. This system defines five stages of the disease (BCLC 0, A, B, C, and D) based on three parameters: tumour burden, liver function, and patient performance status, and recommends the best therapeutic options for each stage. In the latest version published in 2022, intra-arterial liver treatments such as transarterial chemoembolization (TACE) and selective internal radiation therapy (SIRT) are proposed as alternatives when curative treatments are not feasible. This study aims to evaluate the efficacy and safety of TACE in patients with very early and early-stage HCC (BCLC 0 and A) by assessing response rates, overall survival (OS), progression-free survival (PFS), and toxicity profiles.

Aim: The primary objective was to assess efficacy through tumour response rates, OS, and PFS; the secondary objective was to evaluate the safety of the technique.

Methods: This retrospective monocentric study, approved by the local ethics committee (P2024-391), included patients with BCLC 0 and A HCC treated with TACE in a university hospital between January 2017 and December 2023. Patients with prior locoregional treatments targeting active HCC nodules or concurrent active malignancies were excluded. Each HCC nodule was treated as selectively as possible using transarterial chemoembolization with 100 µm microspheres loaded with 75 mg doxorubicin (DEM-TACE). Tumour response was evaluated using mRECIST criteria, and toxicity was assessed based on CTCAE version 5 and the CIRSE classification.

Results: The study cohort included 66 patients, the majority (85%) being male, with a median age of 66 years. All patients were cirrhotic, with alcohol (36%) and viral hepatitis (33%) as the leading aetiologies. Most patients had preserved liver function: median MELD of 9, 86% Child-Pugh A, and 86% ALBI grade 1. According to the BCLC classification, 11% had BCLC 0 HCC, while 89% had BCLC A HCC. The median sum of nodule diameters per patient was 31 mm. Baseline alpha-fetoprotein levels were often normal, with a median of 7 ng/mL. Most patients (68%) received a single TACE session, while 24% underwent two sessions, and 7.6% had three sessions. After a median follow-up of 22 months, disease control was achieved in over 90% of cases, with a complete response rate of 69%. Median OS was 39 months, with significantly prolonged survival observed in transplanted patients ($p=0.001$). Median PFS was 14 months. Regarding safety, 75% of patients experienced no complications, and adverse events were predominantly grade 1 or 2. One treatment-related death due to a hepatic abscess was reported.

Conclusions: This study confirms the efficacy and favourable safety profile of TACE in the treatment of very early and early-stage HCC (BCLC 0-A). A prospective study comparing TACE and SIRT should be conducted to determine the optimal cost-benefit therapeutic strategy for patients with BCLC 0 and A HCC.

- 006 -

ANALYSIS OF THE EFFECTIVENESS OF THE COMBINATION OF ATEZOLIZUMAB AND BEVACIZUMAB AS FIRST-LINE TREATMENT FOR ADVANCED HEPATOCELLULAR CARCINOMA. A REAL-WORLD RETROSPECTIVE MULTICENTRE STUDY IN BELGIUM. S. Haxhe (1), A. Van Thillo (2), F. Peeters (2), A. Collard (3), G. Verset (4), H. Van Vlierberghe (5), G. Houbiers (6), T. VanDamme (7), J. Carrasco (8), J. Dekervel (2), I. Borbath (1) / [1] UCLouvain, Cliniques Universitaires St Luc, Belgium, Hepato-Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive oncology, [3] UCLouvain, Cliniques Universitaires St Luc, Belgium, Statistics, [4] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Hepato-Gastroenterology, [5] Universitair ziekenhuis Gent, Belgium, Hepato-Gastroenterology, [6] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Hepato-Gastroenterology, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [8] Grand Hôpital de Charleroi, Charleroi, Belgium, Oncology.

Introduction: The IMbrave150 study revolutionized first-line treatment for advanced hepatocellular carcinoma (HCC), demonstrating the superiority of the Atezolizumab-Bevacizumab (AtezoBev) combination compared to Sorafenib in a selected group of patients. Median overall survival (OS) and progression free survival (PFS) were 19 and 6.8 months (m) respectively, with an objective response rate (ORR) of 30% and a trend toward better responses in patients with viral-based HCC.

Aim: Our objectives were to evaluate the safety and efficacy of AtezoBev in a Belgian population, assessing the impact of aetiology, Child-Pugh score (CP), ALBI grade, and performance status (PS) on OS and PFS, as well as the number of patients treated with second- and third-line therapy.

Methods: The study, conducted in 7 Belgian centres from 07/2023 to 07/2024, included patients treated with AtezoBev as first-line therapy between 01/2019 and 07/2022. OS and PFS were assessed using Kaplan-Meier and ORR was evaluated by RECIST 1.1. Uni- and Multivariate analyses were performed to study prognostic factors for OS and PFS.

Results: 146 patients with advanced HCC were included in the analysis. The patients were predominantly male (76.7%), cirrhotic (66.4%), CP-A (56.7%), PS 0 (51.9%) or 1 (39.8%), with non-viral aetiology (49.3%). Median age was 70y. Patients were classified as BCLC A (10.3%), B (37.9%) and C (51.7%); 27.6% showing tumoural portal vein thrombosis and 37.7% having metastases; 34.2% of patients had received prior locoregional treatment. Compared to IMbrave150, our population is characterized by a higher proportion of CP-B (10.6% vs 0%) and a predominantly non-viral etiology (49.3% vs 30%). After a median follow-up of 14.5m, the median OS and PFS were 15.1m (95% CI: 13.7-20) and 7.9m

(95% CI: 5.1-11.3), respectively. Among patients evaluable for response (n = 140), the ORR was 29.7%, including 3.5% complete response and 26.2% partial response. Because of the large proportion of non-cirrhotic patients (31.5%), we analysed separately the whole cohort and cirrhotic patients only for prognostic factors. By univariate analysis in the whole population (N=145), several factors were associated with reduced OS: ALBI grade (2 vs 1: HR 1.89, p=0.014; 3 vs 1: HR 20.97, p=0.0001), impaired PS (1 vs 0: HR 1.91, p = 0.018; 2 vs 0: HR 6.86, p<0.0001), and portal vein involvement at diagnosis (HR 1.69, 95% CI: 1.09–2.61, p=0.02). In multivariate analysis, ALBI grade (3 vs 1: HR 30.37, 95%CI 5.34–172.53, p=0.0001 and PS (2 vs 0: HR 9.66, 95% CI 3.16–29.55, p<0.0001) remained associated with shorter OS. Factors significantly associated with poorer PFS in multivariate analysis were impaired PS (2 vs 0, HR 4.25, p=0.0004) and AFP level > 400 ng/mL at diagnosis (HR 1.72, p=0.02). In cirrhotic patients only (N=96), univariate analysis revealed better OS and PFS outcomes for CP-A versus B (OS: HR 0.28, p = 0.0002; PFS: HR 0.47, p = 0.01). Multivariate analysis confirmed worse OS and PFS outcomes for higher ALBI grade (OS: 3 vs 1, HR 30.37, 95% CI: 5.34–172.53, p = 0.0001; PFS: 3 vs 1, HR 7.53, 95% CI: 1.59–35.73, p=0.01), impaired PS (OS: 2 vs 0, HR 9.66, 95% CI: 3.16–29.55, p<0.0001; PFS: 2 vs 0, HR 6.51, 95% CI: 2.52–16.8, p=0.0001) and male sex (OS: HR 3.31, 95% CI: 1.30–8.40, p=0.011; PFS: HR 3.09, 95% CI: 1.41–6.81, p=0.005). In contrast, the presence of cirrhosis, BCLC stage, extrahepatic spread, and prior locoregional treatment did not significantly affect survival. Overall, 17 patients (13.1%) developed treatment-related adverse events. Finally, 55% and 22% of patients received second-line and third-line therapy, respectively.

Conclusions: This real-world observational study in a Belgian population confirms the reproducible safety and efficacy of AtezoBev, with a similar ORR and superior PFS compared to the IMbrave150 study, though a slightly lower OS in a significantly different population. The differences in liver function may contribute to these outcomes. These results highlight the big impact of a higher ALBI grade and impaired PS on both OS and PFS, suggesting that these factors should be key when treating patients with advanced HCC.

- O07 -

NET-IMPRESS: A NOVEL METHYLATION-BASED ASSAY TO DIAGNOSE AND MONITOR NET PATIENTS USING LIQUID BIOPSIES. L. Mariën (1), J. Ibrahim (2), N. De Meulenaere (2), S. Chhajlani (2), I. Neefs (2), J. Vandenhoeck (2), T. Vanpoucke (2), W. Lybaert (3), M. Peeters (4), G. Van Camp (2), K. Op de Beeck (5), T. Vandamme (6) / [1] University of Antwerp, Antwerp, Belgium, Centre for Medical Genetics, [2] University of Antwerp, Antwerp, Belgium, Centre for Medical Genetics, [3] NETwerk, VITAZ/UZA, Edegem, Belgium, Department of Medical Oncology, [4] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Centre for Oncological Research, [5] University of Antwerp, Antwerp, Belgium, Centre for Medical Genetics and Centre for Oncological Research, [6] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Centre for Oncological Research and Department of Oncology.

Introduction: Previously, we showed that analysing copy number alterations (CNAs) in cell-free DNA (cfDNA) of patients with a neuroendocrine tumour (NET) using shallow whole genome sequencing (sWGS) can serve as a potential biomarker for diagnosis and follow-up (PMID: 34759042). We now present NET-IMPRESS, an easy, cost-effective methylation-based assay for detecting circulating tumour DNA (ctDNA) in NET samples.

Aim: We aimed to assess the diagnostic and follow-up potential of our novel NET-IMPRESS assay in the cfDNA of NET patients and compare it to the CNA-based approach.

Methods: We established a biomarker panel including 1152 NET-specific hypermethylated CpG sites and developed a novel bisulfite-free DNA methylation detection method called IMPRESS (Improved Methylation Profiling using Restriction Enzymes and smMIP Sequencing) which we combined into the NET-IMPRESS assay. Using this assay, we analysed 56 cfDNA samples from 25 NET patients and 16 samples from healthy controls. For each sample, a relative methylation level (RML) was calculated. Based on the RML cutoff, determined from the healthy controls, NET samples were classified as ctDNA-positive or -negative. All patient samples had already been analysed using the CNA-based approach that uses sWGS and ichorCNA analysis. CtDNA status was then compared between our new methylation-based assay and the CNA-based approach.

Results: We observed 84% (47/56) concordance in ctDNA status between our NET-IMPRESS assay and the CNA-based approach. Of the 9 discordant samples, our new assay detected ctDNA in 4 cases which the CNA-based method failed to detect. The 5 remaining were negative according to our assay but were considered positive by the CNA-based method. However, all 5 samples exhibited values near the 3% cutoff of ichorCNA suggesting potential false positives. For two patients, over 10 longitudinal samples collected over 18 and 25 months respectively, were analysed. The RML values closely mirrored the tumour fractions calculated by ichorCNA ($R^2 = 0.9561$ and $R^2 = 0.8899$) and accurately reflected each patient's clinical course over time. In one patient, a first positive sample was observed during a treatment break; however, subsequent samples returned negative upon resumption of therapy. Over time, RML and ichorCNA values began to rise sharply, coinciding with an increase in tumour size and investigator-assessed disease progression. Following a switch in treatment, a significant reduction in RML and ichorCNA values was observed, accompanied by a decrease in tumour size.

Conclusions: We present the first results on NET-IMPRESS performance in liquid biopsies, showing its strong potential for diagnosis and follow-up of NET patients in a minimally-invasive way. Further validation in extra samples is ongoing.

A NOVEL IMMUNE-BASED SCORE AND ITS IMMUNE CONTEXTURE EXPLORATION IN COLORECTAL CANCER. Q. Wu (1), A. Peddle (1), S. Rusakiewicz (2), K. Yin (1), Z. Hu (1), F. Van Herpe (3), A. D'Hoore (4), Y. Hong (1), S. Verbandt (1), S. Tejpar (3), G. Rasschaert (3) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory for Digestive Oncology, [2] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Immune Landscape Laboratory, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery.

Introduction: The majority of currently available biomarkers in colorectal cancer (CRC) perform poorly with respect to prognostication and prediction of response. Immunoscore (IS) has been proposed as a signature of host immune cancer response reflecting a favourable prognosis. Next, through AtezoTRIBE, 'Immunoscore immune checkpoint' (IS-IC) was introduced, indicating its potential predictive value for immune checkpoint blockade (ICB) in pMMR metastatic CRC. IS-IC is computed through quantitative and spatial variables related to density and proximity of CD8 cells and programmed cell death-ligand 1 (PD-L1) cells in the tumour core (TC). There are little confirmatory studies.

Aim: In this work we test the application of IS-IC through multiplex immunofluorescence (mIF) on our own cohort of patients. Next we explore immune contexture differences through subgroup analysis.

Methods: 15 prospectively collected, treatment naïve, primary CRC samples (9 dMMR/MSI-H, 6 pMMR/MSS) were analysed with mIF (Table). Cell density, proximity between cells, cell clustering and spatial distribution of selected mIF biomarkers (CD3, CD20, CD11c, CD163, CD15, CD4, CD8, Foxp3, CD56, Granzyme B, PD-L1, programmed cell death protein 1 (PD-1), pan-cytokeratin (CK) and Ki67) were analysed both at the invasive margin (IM) and TC using digital pathology. All slides subjected to digital image analysis met predefined quality control criteria.

Results: Serial mIF showed PD-L1 was enriched in stromal cells (CK-) within IM ($p=0.0148$) and confirmed its co-localization with macrophages (CD163+) ($p=0.0092$). Hence, both TC and IM were included to quantify the densities of CD8, PD-L1 and the proximity between them, as a suggested novel IS-ICTC+IM. During exploration of the immune context we found that both IS-IC and IS-ICTC+IM high groups exhibited significantly increased infiltration of PD-1+ cells ($p=0.0074$ and $p=0.0058$, respectively) and CD8+PD-1+ cells ($p=0.0101$ and $p=0.0062$, respectively), compared to the corresponding low groups. Whereas only the IS-ICTC+IM high group showed increased natural killer (NK) cells (CD56+) ($p=0.0192$), found mainly at IM ($p=0.0167$) in contrast to TC ($p=0.0824$). The novel IS-ICTC+IM scoring system captures the immunosuppressive and immune responsive interaction among PD-1+ cells, PD-L1+ cells, NK cells and CD8+ cells in TC and IM from the cell numbers and cell-cell proximity. A validation cohort is underway.

Conclusions: In this study we confirm the ease of replicating IS-IC and the presence of ICB sensitive stroma in the high score group. This study further explored the immune context in both TC and IM, emphasizing the importance of regional differences. Additionally, it was found that NK cells were only increased at IM. Altogether we suggest adding dual quantification in TC and IM as a novel IS-ICTC+IM, which may be a more sufficient reflection of the tumour microenvironment.

IS INTENSIVE ISCHEMIA-REPERFUSION INJURY INCREASING THE RISK OF HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION? M. Foguene (1), O. Ciccarelli (2), L. Coubeau (2), G. Dahlqvist (3), E. Bonaccorsi Riani (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Abdominal Surgery and Transplantation, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Abdominal Surgery and Transplantation, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepato-Gastro-Enterology.

Introduction: Liver transplantation (LT) is the only curative treatment for hepatocellular carcinoma (HCC) developed in cirrhotic liver, with 5-year overall survival (OS) rate above 70% under appropriate selection criteria. Nevertheless, HCC recurrence (HCC-recr) impacts long-term patient survival, which is associated with pre-LT (tumour morphology and biology) and post-LT (immunosuppression) characteristics. Recent clinical evidence has suggested that also perioperative factors, such as ischemia-reperfusion injury (IRI), can facilitate HCC-recr.

Aim: The aim was to investigate the influence of IRI intensity on HCC-recr.

Methods: Medical records of 248 patients transplanted for HCC in our centre between 2009 and 2021 were reviewed, with follow-up until November 2024. IRI intensity was quantified through 2 markers. Firstly, the occurrence of one of the following clinical events (primary non-function (PNF), early allograft dysfunction (EAD) and ischemic-type biliary lesions (ITBL)) classified the patient in the severe-IRI (Sev-IRI) group. Indeed, these are known to be complications related to severe IRI phenomena. PFN was defined following Ploeg et al., EAD corresponded to Olthoff criteria and ITBL was diagnosed according to Verhoeven et al. Reperfusion-syndrome (RPS), defined by a drop of mean arterial blood pressure above 30% in the first minute after graft reperfusion, was considered as the other marker for intensive IRI.

Results: 37 patients recurred (14.9%) with a mean interval of 29.9 months (± 32.9) between LT and HCC-recr diagnosis. Patient survived less than 2 years (20.4 (± 21.6) months, mean) when recurrence was diagnosed. 109 (44.0%) patients presented an Sev-IRI event (95 EAD (38.3%), 7 PNF (2.8%) and 7 ITBL (2.8%)). 23 recipients of Sev-IRI

cohort (23/109, 21.1%) suffered from HCC-recr, compared to 14 patients (14/139, 10.1%) in non-Sev-IRI ($p=0.016$). Both groups were comparable according to MELD-score, cirrhosis aetiology, demographic data and immunosuppressive exposure after LT. At pathology, Milan-out status was similar in Sev-IRI (26/109, 23.8%) and non-Sev-IRI groups (36/139, 25.9%) ($p=0.711$). Mean disease-free survival (in months) was shorter in Sev-IRI cohort: $87.2 (\pm 7.7)$ vs. $132.4 (\pm 7.0)$ ($p < 0.001$). Similarly, OS (in months) was reduced in Sev-IRI group: $93.6 (\pm 7.6)$ vs. $134.8 (\pm 6.9)$ ($p < 0.001$). 119 patients suffered from RPS (119/248, 48.0%). HCC-recr rate was also higher in this subgroup: 26/119 (21.9%) vs. 11/129 (8.5%) in non-RPS group ($p=0.003$). Again, no difference was noticed between both groups in terms of MELD-score, cirrhosis aetiology, tumoural load and immunosuppressive exposure after LT.

Conclusions: Our findings suggest that intensive IRI, defined by the occurrence of an IRI-related complications (PNF, EAD, ITBL) or RPS, could increase HCC recurrence rate after LT, independently to Milan status. Further studies with larger patient series are required to confirm such results. If so, IRI modulation could be a strategy to decrease HCC recurrence.

- O10 -

BASILINE NEUTROPHIL-TO-EOSINOPHIL RATIO AND NEUTROPHIL-TO-LYMPHOCYTE RATIO TO PREDICT RESPONSE TO GEMCITABINE-CISPLATIN-DURVALUMAB IN UNRESECTABLE CHOLANGIOCARCINOMA: AN INTERNATIONAL, MULTICENTRE, RETROSPECTIVE COHORT STUDY. H. Vandeputte (1), F. Peeters (2), A. Casadeigardini (3), M. Rimini (3), L. Fornaro (4), M. Rizzato (5), L. Antonuzzo (6), F. Rossari (3), S. Tomoyuki (7), C. Vivaldi (4), T. Pressiani (8), J. Lucchetti (9), J. Won Kim (10), A. Oluseyi (11), I. Giovanni Rapposelli (12), S. Tamberi (13), F. Finkelmeier (14), G. Giordano (15), F. Nichetti (16), H. Jae Chon (17), C. Braconi (18), C. Pirrone (19), F. Castet (20), E. Tamburini (21), C. Yoo (22), A. Parisi (23), A. Diana (24), M. Scartozzi (25), G. Prager (26), A. Avallone (27), M. Schirripa (28), I. Hwan Kim (29), L. Perkhofer (30), E. Oneda (31), M. Verrico (32), J. Adeva (33), S. L Chan (34), G. Spinelli (32), N. Personeni (35), I. Garajova (36), M. Rodriquenz (37), S. Leo (38), F. Salani (39), A. De Rosa (40), D. Lavacchi (6), S. Foti (3), M. Ikeda (7), M. Niger (16), R. Balsano (8), G. Tonini (39), M. Kang (10), T. Bekaii-Saab (11), L. Esposito (12), A. Boccaccino (13), V. Himmelsbach (14), M. Landriscina (15), S. Ahcene Djaballah (40), V. Zanuso (8), G. Masi (4), S. Lonardi (40), L. Rimassa (8), J. Dekervel (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Algemene basisopleiding, [2] KUL - University of Leuven, Leuven, Belgium, digestive oncology, [3] Vita Salute San Raffaele University, Milan, Italy, digestive oncology, [4] Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy, digestive oncology, [5] Veneto Institute of Oncology IOV, Padua, Italy, digestive oncology, [6] Careggi University Hospital, Florence, Italy, digestive oncology, [7] National Cancer Centre Hospital East, Kashiwa, Japan, digestive oncology, [8] IRCCS Humanitas Research Hospital, Milan, Italy, digestive oncology, [9] Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy, digestive oncology, [10] Seoul National University Bundang Hospital, Seoul, Korea (the Republic of), digestive oncology, [11] Mayo Clinic, Phoenix, United States, digestive oncology, [12] IRCCS Istituto Romagnolo per lo Studio dei Tumori, Meldola, Italy, digestive oncology, [13] Santa Maria delle Croci Hospital, Ravenna, Italy, digestive oncology, [14] University Hospital Goethe-University, Frankfurt, Germany, digestive oncology, [15] Policlinico Riuniti, Foggia, Italy, digestive oncology, [16] Fondazione IRCC Istituto Nazionale dei Tumori, Milan, Italy, digestive oncology, [17] CHA Bundang Medical Centre, Seongnam, Korea (the Republic of), digestive oncology, [18] University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom, digestive oncology, [19] IRCC Ospedale Policlinico San Martino, Genova, Italy, digestive oncology, [20] Fundació Hospital Universitari Vall d'Hebron - Institut de Recerca, Barcelona, Spain, digestive oncology, [21] Cardinale Panico Tricase City Hospital, Tricase, Italy, digestive oncology, [22] ASAN Medical Centre, University of Ulsan College of Medicine, Ulsan, Korea (the Republic of), digestive oncology, [23] Azienda Ospedaliero-Universitaria delle Marche, Ancona, Italy, digestive oncology, [24] Ospedale del Mare, Napoli, Italy, digestive oncology, [25] University of Cagliari, Cagliari, Italy, digestive oncology, [26] Medical University of Vienna, Vienna, Austria, [27] Istituto Nazionale Tumori-IRCCS Fondazione G. Pascale, Napoli, Italy, digestive oncology, [28] Belcolle Hospital, Viterbo, Italy, digestive oncology, [29] Haeundae Paik Hospital, Busan, Korea (the Republic of), digestive oncology, [30] Institute of Molecular Oncology and Stem Cell Biology, Ulm, Germany, digestive oncology, [31] Fondazione Poliambulanza, Brescia, Italy, digestive oncology, [32] Sapienza University of Rome, Rome, Italy, digestive oncology, [33] Spanish Society of Medical Oncology, Madrid, Spain, digestive oncology, [34] The Chinese University of Hong Kong, Hong Kong, China, digestive oncology, [35] ASST Garda, Brescia, Italy, digestive oncology, [36] University Hospital of Parma, Parma, Italy, digestive oncology, [37] Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy, digestive oncology, [38] Vito Fazzi Hospital, Lecce, Italy, digestive oncology, [39] Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy, digestive oncology, [40] IRCCS Padua, Padua, Italy, digestive oncology.

Introduction: Cholangiocarcinoma (CCA) is a highly lethal malignancy from the epithelial cells of the liver and biliary tract. Its incidence has been steadily increasing worldwide and despite the recent advances in the diagnosis and treatment, CCA continues to have a high mortality rate, with 5-year overall survival rates ranging from just 7% to 20%. Until 2022, gemcitabine and cisplatin chemotherapy continued to be the cornerstone of treatment, yielding a median overall survival

of 11.7 months. However, in 2022, the TOPAZ-1 phase 3 trial demonstrated the benefit of combining immune checkpoint inhibition (ICI) with chemotherapy, establishing the combination of gemcitabine, cisplatin, and durvalumab (anti-PDL1) as the new standard-of-care first-line treatment for advanced CCA. Recent studies in other tumour types treated with ICI have highlighted the pre-treatment neutrophil-to-eosinophil ratio (NER) and neutrophil-to-lymphocyte ratio (NLR) as potential prognostic biomarkers for response to ICI.

Aim: The objective of this study was to assess whether NER and NLR could predict overall survival (OS), progression-free survival (PFS) and objective response rate (ORR) in advanced CCA patients treated with gemcitabine-cisplatin-durvalumab.

Methods: Patient data was retrospectively collected from 39 sites in 11 countries (Italy, Germany, Austria, Spain, United Kingdom, United States of America, Republic of Korea, China, Hong Kong Special Administrative Region of China, Japan and Belgium). The study population comprised patients with unresectable, locally advanced, or metastatic biliary tract cancers, including intrahepatic cholangiocarcinoma (iCCA), extrahepatic cholangiocarcinoma (eCCA), and gallbladder carcinoma. Leukocyte values, including total white blood cell count, eosinophil count, neutrophil count, and lymphocyte count, were measured at the initiation of treatment. NER and NLR were calculated by dividing the absolute neutrophil count by the absolute eosinophil count and lymphocyte count respectively. The primary outcome was OS, defined as the time from initiation of gemcitabine-cisplatin-durvalumab to death. The secondary outcomes were PFS, defined as the time from initiation of treatment to disease progression, and ORR, assessed using the modified Response Evaluation Criteria in Solid Tumours (mRECIST) and defined as the proportion of patients achieving complete or partial response.

Results: A total of 509 patients were included in the analysis, with a median age at the initiation of treatment of 67 years (IQR 15). The median follow-up duration was 6.5 months (IQR 7.7 months), with a median OS of 15.1 months (IQR 21 months) and a median PFS of 8.4 months (IQR 8.2 months). After applying a Bonferroni correction for multiple testing, a univariate Cox regression analysis revealed that patients with metastatic disease (HR 2.1, 95% CI 1.4-3.0, $p < 0.01$), an ECOG performance status more than 0 (HR 1.6, 95% CI 1.3-2.1, $p < 0.01$), and a NLR above the median value (HR 1.6, 95% CI 1.2-2, $p = 0.0063$) had significantly shorter PFS. For OS, significant associations were found for metastatic disease (HR 3.1, 95% CI 1.8-5.5, $p < 0.01$), ECOG performance status more than 0 (HR 2.4, 95% CI 1.7-3.3, $p < 0.01$), NLR above the median value (HR 2, 95% CI 1.5-2.8, $p < 0.001$), and a NER above the median value (HR 1.7, 95% CI 1.2-2.3, $p = 0.039$). In a multivariate Cox regression model, PFS was significantly shorter for patients with metastatic disease (HR 2.2, 95% CI 1.4-3.4, $p < 0.001$), ECOG performance status more than 0 (HR 1.8, 95% CI 1.3-2.4, $p < 0.001$), higher CA 19-9 levels (HR 1, 95% CI 1-1 $p = 0.038$), and an NLR above the median (HR 1.6, 95% CI 1.2-2.1, $p = 0.002$). OS was significantly shorter for patients with metastatic disease (HR 2.1, 95% CI 1.2-4, $p = 0.014$), ECOG performance status more than 0 (HR 2.5, 95% CI 1.7-3.7, $p < 0.001$), and NLR above the median value (HR 2, 95% CI 1.4-3, $p < 0.001$). There was no significant difference in objective response rate (ORR) between patients stratified based on NER- or NLR-value.

Conclusions: A higher baseline NLR was significantly associated with worse PFS and OS. No significant association was found between NER and OS or PFS. These findings suggest that NLR has the potential to serve as a prognostic biomarker for patients with advanced CCA treated with gemcitabine-cisplatin-durvalumab.

- O11 -

STATUS AND ROLE OF HELICOBACTER PYLORI INFECTION IN IMMUNOTHERAPY RESPONSE IN OESOGASTRIC ADENOCARCINOMA. E. Lam (1), L. Verset (2), A. Nebbioso (3), A. Bucalau (1), J. Van Laethem (1) / [1] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Gastroenterology and digestive oncology, [2] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Pathology, [3] Hôpitaux Iris Sud, Brussels, Belgium, Paediatrics.

Introduction: *H.pylori* is a common world-wide infection leading to gastric cancer. The combined positive score (CPS) is a pathological score using PDL-1 coloration and indicates a potential response to immunotherapy. Pre-clinical studies on human gastric epithelial cells have shown that PD-L1 expression was significantly up-regulated after *H.pylori* infection (Wu et al 2010). A recent Chinese meta-analysis involving 1,870 patients found that *H. Pylori* infection was significantly linked to a higher tumour expression of PD-L1, suggesting that this infection could be a potential predictor of a favorable response to immunotherapy in gastric cancer (Zhu et al 2023). Knowing *H.pylori*'s wide range of immune-modulator properties as it can cause local mucosal inflammation (including cancer), induce systemic immune disease (eg immune thrombocytopenic purpura), reduce systemic inflammation such as Crohn's disease and asthma and cause immunotolerance for its own survival, predicting its impact in real life may be challenging. The influence of *H.pylori* infection on the efficacy of immunotherapy (ICI) is controversial; according to the latest Chinese clinical study, *H.pylori* infection seems to be a favorable factor for advanced gastric cancer treated with ICI as it was associated with a significant longer PFS (Jia et al 2024). Another recent American study compared patients with metastatic gastric cancer receiving ICI with and without *H.pylori* infection and observed a significant worse prognosis associated with the infection in both PFS and OS (Magahis et al 2023).

Aim: In our study, we aim to assess if the presence of H.Pylori lead to a higher CPS score in upper GI adenocarcinoma and to evaluate its impact on predicting the efficacy of immunotherapy.

Methods: We retrospectively collected data from patients with an upper GI adenocarcinoma (stomach, lower oesophagus or eso-gastric junction), a known H.pylori status and a known CPS score. The outcomes were: 1) the association between H.pylori infection and CPS 2) H.pylori infection as a predictive factor for systemic treatment, in particular, immunotherapy. We first compared H.pylori positive and H.pylori negative groups depending on their CPS score, setting the threshold at 1, 5 and 10.

Then, we compared the progression free survival (PFS) of H.Pylori positive and negative patients with advanced GI adenocarcinoma under systemic therapy (stage III and IV), then focused on the sub-group of advanced gastric cancer under systemic therapy. Finally, we compared the overall survival (OS) and PFS of patients with oesogastric adenocarcinoma under immunotherapy according to their H.pylori status.

Results: We collected data from 117 patients with oeso-gastric adenocarcinoma, a known CPS score and a known H.pylori status. 1. Association between H.pylori infection and CPS score There was no association between the positive or negative H.Pylori status and CPS score whatever the chosen threshold (1, 5, 10) (p-value 0.602). 2a. H.pylori infection as a predictive factor for systemic treatment There was no significant difference in PFS comparing the H.pylori positive and negative patients with advanced oeso-gastric adenocarcinoma under systemic therapy (N=44, stage III and IV)) (p-value 0.507). There was a significant longer PFS in H.pylori positive in the sub-group of patients with advanced gastric adenocarcinoma treated with systemic treatment (N=20) (p-value 0.037). 2b. H.pylori infection as a predictive factor for immunotherapy There was no significant difference in PFS (p-value 0.226) and OS (p-value 0.083) comparing the H.pylori status in the sub-group of patients with advanced oeso-gastric adenocarcinoma receiving immunotherapy (N=21).

Conclusions: We did not find an association between CPS and H.pylori presence. H.pylori's predictive impact on immunotherapies is still unclear due to its complex immune regulation. In this study, we found that H.pylori infection seems to be associated with a significant longer PFS in patients with advanced gastric adenocarcinoma treated with systemic treatment while we did not find a significant difference in OS and PFS in patients with advanced oeso-gastric adenocarcinoma under immunotherapy. Further research is needed to determine H.pylori's impact on immunotherapy, as it can give prognosis insight and help making therapeutical decisions for patients.

- O12 -

EFFICACY AND SAFETY OF CAPECITABINE-TEMOZOLOMIDE (CAPTEM) REGIMEN IN PATIENTS WITH NEUROENDOCRINE NEOPLASMS – A SYSTEMATIC REVIEW AND EXPERIENCE FROM NETWORK, A BELGIAN ENETS CENTRE OF EXCELLENCE. S. Chhajlani (1), C. Lambrechts (2), O. Islam (1), C. De Weerd (1), L. Mariën (3), L. Verbruggen (1), M. Simoens (4), M. Ulenaers (5), D. Galdermans (6), W. Demey (7), I. Van der Massen (1), W. Lybaert (8), T. Vandamme (1) / [1] UZA - NETwerk, Edegem, Belgium, Medical Oncology, [2] AZ Heilig Hart ziekenhuis Mol, Mol, Belgium, Gastroenterology, [3] Universiteit Antwerpen - NETwerk, Antwerp, Belgium, Medical Genetics, [4] ZAS - NETwerk, Antwerp, Belgium, Gastroenterology, [5] AZ Rivierenland - NETwerk, Bornem, Belgium, Gastroenterology, [6] ZAS - NETwerk, Antwerp, Belgium, Respiratory medicine, [7] AZ Klina - NETwerk, Brasschaat, Belgium, Medical Oncology, [8] VITAZ - NETwerk, Sint-Niklaas, Belgium, Medical Oncology.

Introduction: Neuroendocrine neoplasms (NEN) are rare tumours originating from neuroendocrine cells, commonly found in the gastrointestinal tract and the pulmonary tract. Current treatment guidelines remain inconclusive due to scarcity of data regarding the optimal systemic treatment for metastatic gastroenteropancreatic (GEP) neuroendocrine tumours (NET) grade 3 and aggressive GEP NET grade 2. Similarly, for metastatic pulmonary typical (TC) and atypical carcinoids (AC), the indication for chemotherapy is unclear. Recent evidence highlights a promising role for CAPTEM, combining temozolomide (TEM) with capecitabine (CAP), showing encouraging antitumoural activity and safety profiles for these indications.

Aim: To study the efficacy and safety of capecitabine-temozolomide (CAPTEM) regimen in patients with GEP NET, TC, and AC.

Methods: A systematic review was conducted to gather efficacy and safety data for CAPTEM use in GEP NET and pulmonary NEN from 2005-2024. Retrospective data from the NETwerk (Belgian ENETS CoE) database, comprising 36 patients with GEP NET grades 1-3 and pulmonary NEN treated with CAPTEM between June 2016 and January 2024, was also analysed.

Results: The systematic review showed benefit for CAPTEM in terms of median progression-free survival (mPFS), median overall survival (mOS), overall response rates (ORR), and disease control rates (DCR), particularly in pancreatic NET, TC, and AC. CAPTEM was safe and well tolerated, with low rates of grade 3-4 toxicities. In the NETwerk cohort, the mPFS was 13m, mOS was 17m, ORR was 25.8%, and DCR was 67.7%. NET grade 2 patients had the highest mPFS, while NET grade 3 exhibited the most favorable mOS. Subgroup analysis showed that panNEN had superior mPFS and mOS compared to other primary tumour sites, with significant differences in mOS based on NEN type. Safety analysis in 20 patients indicated good tolerance and safety.

Conclusions: Currently available data demonstrates that CAPTEM is an effective, safe and well tolerated regimen especially in metastatic pancreatic NET, TC, and AC. Additional analyses within the review are ongoing to assess CAPTEM's efficacy in combination with somatostatin analogs (SSA), peptide receptor radionuclide therapy (PRRT), and liver-directed therapies.

- O13 -

CLINICAL UTILITY OF [¹⁸F]AIF-NOTA-OCTREOTIDE FOR SOMATOSTATIN RECEPTOR PET/CT: A RETROSPECTIVE STUDY IN 288 PATIENTS WITH NEUROENDOCRINE NEOPLASMS. H. Leupe (1), J. Dekervel (2), F. Cleeren (3), K. Goffin (4), C. Doooms (5), S. Jentjens (4), L. Boeckxstaens (4), E. Van Cutsem (2), F. Van Herpe (2), P. Clement (6), G. Rasschaert (2), K. Van Laere (4), G. Bormans (3), C. Verslype (2), C. Deroose (4) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nucleaire geneeskunde, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology, [3] KUL - University of Leuven, Leuven, Belgium, Radiopharmaceutical Research, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Respiratory Diseases, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Oncology.

Introduction: [¹⁸F]AIF-NOTA-Octreotide has established itself as a reliable tracer for somatostatin receptor (SSTR) PET/CT in patients with neuroendocrine neoplasms (NENs). However, despite its efficacy and logistical benefits, data on its clinical use, particularly in specific subtypes such as NET G3 or non-GEP-NEN remains sparse.

Aim: This study aims to evaluate the real-world clinical application of [¹⁸F]AIF-NOTA-Octreotide PET/CT, focusing on uptake patterns and referral trends at our institution.

Methods: A retrospective analysis was performed on all patients referred for SSTR PET/CT at University Hospitals Leuven between March 1, 2023, and January 18, 2024. Clinical and demographic information, as well as procedural details, were collected. PET/CT imaging data were analysed to quantify uptake parameters.

Results: A total of 322 [¹⁸F]AIF-NOTA-Octreotide PET/CT scans from 288 patients were analysed, including 93 patients with WHO G1 NET, 84 with G2 NET, 15 with G3 NET, 5 with NEC, and 40 with lung NENs. Additional cases included patients with tumour of unknown primary (CUP-NET) and meningioma. Referral patterns based on SNMMI appropriate use criteria (AUC) revealed that most patients were referred for 'Monitoring of NETs seen predominantly on SSTR PET,' followed by 'Initial staging after histologic diagnosis.' The average injected activity was 208.5 ± 73.6 MBq, with a mean uptake time of 121 ± 14 minutes before imaging. Ongoing quantitative analysis is focused on exploring correlations between uptake values and NET grading, as well as assessing diagnostic accuracy in comparison to other available imaging modalities.

Conclusions: This study provides essential real-world data supporting the use of [¹⁸F]AIF-NOTA-octreotide PET/CT in NET patient management. Our findings validate [¹⁸F]AIF-NOTA-octreotide for routine clinical use.

- O14 -

ANALYSIS OF THE CLINICAL, BIOLOGICAL, AND PROGNOSTIC FEATURES OF PATIENTS WITH COLORECTAL CANCER EXHIBITING MULTIPLE RAS GENE MUTATIONS. R. Di Giugno (1), M. Meyers (2), F. Sclafani (2) / [1] CUB Hôpital Erasme, Belgium, Gastroenterology, [2] Institut Jules Bordet, Brussels, Belgium, Oncology.

Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide, representing the fourth most common type of cancer. CRC progression primarily follows three pathways: the adenoma-carcinoma sequence, the serrated/methylated pathway, and the microsatellite instability (MSI) pathway. Among the genes frequently mutated in CRC, the RAS family (KRAS, NRAS, HRAS) plays a pivotal role. Mutations in these genes result in the continuous activation of intracellular signalling pathways, such as MAPK, which promote tumour growth and metastasis. Screening for RAS mutations has become a standard practice in the management of advanced CRC due to its prognostic implications and its role in guiding targeted therapies.

Aim: In this study, we aim to examine the clinical, pathological, and molecular characteristics, as well as the overall disease outcomes potentially associated with this specific genomic feature.

Methods: This retrospective study analysed histological samples of colorectal tumours collected between March 2007 and December 2023 from Erasme and Jules Bordet hospitals. Inclusion criteria were a confirmed CRC diagnosis and the presence of at least two mutations within the RAS gene family (KRAS, NRAS, or HRAS). Patients who received systemic treatment prior to tumour biopsy were excluded. Mutation analysis was performed using targeted sequencing and NGS, and Kaplan-Meier curves were employed to assess overall survival (OS) and progression-free survival (PFS).

Results: Eight patients (5 women, 3 men) with a mean age of 74 years were included. Among them, 5 presented with metastases, predominantly in the lungs. A total of 17 RAS mutations were identified: 15 in KRAS and 2 in NRAS. No mutations were found in HRAS. Regarding survival outcomes, the median OS was 67 months for all patients and 57.6

months for metastatic patients. The median PFS was 32 months for all patients and 21 months for those with metastases. No systematic genomic correlation was identified between RAS mutations and other genetic alterations.

Conclusions: This study suggests that CRC cases with multiple mutations in the RAS gene may be associated with prolonged survival, in contrast to the generally observed poorer prognosis for KRAS-mutated patients. The complex interaction between these mutations might mitigate their negative impact, although the underlying mechanisms remain unclear. These findings align with other studies suggesting that KRAS-mutated CRCs exhibit a higher propensity for lung metastases, potentially pointing to specific biological mechanisms. However, the study's limitations, particularly the small sample size, underscore the need for further research to validate these observations.

- O15 -

THE RELATIONSHIP BETWEEN PRETHERAPEUTIC MALNUTRITION ACCORDING TO GLIM CRITERIA AND CLINICAL OUTCOMES IN PATIENTS WITH COLORECTAL CANCER. S. Zaouga (1), S. Ben Hamida (1), H. Elloumi (1), I. Cheikh (1) / [1] Habib Bougatfa Hospital, Tunisia, Gastroenterology.

Introduction: Malnutrition is a highly prevalent condition in patients with cancer that has a negative impact on clinical outcomes. The GLIM criteria for malnutrition aim to standardize its diagnosis. In colorectal cancer, poor nutritional status is associated with increased morbidity and mortality and reduce tolerance to treatment.

Aim: We aimed to assess the prevalence of malnutrition base on the GLIM criteria and to correlate this with patient outcomes and survival in colorectal cancer.

Methods: Patients with colorectal cancer diagnosed from January 2015 to December 2022 were included. All of them were screened for malnutrition using the GLIM criteria. The relationships between GLIM-malnutrition and survival were analysed.

Results: Sixty patients were included. The mean age was 54 years [35 - 82] with a sex ratio of 1.8 (M/F). Tumour was located in the right colon in 20 patients (33%), the left colon in 22 patients (36%), and the rectum in 15 patients (25%). According to TNM classification, patients were predominantly classified in stages II and III. In terms of treatment, 20 patients received neoadjuvant chemotherapy (30%), 15 patients received neoadjuvant radiotherapy (25%), and 45 patients underwent surgery (75%). Malnutrition, according to GLIM criteria, was present in 40% of patients. It was classified as mild, moderate, and severe in 40%, 45%, and 15% of cases, respectively. On univariate analysis, Malnutrition was significantly associated with elder age ≥ 65 years ($p=0.008$), bowel obstruction revealing CRC ($p=0.004$) and length of hospital stay ($p = 0.002$). Regarding survival, the difference between the two Kaplan-Meier curves of patients fulfilling GLIM malnutrition criteria versus patients without malnutrition was statistically significant (Log-rank test $p = 0.001$), [HR = 4.35 (95% CI = 2 - 9)], with a mean survival period of 18 ± 4.7 versus 32 ± 5.2 months, respectively ($p = 0.028$). Mild malnutrition was associated with better survival compared to moderate and severe malnutrition: 20 ± 2.3 versus 17 ± 3.2 months, respectively ($p = 0.003$).

Conclusions: Pretherapeutic screening for malnutrition seems to be mandatory due to its negative prognostic impact in patients with colorectal cancer, allowing for better pre-therapeutic stratification.

BELGIAN PANCREATIC CLUB (BPC)

- P01 -

PANCREATIC WALLED-OFF NECROSIS: NOT ALWAYS WHAT IT SEEMS. E. Coppieters (1), C. Buysse (1), D. Persyn (1), A. Billiet (1), M. Cool (1), M. Tresinie (1), S. Van Avermaet (1), P. Dewint (1), G. Lambrecht (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology.

A 69-year-old female presented with fatigue, weight loss, abdominal fullness, and left-sided shoulder pain. Relevant medical history included a pT1b squamous cell carcinoma of the oesophagus, for which she underwent oesophagectomy with gastric pull-up and cervical anastomosis 13 years prior to current presentation. Computed-Tomography (CT) of thorax-abdomen showed a cystic lesion with internal debris situated in the left hypochondrium at the pancreatic corpus (12cm x 8.5cm x 11cm), with compressive effect on neighbouring structures. The radiological image resembled a pancreatic walled-off necrosis (WON) and endoscopic drainage was performed using a lumen-apposing metal stent (LAMS) (Hot Axios, Boston, 20mmx10mm) and a coaxial pigtail stent. Cytological evaluation was suboptimal due to the amount of necrosis but reported the presence of atypical cells. Endoscopic reassessment showed that the LAMS had partially migrated out of the stomach wall. The LAMS was removed, and two new pigtail stents were placed to allow further drainage of the cystic lesion. During the procedure intralesional wall biopsies were taken through the cystogastrostomy. Histopathological evaluation surprisingly showed a squamous cell carcinoma, consistent with a late metastatic recurrence from her prior oesophageal cancer. After drainage of the cyst, the left sided shoulder pain improved but the patient suffered further weight loss (6kg). Additional staging with FDG-PET showed multiple retroperitoneal and para-aortic lymphadenopathies, localised as a conglomerate between stomach, spleen and pancreatic tail. After multidisciplinary oncologic discussion the patient was started on chemoradiotherapy (intravenous weekly administration of carboplatin and paclitaxel) with concurrent radiotherapy (41,4 Gy, given in 23 fractions of 1,8 Gy). The patient completed the treatment course with good tolerance, however, she unexpectedly passed away at home before new staging examinations could be performed.

Conflicting evidence exists regarding treatment and the superiority of LAMS versus plastic stents for the drainage of WON (1,2). While LAMS, such as the Hot AXIOS, provide better stability, larger luminal diameter, and direct access for therapeutic interventions, the risks of adverse events such as bleeding and stent migration are not negligible. For symptomatic relief and diagnosis, a cystogastrostomy performed with a LAMS offers a dual advantage: effective drainage of the cyst and the ability to obtain tissue biopsies for histopathological examination. This approach is particularly relevant in cases where malignancy is suspected and initial cytologic analysis is inconclusive. To the best of our knowledge, only 6 cases of oesophageal cancer with pancreatic metastasis are reported in the literature (3-8).

This case describes a very rare situation of a metastatic recurrence of an oesophageal squamous cancer, presenting as a pancreatic WON, occurring 13 years after seemingly curative treatment. It highlights the need for strict awareness in oesophageal cancer, even beyond standard follow-up periods, as late recurrences can present diagnostic challenges.

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- P02 -

A RARE CASE OF PANCREATIC MASS MIMICKING MALIGNANCY. E. Gökce (1), P. Hindryckx (1) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology.

We present the case of a 39-year-old Nigerian woman, referred in September 2024 after a pancreatic mass was identified on transabdominal ultrasound. The patient was asymptomatic at presentation, with no reports of abdominal pain, jaundice,

pruritus, stool changes, or fever. The ultrasound was requested due to mild elevations in liver enzymes (gamma-glutamyl transferase and alkaline phosphatase) following childbirth. Further examination with CT abdomen revealed a 1.9 cm hypodense solid nodule in the body of the pancreas and multiple intra-abdominal lymphadenopathies. Upon reviewing her medical records, we found that abdominal lymphadenopathies had already been described on an abdominal CT in October 2023. A follow-up MRI in January 2024 showed no significant growth of the lymph nodes. Endoscopic ultrasound (EUS) was recommended for further examination but was postponed due to pregnancy. The most recent CT showed no significant change in lymph node size over time. Biochemical work-up revealed no additional abnormalities, with normal Ca19-9 and IgG4 levels and negative infectious serologies (including HIV, HAV, HBV, HCV, CMV, and EBV). A thoracic CT showed a nonspecific micronodule in the right lower lung lobe. EUS identified two solid lesions in the pancreatic parenchyma, multiple pathologic lymphadenopathies, and numerous splenic lesions. A PET-CT was performed to assess disease extent, which confirmed involvement of the pancreas, spleen, and liver, as well as new bilateral lung micronodules. Histopathological examination of biopsy samples revealed necrotic tissue with focal granulomas, suggestive of mycobacterial infection or tuberculosis. The patient was referred to the internal medicine department for further management. A repeat EUS was performed for PCR analysis and to obtain a culture for antibiotic resistance testing. PCR confirmed mycobacterium tuberculosis, with no resistance detected. Appropriate antituberculosis therapy with isoniazid, rifampicin, pyrazinamide, and ethambutol was initiated, and family members were screened using a Mantoux test. This case highlights the rarity, clinical significance, and diagnostic challenges of pancreatic tuberculosis. Recognizing and correctly diagnosing pancreatic tuberculosis is crucial for correct management.

- P03 -

WEIGHT LOSS AND PAIN IN A PATIENT WITH CHRONIC PANCREATITIS: NO GOOD, ONLY THE BAD AND THE UGLY. C. Gulkilik (1), M. Pezzullo (2), L. Verset (3), L. Mans (1), M. Fernandez Y Viesca (1), P. Eisendrath (4), M. Arvanitakis (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology, [2] HUB Hôpital Erasme, Brussels, Belgium, Radiology, [3] HUB Hôpital Erasme, Brussels, Belgium, Pathology, [4] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology

Introduction: Chronic pancreatitis (CP) is a progressive inflammatory disease of the pancreas characterized by irreversible structural damage, often leading to abdominal pain, malnutrition, exocrine and endocrine insufficiency. Importantly, CP is a recognized risk factor for the development of pancreatic cancer, and its incidence increases with disease duration. This case report examines the challenges of managing CP progression to pancreatic cancer, focusing on early diagnosis and comprehensive care strategies.

Case Presentation: A 54-year-old male patient with a diagnosis of CP since 2019 presented in August 2023 with recurrent episodes of abdominal pain, persistent weight loss and vomiting. Initial investigations, including a CT scan and magnetic resonance cholangiopancreatography (MRCP), showed features of CP with pancreatic ductal abnormalities and calcifications, but no evidence of malignancy. The patient underwent extracorporeal shock wave lithotripsy (ESWL) in August 2023 to treat the pancreatic duct stones. Following ESWL, pancreatic duct drainage through endoscopic retrograde cholangiopancreatography (ERCP) failed; therefore, an EUS-guided pancreatico-duodenostomy was performed in September 2023. A surgical gastrojejunostomy was also performed for suspected superior mesenteric artery (SMA) syndrome with symptoms of gastric outlet obstruction. Despite these interventions, the patient continued to experience abdominal pain although imaging confirmed adequate drainage of the main pancreatic duct. In February 2024, MRCP imaging revealed tissue around the SMA, prompting further evaluation. An endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) performed in April 2024 showed no evidence of malignancy. This was followed by ERCP, during which a plastic stent was placed to treat a biliary stricture known since 2023. Unfortunately, during follow-up in July 2024, a CT scan and MRI revealed an increase in perivascular infiltration and the development of multiple hepatic lesions. A second EUS-FNB focused on the perivascular infiltration allowed the diagnosis of pancreatic cancer and the onset of chemotherapy.

Discussion: This case illustrates the importance of careful assessment of vascular structures in the diagnostic evaluation of patients with CP. Inflammation and structural changes in CP complicate imaging and make the differentiation between neoplastic and fibrotic tissue challenging due to their similar characteristics (similar texture, signal and behaviour). Regular follow-up with cross-sectional imaging such as CT and MRI, interpreted by experienced radiologists and reviewed by comparative assessment in multidisciplinary discussions, is essential. EUS-FNB has proven to be a valuable tool in differentiating pseudotumoural masses from solid neoplasms in CP. With higher sensitivity and diagnostic accuracy compared to EUS-FNA, it is increasingly recognized as the preferred method for cancer diagnosis in this context [1]. However, EUS-guided tissue sampling presents several challenges due to the heterogeneity of pancreatic tissue, compounded by calcifications and posterior infiltration around arteries. To address these limitations, advanced echo-endoscopic modalities, including EUS elastography and contrast-enhanced EUS (CE-EUS), have been developed to improve diagnostic accuracy. EUS elastography shows a good sensitivity for the diagnosis of pancreatic tumours, but a lower specificity, mainly due to the difficulty in distinguishing highly fibrotic CP from tumour lesions [2]. CE-EUS improves the characterization of microvascularization within the target tissue and provides good sensitivity and specificity for the detection of tumour tissue [3]. Finally, a study confirmed the complementary role of EUS elastography

and CE-EUS in differentiating focal pancreatic masses, with the best diagnostic accuracy achieved through a sequential algorithm starting with elastography followed by contrast enhancement [4].

Conclusion: This case highlights the challenges of diagnosing pancreatic cancer in CP and underscores the need for advanced diagnostic techniques, multidisciplinary care, and vigilance to improve outcomes. Refining EUS-guided biopsy techniques and developing standardized protocols are crucial for early detection and effective management in this high-risk population.

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- P04 -

ENDOSCOPIC MANAGEMENT OF PANCREATIC STENTS WITH A DEEP MIGRATION IN THE PANCREAS. P. Deprez (1), T. Moreels (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepatogastroenterology.

Pancreatic stents can migrate both distally as well as proximally into the pancreatic duct. Migrated stents can cause recurrent pancreatitis, infection, perforation, as well as stenosis of the duct. Incidence of stent migration has been reported at about 1.5% in the medical literature. Retrieval of the migrated stent is challenging and may even be more complicated in case of anormal anatomy of the minor or major papilla, and main pancreatic and in patients with altered anatomy. Location as well makes stent retrieval challenging and usually starts with attempts of retrieval with a rat tooth forceps, a Dormia basket, or a metallic spiral stent retriever, or the use of a pancreatoscope. Use of SpyGlass Direct Visualization System enables direct and fluoroscopic visualization of the pancreatic duct. Success rate of endoscopic retrieval is estimated from 70% to 100%. If endoscopic retrieval is not possible, surgical retrieval may be necessary. We report various cases in whom these techniques have been used successfully.

- P05 -

ISOTRETINOÏN INDUCED PANCREATITIS: IS IT TIME TO DEFINITELY RECOGNIZE IT? - A CASE REPORT. E. Gregoire (1), J. Barras (1), J. Loly (2) / [1] CHU Liege, Liège, Belgium, Gastroenterology, [2] CHU Liege, Liège, Belgium, Gastroenterology.

Background: Although often overlooked, drug-induced pancreatitis is a frequent cause of pancreatitis. Pancreatic drug toxicity is defined according to the Mallory et al. and Trivedi et al. classification. Isotretinoin is only classified as possibly toxic to the pancreas (class 3). We report the first case of recurrence of pancreatitis after rechallenging, which argues for a modification of the classification of drug induced pancreatitis.

Case presentation: We present here the case of a 20-year-old Caucasian man who suffered several episodes of acute pancreatitis for which no aetiology could be identified despite an exhaustive assessment. Eventually, as a precaution, Isotretinoin was discontinued and there was no recurrence until it was reintroduced.

Conclusion: This is the 25th case described in the literature, but the first with a positive rechallenge on two occasions. This case therefore implies that isotretinoin should definitely be considered a class 1 toxic drug for the pancreas and should be incriminated in acute pancreatitis in patients treated with this drug.

BELGIAN WORKING GROUP ON DIGESTIVE PATHOLOGY

- R01 -

SPATIAL IDENTIFICATION OF FAVORABLE MOLECULAR MODULATIONS AFTER STEREOTACTIC BODY RADIOTHERAPY IN PANCREATIC CANCER WITH A PRACTICAL STAINING-BASED CLASSIFIER. C. Bouchart (1), E. Michiels (2), J. Navez (3), L. Verset (4), O. Azurmendi Senar (5), T. Arsenijevic (5), I. Rooman (2), J. Van Laethem (6) / [1] Institut Jules Bordet, Brussels, Belgium, Laboratory of Experimental Gastroenterology / Radiation Oncology, [2] Vrije Universiteit Brussel (VUB), Jette, Belgium, Laboratory of Medical and Molecular Oncology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Hepato-biliary-pancreatic surgery, [4] Institut Jules Bordet, Brussels, Belgium, Pathology, [5] ULB, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Oncology.

Introduction: Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest tumours. Consensus have been recently made regarding the existence of two main molecular subtypes in PDAC named Classical and Basal-like, associated with opposite prognosis and different chemosensitivity. However, the determination of molecular subtype is currently performed through transcriptomic gene profile analysis which is inadequate for daily practice. We previously developed a practical RNAScope staining-based classifier of the two main molecular subtypes in PDAC, allowing to spatially visualize intraductal heterogeneity.

Aim: Here, our aim is to better characterize in situ the molecular modulations following neoadjuvant treatments, including isotoxic high-dose stereotactic body radiotherapy (iHD-SBRT).

Methods: Using differential gene expression from two published RNAseq PDAC databases, two practical RNAScope multiplex panels were created to differentiate Classical and Basal molecular subtypes and were previously validated on an independent PDAC cohort. The Classical panel (CLP) included GATA6, CTSE and EPS8L3 while the Basal panel (BLP) included: AHNK2, MUC16 and S100A2. To spatially study molecular modulations after neoadjuvant treatments, paraffin-embedded residual tumoural tissues of 23 localized PDAC resected between 2014 and 2020 were used: eight patients had surgery first, eight received an induction chemotherapy with FOLFIRINOX (FFX) only and seven with FFX followed by an iHD-SBRT designed to individually maximize the dose prescribed to the tumour and vessels interfaces up to $D_{max}(0.5cc) < 53Gy$ in 5 fractions. Quantitative analysis was carried out using the HALO™ software in 10 ducts per sample randomly chosen within the tumoural area.

Results: Labelling of the treatment naïve cohort highlighted the high level of molecular intratumoural heterogeneity of PDAC regarding molecular subtypes, including within a single duct. After FFX alone, a shift was visually observed towards the BLP, whereas tumours treated with FFX + iHD-SBRT displayed a more enhanced CLP profile. After ductal quantification, tumours treated with FFX+SBRT were significantly associated with more Classical and less Basal-like cells than the tumours treated with FFX alone or treatment-naïve. Similarly, a nearly significant trend in decreased level of KRT17+ cells, a marker associated with Basal-like and poor prognosis, was identified in the FFX + SBRT cohort compared to FFX alone.

Conclusions: We successfully applied a practical multiplex staining-based classifier allowing to easily display the molecular heterogeneity of PDAC, including at the intraductal level. Contrary to the non-treated and FFX cohorts, tumours treated with FFX + iHD-SBRT were significantly enriched in cells displaying a Classical subtype, associated with a better prognosis, suggesting either a selection or a reprogramming effect of SBRT on the Basal-like cells.

- R02 -

GASTROINTESTINAL MANIFESTATIONS IN COMMON VARIABLE IMMUNODEFICIENCY DISORDER (CVID): HISTOPATHOLOGICAL PATTERNS, CLUES, AND PITFALLS FOR THE PATHOLOGIST AND GASTROENTEROLOGIST. L. Velthof (1), J. Geldof (2), M. Truyens (2), J. Van Dorpe (1), L. Ferdinande (1), T. Kerre (3), F. Haerynck (4), T. Lobaton (2), A. Hoorens (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Pathology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Hematology and Clinical Chemistry, [4] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Paediatric Immunology and Pulmonology.

Introduction: Gastrointestinal diseases are a major cause of morbidity in common variable immunodeficiency disorder (CVID), clinically often mimicking other conditions such as celiac disease or inflammatory bowel disease (IBD). CVID has a high mortality rate. Diagnosis remains challenging and is often delayed, potentially leading to life-threatening complications, hence the importance of early recognition.

Aim: This case series aims to contribute to higher awareness of CVID, highlight histopathological clues for CVID in intestinal biopsies, and emphasize pitfalls for both the pathologist and gastroenterologist in making the diagnosis.

Methods: We present a case series overlooking 63 biopsies and case histories from 7 CVID patients, including 18

duodenal, 23 ileal and 22 colonic biopsies, obtained over a 31-year period, with particular attention to features suggestive of CVID. We investigated active inflammation, intraepithelial lymphocytosis, the number of plasma cells, lymphoid hyperplasia, distortion of crypt/villous architecture, thickening of the subepithelial collagen layer, increased apoptosis, granulomas, and infections. Clinical information of 41 pathology requests was reviewed for mention of known/suspected CVID.

Results: Patients presented with variable gastrointestinal symptoms, diarrhoea (7/7) and abdominal discomfort (6/7) being the most frequent. CVID was often associated with autoimmune diseases (2/7). Observed histological features were variable and could be divided into patterns, including an IBD-like pattern (3/7), a celiac disease-like pattern (2/7), a graft-versus-host disease (GVHD)-like pattern (2/7), a lymphocytic sprue/lymphocytic colitis-like pattern (3/7), a collagenous colitis-like pattern (2/7), and an acute colitis-like pattern (4/7). Histological patterns often overlapped (2/7) and/or changed over time (3/7). Lymphoid hyperplasia was seen in 3/7 patients and an intestinal infection was identified in 1/7 patients. A low number of plasma cells was observed in 5/7 patients, mostly only focally in one part of the gut (3/5). Clinical information of 12/41 (29%) pathology requests mentioned suspected/known CVID, despite that, in 33/41 (80%) pathology requests, this information was on file in medical records.

Conclusions: Histological and clinical features of CVID in the gut are diverse and show similarities to other conditions, including IBD, microscopic colitis, celiac disease and GVHD, hence the importance of adequate clinical information. Some histological features, however, are atypical of these established entities and may indicate CVID, as may overlapping and/or changing histological patterns. A low number of plasma cells in biopsies is highly suggestive of CVID, though often only focal and easily overlooked. Higher awareness of the heterogeneous clinical presentation and histopathological indicators of CVID may improve diagnosis.

- R03 -

WHEN THE ORDINARY LOOKS EXTRAORDINARY: GALT-ASSOCIATED CARCINOMA, A UNIQUE COLON CANCER MORPHOLOGY. J. Fallas (1), M. Arvanitaki (2), N. D'Haene (1), M. Gómez Galdón (1), L. Verset (1) / [1] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Pathology, [2] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Background: GALT-associated carcinoma, also known as dome-type carcinoma, is a rare morphological variant of colorectal adenocarcinoma. It is characterised by cystically dilated glands filled with an amorphous eosinophilic material and embedded in a dense lymphoid stroma. Since its initial description in 1999, 24 cases have been reported in the scientific literature. The tumour's close association with lymphoid tissue, presence of intraepithelial B lymphocytes, and absence of goblet cells have led to the hypothesis that it originates from M-cells from the dome epithelium of gut-associated lymphoid tissue.

Case presentation: We report the case of a 68-year-old asymptomatic woman who was found to have a large sessile polyp in the sigmoid colon during routine screening colonoscopy. A superficial biopsy revealed an intramucosal colonic adenocarcinoma. Subsequent sigmoidectomy uncovered a 22 mm elevated submucosal lesion. Histologically, the lesion was well-demarcated and confined to the lamina propria. Although the tumour bulged into the submucosa, desmin immunostaining confirmed that muscle fibres from the muscularis mucosae wrapped around it. The lesion consisted of cystic glands containing an amorphous eosinophilic material, within a dense lymphoid stroma with germinal centres. The glands were lined by a columnar epithelium with eosinophilic cytoplasm and moderate nuclear atypia. The tumour was well-differentiated, with only a few cribriform clusters and no evidence of tumour budding or desmoplastic reaction. Surface examination revealed severe dysplasia and adenocarcinoma, consistent with the initial biopsy findings. All 16 harvested lymph nodes were free of neoplastic infiltration. Immunohistochemical examination revealed a complete absence of goblet cells, confirmed by negative MUC2 staining. The tumour was positive for CDX2, SATB2, and cytokeratin 20, and negative for cytokeratin 7, consistent with typical colorectal adenocarcinoma profiles. Rare intraepithelial lymphocytes were identified as T lymphocytes (CD3⁺/CD20⁺), with no intraepithelial B lymphocytes detected. Mismatch repair proteins were preserved, showing nuclear positivity for MLH1, MSH2, MSH6, and PMS2. Epstein-Barr virus in situ hybridisation was negative. Next-generation sequencing using a 168-gene panel revealed a mutation in the TP53 tumour suppressor gene.

Discussion: The hypothesis that this tumour originates from M-cells is supported by weak evidence. While the presence of a dense lymphoid stroma is noteworthy, key features such as intraepithelial B lymphocytes are not consistently reported in the literature. Furthermore, published cases did not show M-cell specific immunostaining, and electron microscopy studies identified microvilli at the apical membrane of tumour cells. Additionally, the molecular profile appears nonspecific. Despite its distinct morphology, we believe there is insufficient evidence to conclude that it originates from M-cells. Nevertheless, we propose that the unusual morphological features of this tumour—such as the coalescence of glands with lymphoid stroma and its characteristic pushing invasion pattern—justify its recognition as a distinct morphological subtype of colorectal carcinoma. Another important consideration is that this lesion is an ideal candidate for endoscopic resection, and better understanding could lead to more accurate diagnoses, potentially avoiding colectomy in future cases. Given the limited number of reported cases, it is unclear whether these tumours are truly rare

or simply under-recognised. By providing detailed histopathological and molecular insights, this case contributes to the limited literature on GALT-associated carcinoma.

- R04 -

RECURRENT LEUKEMOID REACTION IN ALCOHOL-ASSOCIATED STEATOHEPATITIS: A DIAGNOSTIC CHALLENGE. L. Duchêne (1), N. Lanthier (2), V. Havelange (3), S. Haxhe (2), S. Aydin (1), P. Baldin (1) / [1] UCLouvain, Cliniques Universitaires St Luc, Belgium, Pathology, [2] UCLouvain, Cliniques Universitaires St Luc, Belgium, Gastroenterology and hepatology, [3] UCLouvain, Cliniques Universitaires St Luc, Belgium, Haematology.

A 36-year-old woman of Hispanic descent presented in 2019 with abdominal pain and jaundice. Physical examination revealed abdominal stiffness and hepatosplenomegaly. Laboratory investigations showed severe leukocytosis, bicytopenia, inflammatory markers, coagulopathy, and cholestatic liver enzyme elevations. A liver biopsy revealed histological features of steatosis, severe portal and lobular neutrophilic inflammation, hepatocyte ballooning, Mallory-Denk bodies and pericellular fibrosis. The findings suggested alcohol-associated steatohepatitis (ASH), though the patient denied alcohol consumption. Other etiologies, including viral hepatitis and drug-induced liver injury, were ruled out. Given the systemic leukocytosis, bicytopenia, and splenomegaly, a bone marrow biopsy was performed. It demonstrated hypercellularity with granulocytic hyperplasia and numerous megakaryocytes raising suspicion for an atypical myeloproliferative neoplasm, specifically chronic neutrophilic leukemia (CNL). However, next-generation sequencing (NGS) did not identify any molecular alterations. Following consultation with a liver pathology specialist, a working diagnosis of chronic steatohepatitis associated with exaggerated neutrophilic infiltration in the context of possible CNL was proposed. The patient's clinical condition improved with treatment directed at leukocytosis and supportive care, but she was subsequently lost to follow-up. Three years later, she presented again with recurrent abdominal pain and jaundice. Laboratory findings and clinical features were strikingly similar to the prior episode. A repeat liver biopsy revealed severe neutrophilic portal and lobular inflammation, macrovesicular steatosis, satellitosis, prominent Mallory-Denk bodies, and pericellular fibrosis. This time, the patient admitted to significant alcohol consumption preceding both episodes. Reevaluation of the bone marrow biopsy excluded persistent myeloproliferative disease and repeat NGS testing remained negative for mutations. The recurrent leukocytosis was reinterpreted as a leukemoid reaction associated with alcohol-associated steatohepatitis. The patient was diagnosed with recurrent ASH, accompanied by an unusual and underreported phenomenon of a leukemoid reaction. This case underscores the diagnostic complexities associated with recurrent leukemoid reactions in ASH, a rare clinical presentation. While the histological features in this case were consistent with ASH, the initial diagnosis was confounded by the patient's denial of alcohol use and the atypical systemic findings, including significant leukocytosis and splenomegaly. The leukemoid reaction, characterized by extreme neutrophilia, is a rare occurrence in ASH and led to the initial consideration of a myeloproliferative disorder. This case brings to light several diagnostic challenges that underscore the complexities of chronic hepatitis with steatosis, especially in the presence of systemic symptoms like severe leukocytosis. One key issue is the histological overlap in chronic hepatitis. While the liver biopsy revealed hallmark features of alcohol-associated steatohepatitis (ASH)—such as neutrophilic inflammation, Mallory-Denk bodies, and pericellular fibrosis—these findings can be seen in conditions such as drug-induced liver injury, autoimmune hepatitis, or infectious aetiologies, particularly hepatitis E. Neutrophilic inflammation could be observed in ASH, but when exuberant is an atypical finding. Equally important is the role of clinical context in guiding the diagnostic workup. This case highlights how incomplete or inaccurate clinical history can skew the interpretation of pathological findings. The patient's initial denial of alcohol consumption prompted an alternative diagnostic pathway focused on myeloproliferative disorders. It was only after the patient admitted to heavy drinking that the clinical and pathological findings aligned, enabling a definitive diagnosis of ASH. This underscores the critical need for open communication and thorough history-taking in complex cases. Lastly, this case sheds light on rare manifestations of ASH, specifically the occurrence of a leukemoid reaction. Extreme neutrophilia is an unusual systemic feature in ASH, and this case is among the first to document its recurrence. Such a presentation broadens the recognized spectrum of systemic manifestations associated with ASH, reminding pathologists to consider this phenomenon when faced with severe leukocytosis in the setting of compatible liver pathology. This case illustrates the diagnostic intricacies in evaluating chronic hepatitis with systemic neutrophilia. It emphasizes the importance of comprehensive clinical correlation, particularly regarding alcohol use, in avoiding diagnostic pitfalls. Pathologists should consider leukemoid reactions as a rare but possible systemic manifestation of ASH, especially in patients with unexplained extreme neutrophilia.

- R05 -

METASTASES: THE DEFAULT DIAGNOSIS UNTIL DISPROVEN. K. De Corte (1), T. Chapelle (2), B. Op de Beeck (3), S. Francque (4), A. Driessen (1) / [1] University Hospital Antwerp, Edegem, Belgium, Pathology, [2] University Hospital Antwerp, Edegem, Belgium, Hepatobiliary, Transplant and Endocrine Surgery Department, [3] University Hospital Antwerp, Edegem, Belgium, Radiology, [4] University Hospital Antwerp, Edegem, Belgium, Gastroenterology and Hepatology.

The liver, due to its dual blood supply and its role in filtering blood from the gastrointestinal tract, is the most common site of metastatic cancer. In fact, the majority of liver tumours are metastases, which are more prevalent than primary liver cancers. These metastases have diverse origins, with colorectal cancer being the most common source.

We present the case of a 65-year-old female with metabolic associated steatotic liver disease (MASLD), linked to a high BMI and disturbed glucose tolerance with hyperinsulinism. A past liver biopsy revealed steatohepatitis with mild perisinusoidal fibrosis. Recently, she was diagnosed with ductal adenocarcinoma of the breast, which was treated with lumpectomy and adjuvant radiotherapy. During follow-up, an abdominal MRI revealed a liver with an irregular surface, resembling cirrhosis. Several intensely white spots of varying size were detected in the liver parenchyma. To rule out metastatic disease, a surgical biopsy was performed. However, pathological examination revealed no signs of malignancy. The white spots corresponded to multiple von Meyenburg complexes of varying sizes. Mild steatosis was found in the surrounding liver parenchyma.

Von Meyenburg complexes, or biliary hamartomas, first described by Van Meyenburg in 1918, are not tumours but rather result from ductal plate malformation involving the smallest intrahepatic bile ducts. These biliary hamartomas consist of cystic remnants of the ductal plate, lined by a single layer of cuboidal cells, and surrounded by fibrocollagenous stroma. They can occur as solitary lesions or in association with other fibropolycystic disorders, such as autosomal dominant polycystic kidney disease (ADPKD), congenital liver fibrosis, or Caroli syndrome. These subcapsular lesions, typically 5 to 10 mm in size, are usually benign. However, in some cases, they can grow up to 2-3 cm, raising concern for metastatic disease. While these lesions can sometimes be identified on imaging alone, a liver biopsy is recommended to exclude malignancy. Although rare, these lesions can occasionally progress to cholangiocarcinoma, making follow-up essential, as in the case of our patient.

- R06 -

ACUTE HEPATIC FAILURE SECONDARY TO AMYLOIDOSIS AT THE ORIGIN OF THE DIAGNOSIS OF MULTIPLE MYELOMA. I. Mariz (1), S. Negrin Dastis (2), P. Baldin (1), G. Dahlqvist (3), E. Bonaccorsi-Riani (4), S. Aydin (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Histopathology, [2] Grand Hôpital de Charleroi, Charleroi, Belgium, Gastroenterology and hepatology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology and hepatology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Surgery.

An active 58-year-old man with no significant medical history had been suffering for several months from progressive fatigue and general health decline over the course. He used to drink about a bottle of wine daily, which he had stopped a few months before the onset of symptoms. He was followed by his GP for this fatigue with monthly blood tests revealing isolated thrombocytosis, progressing to cholestasis and eventually liver cytolysis. Early imaging showed hepatomegaly and marked steatosis, suggesting cirrhotic decompensation with fluid accumulation in the perihepatic regions and the pouch of Douglas. Further evaluation via suprahepatic catheterisation identified a rapidly progressing cholestatic hepatitis of indeterminate origin. All viral and autoimmune serologies were negative, with no evidence of storage disease or drug-induced liver injury (DILI). However, elevated LDH levels raised suspicion for an underlying neoplastic process or a myeloproliferative syndrome. A liver biopsy was performed during the procedure for further diagnostic investigation. Liver biopsy revealed diffuse sinusoidal thickening with Congo red positive amyloid deposits located in both sinusoids and vessel walls, confirmed by immunofluorescence as AL lambda amyloid deposits. Minimal fibrosis was observed (Metavir score system: F0-F1), no significant steatosis or necrosis was noted and a mild bilirubinostasis and ductal proliferation were mentioned. Two days later, the patient developed abdominal pain, jaundice and moderate haemorrhagic ascites in the perihepatic and parietocolic regions. Tests revealed marked hyperbilirubinaemia (13 mg/dL) and worsening cytolysis and cholestasis. These findings were consistent with cholestatic hepatitis rapidly progressing to hepatic decompensation, leading to transfer to specialist care. After transfer, haematological investigation revealed multiple myeloma, with >30% plasmacytosis and an excess of mast cells. Protein electrophoresis showed a monoclonal band of lambda-type IgG in the gamma zone, with an estimated monoclonal band of 11,8 g/L. The final diagnosis was a sub-fulminant hepatitis due to AL amyloidosis in the context of multiple myeloma, leading to acute liver failure. This was complicated by portal hypertension, grade 1 oesophageal varices, hepatorenal syndrome and ascites requiring drainage. The patient also developed acute hypoxaemic respiratory failure, probably related to ascites and pleural effusions. Cardiac evaluation revealed mild mitral insufficiency and sinus tachycardia without left ventricular hypertrophy (LVH), and MRI showed no evidence of cardiac amyloidosis. The patient was treated with chemotherapy for his multiple myeloma, glypressin for his hepatorenal syndrome, and a liver transplant was performed few days after the final diagnosis.

Liver involvement in light chain amyloidosis is uncommon but not rare and often manifests with a wide range of symptoms, the most common being hepatomegaly. Cholestatic jaundice and portal hypertension are less frequent, and acute liver failure is rare, especially as a primary manifestation of AL amyloidosis. The broad spectrum of presentations, combined with the fact that altered liver test results are usually mild and appear late in the disease course, often delays the diagnosis of hepatic amyloidosis. The literature suggests that diagnostic clues for light chain amyloidosis include involuntary weight loss, unexplained hepatomegaly, elevated alkaline phosphatase levels, proteinuria (reflecting frequent renal involvement), hyposplenism, and the presence of monoclonal protein in serum, urine or both. However, the gold

standard for confirming amyloid deposit remains tissue biopsy, with Congo red staining, immunohistochemistry or fluorescent dyes to highlight amyloid deposits. The classification of amyloid fibrils (e.g., AL lambda or AL kappa) is also important for guiding treatment.

We share this case to draw attention to the challenges in the diagnosis of hepatic amyloidosis. It is important to recognise this disease despite its generally poor prognosis in advanced stages, as some patients may benefit from treatments such as chemotherapy to treat the underlying cause and, in some cases, eventual organ transplant to replace failing organs. Furthermore, randomised trials of novel chemotherapies have shown significant improvements in survival and symptoms in patients who received adequate treatment.

ULTRASOUND

- U01 -

EVALUATION OF NASOGASTRIC TUBE PLACEMENT BY BEDSIDE ULTRASOUND IN CRITICALLY ILL PATIENTS. E. Stiers (1), K. Vanderbiest (1), K. Colpaert (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Intensive Care Medicine.

Introduction: Nasogastric tube (NGT) feeding is the preferred and a commonly used nutritional intervention for critically ill patients in the intensive care unit (ICU). Accurate placement is essential to prevent severe complications such as aspiration, pneumothorax, and pneumonia, which increase the risk of mortality. Thorax radiography is the conventional method for placement verification, but it introduces increased costs, care delays, and radiation exposure. Bedside ultrasound has emerged as a fast, cost-effective, and radiation-free alternative that enables real-time soft tissue assessment. Although recent research demonstrates high sensitivity and specificity of ultrasound for confirming NGT placement, concerns persist regarding the safety of air or water injections for visualization, highlighting the need for an additional verification technique.

Aim: This study aimed to assess the accuracy and feasibility of bedside ultrasound, particularly subxiphoid ultrasound, combined with pH analysis of gastric aspirates, as a non-invasive, cost-effective alternative to chest radiography for confirming nasogastric tube (NGT) placement in critically ill patients. Additionally, it explored the impact of proton pump inhibitor (PPI) use on pH measurement.

Methods: This single-centre, prospective, single-blind study assessed NGT placement by identifying a hyperechoic ultrasound image of the NGT within the esophagus and subxiphoid region of the antrum. Additionally, pH measurements of aspirated fluids were obtained and analysed. A pH lower than 5.5 is considered gastric fluid. The effectiveness of the combined ultrasound and pH methods was compared against standard chest radiographs.

Results: The study included 39 patients (17 male, 22 female) with a mean age of 58.9 ± 13.6 years. Outcome measures focused on the accuracy of verification using ultrasound compared to thorax radiography, alongside pH analysis of aspirated gastric fluid. Ultrasound demonstrated a sensitivity of 96.9% and specificity of 100% for identifying correctly placed NGTs, with a positive predictive value of 100% and a negative predictive value of 85.7%. Subxiphoid US in combination with pH aspiration gave the same results. In one patient, aspiration showed positive pH results with oesophageal ultrasound confirmation, but subxiphoid ultrasound failed to detect the NGT. Thorax radiography confirmed correct placement of the NGT. In 7/39 patients, the NGT was not visualized via subxiphoid US, of which only one was a false negative as confirmed by radiography. In the remaining 6 it was not possible to aspirate. Oesophageal US has a specificity of only 17%. Subgroup analysis indicated that the use of proton pump inhibitor (PPI) was associated with a slight increase in pH levels (mean pH 4.35 ± 1.13) relative to non-users (mean pH 3.57 ± 0.79). In 3 patients with PPI intake values above the cut-off 5,5 were seen.

Conclusions: These findings suggest that bedside ultrasound, combined with pH analysis, may serve as a reliable, non-invasive method for verifying NGT placement, potentially reducing reliance on chest radiography when ultrasound visualization is achievable. While promising, the study also identified limitations, including occasional false negatives and the need for operator expertise in ultrasound imaging. The influence of PPI intake on pH levels should be considered in the interpretation of aspirate results as values were found that were above the cut-off value. Further investigation is needed to validate these findings and refine the ultrasound protocol.