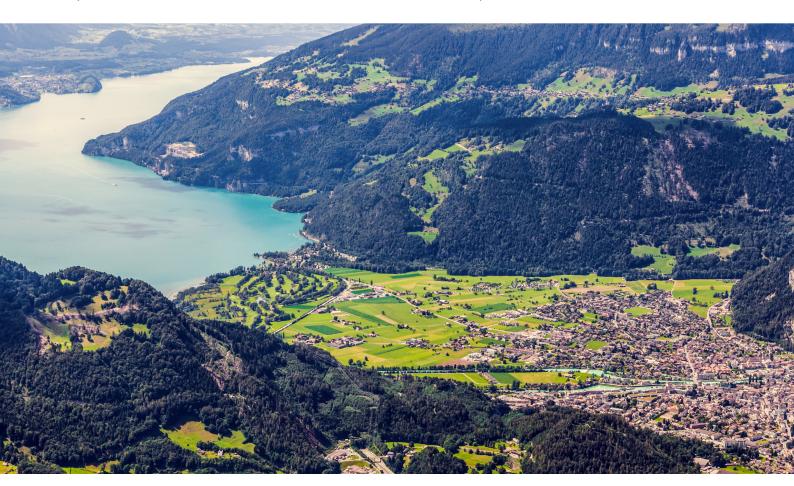
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# SWISS SOCIETY OF GASTROENTEROLOGY (SGG-SSG) SWISS VISCERAL SURGEONS (SGVC-SSCV) SWISS ASSOCIATION FOR THE STUDY OF THE LIVER (SASL) SWISS SOCIETY OF ENDOSCOPY NURSES AND ASSOCIATES (SVEP-ASPE)

#### **ANNUAL MEETING 2022**

INTERLAKEN, SEPTEMBER 15-16, 2022

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#### **SESSION GASTROENTEROLOGY I**

# Longitudinal follow-up of patients with eosinophilic esophagitis variants and their potential to progress to EoE: a clinical, histological and molecular multi-center analysis

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**Background:** Eosinophilic esophagitis (EoE) variants have been recently characterized as conditions with symptoms of esophageal dysfunction resembling EoE, but absence of significant esophageal eosinophilia. As of yet, it remains unknown whether any of several EoE variants can progress to classical EoE over time, and which genes are responsible for such progression.

**Methods:** Treatment-naïve patients from six EoE-centers with symptoms of esophageal dysfunction, but peak eosinophil counts of <60/mm² (<15/hpf) in esophageal biopsies and absence of gastro-esophageal reflux disease with at least one follow-up were included. Clinical, (immuno)-histological and molecular features (sequential mRNA sequencing) were determined and compared with EoE and esophagus-healthy controls.

Results: We included 54 patients with EoE variants (29 EoE-like esophagitis, 53.7%; 7 lymphocytic esophagitis, 13.0%; 18 non-specific esophagitis, 33.3%). Transition from one EoE variant (baseline) to another variant (during follow-up) was seen in 19 patients (35.2%). In 8 patients with EoElike esophagitis (8/29, 27.6%), progression to EoE occurred after a median of 14.0 months (IQR 3.6-37.6). Seven of these patients had detectable, but non-significant esophageal eosinophilia at baseline visit (mean 24 eos/mm<sup>2</sup>, SD 13.2, IQR 14-34.5, range 13-42), while one patient had neither epithelial nor subepithelial eosinophilic infiltration (0 eos/mm<sup>2</sup>). In 5 of these 8 patients, tissue for mRNA sequencing analyses (time baseline vs time eosinophilic infiltration) was available. Sequential mRNA sequencing analyses revealed only few genes involved during the progression from EoE- like esophagitis to EoE (TSG6, ALOX15, MUC5AC, CTSE, RPTN, LTF, SLC26A4, GKN1) with upregulation of a previously attenuated Th2 pathway. Immunohistochemical analyses confirmed an upregulation of TSG6 in epithelial cells paralleling the increase in EPX positive eosinophils during progression from EoE-like esophagitis to EoE. An increase in CD3 positive T-cells, particularly GATA3+ lymphocytes (indicating a Th2 response), was seen during this progression to EoE, resulting in a similar inflammatory response as detected in classical EoE patients when compared to healthy controls.

**Conclusion:** Frequent transition from one EoE variant to another and progression to classical EoE suggest the presence of a disease spectrum. Few genes (such as TSG6) are responsible for this progression to EoE with upregulation of a previously attenuated Th2 signal. These genes including GATA3 as a key Th1/Th2 switch regulator represent potential therapeutic targets for both EoE variants and EoE in general.

## Hierarchical Contribution of Demographics, Lifestyle, and Diet to Adenomatous and Serrated Polyp Risk

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**Background**: Individual risk factors of colorectal polyps are well characterized, however, insights into their joint impact is scarce. We aimed to identify the hierarchical structure of various risk factors and their joint effects on adenomatous (AP) and serrated polyp (SP) risk.

**Methods**: We collected detailed information on 363 variables including demographic data, polyp histology, metabolic parameters, lifestyle, and nutrition from 1'597 randomly recruited participants undergoing colonoscopy, resulting in over 521,000 data points. We used a combination of multivariate statistics and machine-learning approaches to assess the association of single variables and their joint interactions with AP and SP.

**Results**: Our approach showed that age, gender, various lifestyle factors, and diet follow a differential step- wise hierarchical structure for AP and SP risk. While a high BMI and western diet strongly increased AP and SP risk, gender, age, and metabolic syndrome only increased AP risk. Smoking alone was associated with increased SP risk, whereas only its combination with age and male gender increased AP risk. Colorectal cancer (CRC) family history did not impact initiation, but progression of AP to advanced lesions. Obesity and diabetes associated with progression of SP to advanced lesion.

**Conclusions**: Our study suggests that risk factor interactions for adenomatous and serrated pathways for both polyp initiation and progression are strongly different. Our findings may facilitate tailored lifestyle change recommendations, and contribute to a better understanding how risk factors impact the molecular mechanisms underlying adenomatous and serrated pathway.

## A Clinically Applicable Genomic Assay Detects Pathogenic Alterations in Non-Dysplastic Barrett's Esophagus Patients

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**Background:** Current risk prediction for malignant progression in Barrett's Esophagus (BE) is based on the histological diagnosis of dysplasia, which is limited by several factors. Genomic abnormalities precede dysplasia and may allow for objective and early risk stratification. We aimed to identify genomic factors for a clinically applicable targeted sequencing panel predicting progression in BE.

**Methods:** Progressors (P) to high-grade dysplasia/esophageal adenocarcinoma (EAC) and matched non-progressors (NP) from a nested, community-based cohort were identified. DNA from baseline and subsequent (temporal) non-dysplastic endoscopies was assessed. Sequencing was performed utilizing a targeted capture- based panel designed to detect alterations previously identified in BE/EAC. Mutations, homozygous deletions, and high-level amplifications were filtered for likely pathogenic events.

**Results:** 227 BE patients (85% male, median BE length of C3M4) were analyzed. 105 patients progressed after a median of 4 (IQR 3- 6) years. 122 NP had a median follow-up of 6 (IQR 5-7) years. Baseline analysis identified *TP53* in 30% of P compared with 3% of NP, p = <0.0001, and increased to 50% closer to progression. *TP53*, *KMT2D*, *ATM*, and *KDM6A* were identified as risk predictors in univariate Cox regression analysis. Copy number alterations (amplifications, arm level loss) increased in P closer to progression

**Conclusions:** Our study identified multiple mutational and copy number aberrations in non-dysplastic biopsies years before progression. A combination of these markers will best identify non- dysplastic BE patients at high-risk for progression.

# Characterization of small intestinal stoma microbiota in patients with colorectal cancer and inflammatory bowel diseases

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Background: Small intestinal microbes have been shown to substantially impact host metabolism and immunity in experimental animals, but human studies have been limited by the inaccessibility of the ileum without purging and/or deep intubation. Studies on stoma patients have been especially valuable to investigate human digestive processes and the microbial consortia in different intestinal segments. Hence, we designed a study to understand dietary changes in human small intestinal microbiota biomass and its sub-strain composition. Therefore, we show here that there is an inherent instability in the human small intestinal microbiota biomass relating to dietary pulsations within individuals.

**Method**: We characterized stoma content and biopsy samples collected from colorectal cancer patients and inflammatory bowel disease patients using shotgun metagenomic sequencing and mass spectometry. Importantly, we characterized the microbiota profile deeper by examining the sub-strain variants using the *InStrain* pipeline.

**Results**: This study allows real-time access to the distal small intestine and different levels of the large intestine without purgatives or other clinical manipulations. It also shows that there are two types of instability in the host-microbial relationship: i) biomass in the distal small intestine is substantially shed in ileostomas following a fasting period and rapidly blooms in the fed state; ii) proportions of different taxa in the large intestine are stable and there are only minor changes in taxa proportions in the distal small intestine.

**Conclusion**: Overall, we generated a combination of molecular ecological data sets using samples from stoma patients to describe the small intestine using an ecosystems biology approach in which we showed the capacities of small intestinal microbiota to adapt and to increase the biomass dramatically upon dietary intake.

#### Clinical impact of molecular biomarkers in the management of patient with pancreatic cysts

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**Background:** Pancreatic cysts (PCs) represent a diagnostic challenge. Mucinous PCs have the potential to be malignant and should be differentiate from other cysts. Using MRI, EUS, biochemical assay and cytopathology allows a 70% diagnostic accuracy. This number can increase to 90% when using cystic molecular analysis (KRAS and GNAS). We aimed to assess the

impact of molecular biomarkers on the clinical diagnosis and management of patients with PCs.

**Methods:** Retrospective analysis (2014 to 2021) in a single, tertiary university center of patients who underwent EUS-guided FNA for PCs.

Results: 85 patients were analyzed (39% male, mean age of 63 years old). Most cysts were unique (77%), distributed either in the head of the pancreas (42%) or the body (32%) with a median diameter of 23mm. 73% of cysts were discovered incidentally. The other 27% of patients had abdominal pain or pancreatitis. Main type of PCs was intraductal papillary mucinous neoplasm (58%), serous cystadenoma (14%) and mucinous cystic neoplasma (11%). Of the 63 patients with mucinous lesions, KRAS and/or GNAS mutations were present in 17 patients. The presence of KRAS and/or GNAS mutation was observed in 12% of PCs without elevated CEA levels. 25 patients were operated for suspected malignant lesions and only 11 had high grade dysplasia (8/11) or cancer (3/11). Two other patients had advanced unresectable malignancy. Mutations in KRAS and/or GNAS were found in the 6/13 (46%) of malignant lesions and in 3/14 (21%) of the non-malignant lesions. No mutations were found in the 8/25 (32%) patients operated for mucinous lesion, 5 with malignant lesions.

**Conclusion:** Molecular biomarkers impact clinical diagnosis and patient's management with PCs but further studies with larger sample sizes are required to show beneficial input.

# Efficacy and safety of cold snare polypectomy of large colorectal polyps 10–15 mm with a hybrid snare: A prospective observational trial

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Background and Aims: Cold snare polypectomy (CSP) is a safe and effective procedure for small colorectal polyps ≤9 mm. There is only limited data regarding CSP of larger neoplastic lesions. This study evaluated the efficacy and safety of CSP for polyps between 10 and 15 mm in size.

**Methods:** In this prospective single-arm observational study, patients with a least one polyp 10-15 mm were included. These polyps were preferably removed by CSP using a dedicated hybrid snare. The primary outcome was the histological complete resection rate (CRR) determined by pathologically negative margins of the specimen and no neoplastic tissue obtained from biopsies of 4 quadrants of the resection site margin. Secondary outcomes were en bloc resection rate, failure of CSP and conversion to hot snare polypectomy (HSP), and incidence of adverse events.

Results: A total of 61 neoplastic polyps were removed from 39 patients. Overall complete resection rate was 80.3% (49/61). CSP was feasible in 78.7% (48/61) of polyps and the CRR in this group was 85.4% (41/48). When CSP failed (13/61; 21.3%), lesions were successfully resected by immediate HSP using the same snare with a complete resection rate of 61.5% (8/13) in this group. In univariate analysis, CRR was more likely related to polyps 10 mm in size (odds ratio [OR] 7,586; 95% confidence interval [CI], 0,906 – 63,512; P = 0,044) and histological diagnosis of adenoma ([OR], 4,286; [CI],1,058 – 17,363; P = 0,047). One patient presented delayed hemorrhage after HSP of a polyp but successful hemostasis was achieved with two hemoclips. No other adverse events such as post procedural abdominal pain or perforation occurred. No recurrence was seen on follow-up colonoscopy in cases with incomplete resected polyps.

**Conclusions:** CSP seems to be efficient and safe in removing colorectal polyps up to 15 mm. A hybrid snare seems to be particular advantageous for these polyps as it allows immediate conversion to HSP if CSP might fail in larger polyps.

#### **SESSION GASTROENTEROLOGY II**

## Microbial regulation of Math1 expression impedes Paneth cell depletion in germ-free Math1lox/lox VilCreERT2 mice

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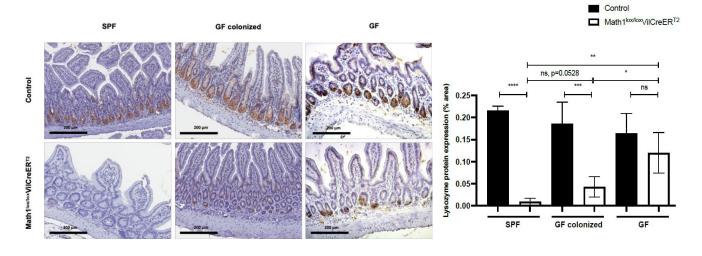
Background: Math1 (Atoh1) is a basic helix loop-helix transcription factor important for the cell fate determination and the role of secretory cells within the intestinal epithelium. We used Math1<sup>flox/flox</sup> VilCre<sup>ERT2</sup> mice to study the effects of depleting Paneth cells (PCs) which are members of intestinal innate immune system. Surprisingly, germ free mice failed to show the phenotype of intestinal-specific ablation of secretory cells such as PCs. Thus, we investigated the effects of intestinal microbiota in this mouse model.

**Methods:** Math1<sup>flox/flox</sup> VilCre<sup>ERT2</sup> and littermate controls were generated under different microbial colonization status as follows: specific pathogen

free (SPF), germ-free and ex-germ-free mice (co-housed with SPF mice for 8 weeks). All mice received three consecutive intraperitoneal injections of tamoxifen to induce the intestinal specific depletion of Math1. After 5 days of the last injection, the intestinal tissues were harvested. The expression of lysozyme and Ki67 were evaluated in the intestinal tissue by immunohistochemistry and quantified using a semiquantitative analysis with ImageJ software. The expression level of Math1 was evaluated by RT-qPCR.

Results: The expression of Math1 in the small intestine was reduced significantly at basal conditions in germ-free conditions as compared to SPF mice. The activation of Cre-lox system resulted in a complete depletion of Paneth cells in SPF mice, while in germ-free conditions, Paneth cells were not depleted (Figure 1). The expression of Ki67 was significantly diminished in the intestinal tissue of germ-free as compared to SPF conditions. Re-colonization of germ-free mice restored the gene expression levels of Math1 at basal conditions promoted by recovered intestinal cell proliferation leading to the Paneth cell depletion phenotype.

**Conclusion:** The absence of intestinal microbiota affects the expression of Math1 in addition to the cell renewal and turnover thereby leading to the loss-of-function of Cre-lox system in Math1<sup>flox/flox</sup> VilCre<sup>ERT2</sup> mice. Therefore, the inducible Math1<sup>flox/flox</sup> VilCre<sup>ERT2</sup> mouse model is not a suitable model to study the depletion of intestinal secretory cells in germ-free mice.



## Diagnostic delay in patients with eosinophilic esophagitis has not changed since first description 30 years ago

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**Background:** Eosinophilic esophagitis (EoE) is a progressive disease. Diagnostic delay (DD) is associated with increased risk of esophageal strictures and food impactions. We aimed to assess the evolution of DD since first description in 1993 until 2021.

**Methods:** We retrospectively analyzed patients included in the Swiss EoE Database. DD was calculated according to the interval between the period of first occurrence of EoE symptoms to confirmed diagnosis, according to established criteria. DD was analyzed annually over time (1989-2021) and focusing on milestone publications in the field. In addition, a cox proportional hazards model was used to describe the relation between diagnostic delay and covariates.

**Results:** Data of n = 1152 patients (male = 857, 74%; median age at diagnosis = 38 years, IQR: 28-49, range, 1-86) were analyzed. Overall, median DD was 4 years (IQR: 1-11, range, 0-56) with DD  $\geq$ 10 years in 32%. Over time, DD did not significantly change, neither annually, nor according to mile stone publications with a persistently stable fraction of roughly a third of all patients with a DD of  $\geq$ 10 years. Both, age at diagnosis and at symptom onset were significantly associated with DD.

Conclusions: DD in EoE has not changed since first description 30 years ago and remains substantial. Even today still about a third of patients has a persistently high DD of ≥10 years. Apparently, and especially with regards to the latter fraction of very long DD EoE patients, huge efforts are needed to increase awareness for EoE and to respect solid-food dysphagia as a red-flag symptom among health-care professionals and the general population in order to lower risks for long-term complications.

# Technical feasibility and clinical success of direct "free hand" EUS-guided gastroenterostomy in patients with gastric outlet obstruction

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**Goals:** This study evaluates the technical feasibility, procedure- associated complications and clinical outcome of direct "free hand" EUS-GE. Background Endoscopic ultrasound-guided gastroenterostomy (EUS-GE) with lumen-apposing metal stents (LAMS) appears to be a promising intervention in the management of gastroduodenal obstruction particularly for patients of surgical high-risk or in a palliative setting.

**Methods:** This retrospective bicenter study included patients who underwent direct EUS-GE (April 2017 to March 2021) investigating technical success (correctly placed LAMS), clinical outcome (successful oral nutrition) and management of procedure-associated complications.

**Results:** 45 patients (58% women/42% men; mean age 65 years) with malignant (n = 39), benign (n = 4) or unclear (n = 2) gastroduodenal obstruction underwent direct "free hand" EUS-GE. The technical success rate was 98% (44/45). 95% (42/44) showed reduced vomiting and the ability of oral food intake after the intervention. In one patient, a second EUS-GE was necessary to achieve sufficient clinical improvement. Procedure-associated complications were observed in 24% (11/45) of cases including stent misplacement (n = 7), leakage (n = 1), development of a gastrojejunocolic fistula (n = 1) and bleeding (n = 2), which could be all managed endoscopically.

**Conclusion**: Direct EUS-GE has a favorable risk-benefit-profile for patients with gastroduodenal obstruction, showing high technical success rates, manageable complications and rapid symptom relief.

#### Indefinite for Dysplasia Diagnosed in Barrett's Esophagus by Expert Pathologists is Associated with a High Risk for Progression to Neoplasia: A Retrospective Cohort Study

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**Background**: Patients with Barrett's esophagus (BE) receive intensified endoscopic surveillance and/or treatment based on the histological diagnosis of dysplasia. The risk of progression and therefore the management of BE patients diagnosed with indefinite for dysplasia (IND) remains controversial.

**Methods**: All BE patients diagnosed with IND between 2010 and 2020 were retrospectively identified using the St. Gallen BE cohort. Diagnosis of IND was reviewed by an expert pathologist. Rate of progression was calculated and logistic regression analysis was used to identify clinical and histological factors associated with risk of progression.

**Results**: 26 patients (median age 68 years (IQR 57-75) with a median BE length of C3M5 were diagnosed with IND. A total of 9/26 (34.6%) progressed to neoplasia within a median follow-up of 7 months (IQR 4-18), resulting in a detection rate of neoplasia of 4.2 per 100 patient-years. Neither positive p53 staining (OR 0.34 (95% CI 0.03-4.47, p = 0.424) nor BE length (OR 0.14 (95% CI -0.05-0.90, p = 0.506) were risk factors for progression

Conclusions: The rate of progression in BE patients with IND confirmed by expert pathologists was high and comparable to expert confirmed low-grade dysplasia. Objective markers are needed to discriminate patients at high-risk for progression justifying intensified endoscopic surveillance from the subgroup of low-risk patients amenable to prolonged surveillance intervals.

#### Autoimmune pancreatitis: the ongoing challenge in the Geneva experience

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**Background:** Two types of autoimmune pancreatitis are recognized (AIP-1 and AIP-2) and AIP-1 is considered to be an IgG4-related disease (IgG4-RD). Management of both rare diseases is challenging. We aimed to evaluate the clinical, radiological, biological and histological features along with the treatment outcomes of patient with AIP, and IgG4-RD.

**Methods:** Retrospective analysis (2010 to 2022) in a single, tertiary university center of patients with AIP and IgG4-RD.

Results: 11 patients with AIP were analyzed (81% of male, mean age of 65.8 years old) with a mean follow-up of 45.3 months. The most common symptom was abdominal pain (54.5%) followed by jaundice and weight loss in 36,3%. 27.25% of patients presented as a pancreatic manifestation of a systemic IgG4-RD. IgG4 levels were high in 81% of the patients and IgG4 infiltrations of the organ were noticed in 45.45% of them. Initial treatment with steroid was given to 10 patients, but relapse occurred in 7/10 patients with a mean follow-up period of 3.5 months requiring subsequent azathioprine. 3 required initiation of rituximab to reach remissions. Furthermore, 23 patients with IgG4-RD without AIP (39.1% male, mean age of 64 years old) were evaluated. Median IgG4 value in this group was low and median plasmablasts (CD27+ CD 38+) titer was 6200 cells/ml. 60.8% of patients were treated with steroid with a mean duration of treatment of 15 months and 26.1% of patients were treated by surgery. Relapsed after initial treatment occurred in 8/23 patients, and 4 patients had multiple relapse requiring additional rituximab treatment.

**Conclusion:** Management of patients with AIP and IgG4-RD remains challenging and requires better understanding of both diseases.

# Endoscopic submucosal dissection (ESD) in the esophagus: is it safe and effective in real life conditions? First results from a single center experience

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**Background:** Endoscopic submucosal dissection (ESD) is a curative treatment of superficial esophageal lesions. However, data regarding its efficacy in routine practice in Switzerland are scarce. We aimed to assess the feasibility, efficacy and potential morbidity of ESD in the esophagus for Barrett's esophagus (BE) and squamous cell carcinoma (SCC)-associated lesions

**Methods:** A retrospective study was conducted on patients treated by ESD for esophageal lesions between November 2014 and September 2021 at the University Hospital of Geneva (HUG). Endoscopic surveillance was carried out at 3 months under general anesthesia or sedation.

**Results:** A total of 18 patients (mean age 65 years, 33% men) were treated by ESD during the study period. No SAE were noted following-ESD (mean follow up: 10.25 months for SCC group and 32.6 months for BE group). The mean hospital stays were 1.2 and 1.6 days in BE and SCC patients, respectively. Lesions in the BE group (n = 13) measured 35 $\pm$ 13 mm versus 40 $\pm$ 18 mm in the SCC group (p = 0.25). En bloc resection rates were 92% and 100%. Histological R0 was confirmed in85% and 60% of specimen in the BE group and the SCC group, respectively.

**Conclusion:** ESD is a safe and effective technique to provide En bloc resections in the esophagus. Since SAE are rare, it should be considered as the first-line option for the histological evaluation and potential curative treatment of early (T1N0) esophageal lesions.

## Inflammation Status Reduces Cytochrome Expression in IBD and Colitis

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**Introduction**: The colonic immune system is exposed to xenobiotics and metabolites derived from the microbiome. The orphan cytochrome Cyp2s1 is mainly expressed in extrahepatic tissues with unknown functions in colitis.

**Methods**: We investigated Cyp2s1 expression under steady-state and inflammatory conditions in colitis models using RNA-sequencing (RNA-seq) and qPCR analysis.

Results: The consultation of the human protein atlas and tissue profiling in mice demonstrated that Cyp2s1 is highly expressed in intestinal tissues, including the colon, in humans and rodents. scRNA-seq revealed expression of Cyp2s1 by epithelial cells, including stem, enteroendocrine and goblet cells, except tuft cells. The highest Cyp2s1 expression among epithelial cells was observed in the mature colonocytes. Besides epithelial cells, bone marrow- derived macrophages as well express Cyp2s1. The Stimulation with the Toll-like receptor ligands LPS, CpG and Pam2CSK4, decreased Cyp2s1 in bone marrow-derived macrophages. The previously suggested Cyp2s1 substrates prostaglandin E2 and all-trans retinoic acid did not modulate Cyp2s1 expression in macrophages. Biopsies of patients with active Crohn's disease or ulcerative colitis revealed have reduced Cyp2s1 expression. Colitis induced by DSS, TNBS, or anti-CD40 injection reduced Cyp2s1 transcript levels, with the latter being higher in epithelial rather than lamina propria cells.

**Conclusion:** Murine colitis models and active inflammation in IBD decreased Cyp2s1 expression. Using a novel generated mouse model, we will further elucidate the impact of Cyp2s1 on colitis.

## Real life and predictive factors of endoscopic antroplyoromyotomy (GPOEM) in refractory gastroparesis

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**Background:** Refractory gastroparesis is a debilitating syndrome. Gastric peroral endoscopic myotomy (GPOEM) show a success rate up to 56% at 12 months follow-up in literature. This study wants to confirm the clinical and technical effectiveness and identify potential predictive factors.

**Methods**: 47 patients were included in a single tertiary centre. The first objective was to confirm the technical (47 patients analysed) and clinical success (37 patients followed) with a GCSI score. Clinical success is defined as at least a 50% reduction in GCSI during the follow-up. The second was to search predictive factors like: diabetes, surgery, previous specific drug therapy, Botox therapy and the time between first symptom and GPOEM.

Results: Technical success was 100%. Clinical success was 67.6%. The evolution of the GCSI score shows a reduction of symptoms over time, the median went from 2.8 to 0.5 at 12 months. The results do not show statistically significant predictor factors. In non-diabetic patients the clinical success rate was 70.8%, in diabetic patients 61.5%. In patients operated <12 months after the first symptom the clinical success rate was 76.2%, in those operated >12 months it was 62.5%. 81.3% of the patients without specific treatment had clinical success, in the group with specific treatment the response rate was 61.9%. 80% patients treated with Botox had clinical success, while in the group without Botox therapy 68.7% patients responded. No surgery appears to be a predictive factor.

**Conclusion**: GPOEM is a safe and very effective intervention. Although there are no statistically significant predictive factors, some factors seem to influence the outcome.

#### **SESSION HEPATOLOGY I**

#### A Genome-Wide CRISPR/Cas9 Screen Identifies a Role for Early Endosomes in Hepatitis E Virus RNA Replication

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Background and Aim: Hepatitis E virus (HEV) is believed to replicate its positive-strand RNA genome in a membrane-associated replication complex, composed of viral proteins (the so called replicase), replicating RNA, altered cellular membranes, and other host factors. However, current understanding of the host factors required for productive HEV infection is limited and the site as well as the composition of the HEV replication complex are elusive. Hence, our study aimed at identifying host factors required for HEV RNA replication.

**Methods:** A genome-wide CRISPR/Cas9 screen was performed in permissive human cell lines harboring newly developed subgenomic HEV replicons allowing for positive and negative selection, followed by next-generation sequencing and bioinformatic analyses. Candidates were validated by siRNA- mediated gene silencing and pharmacological inhibition in cells transfected with HEV replicons.

Results: The newly developed replicons and a library of 120,000 unique guide RNAs were employed in two separate screens, identifying 20 top host factor candidates. Validation yielded five host factors, including GBF1, which had been identified previously by a directed approach, and the Ras-related endosomal protein Rab5A. Colocalization studies revealed close proximity of Rab5A and the viral replicase. Knockdown of APPL-1 and EEA1, partners of Rab5A, significantly reduced HEV RNA replication while knockdown of Rab7A and Rab11A, markers of late and recycling endosomes, respectively, did not show any effect. Pharmacological inhibition of Rab5A and of dynamin 2, required for the formation of early endosomes, resulted in a dose-dependent decrease of HEV RNA replication. These observations point to a role of early endosomes in HEV RNA replication.

**Conclusion:** We exploited CRISPR/Cas9 and selectable subgenomic replicons to identify host factors of a noncytolytic virus. This approach identified a role for early endosomes in HEV RNA replication, likely by serving as a scaffold for the establishment of a functional replication complex. This work yields new insights into the HEV life cycle and the virus-host interactions required for productive infection.

## Recombinant Hepatitis E Viruses Harboring a Split Luciferase Tag in the ORF2 Protein

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Background and Aim: Hepatitis E virus (HEV) infection is the most common cause of acute viral hepatitis worldwide. The viral genome harbors three open reading frames (ORF). The ORF2 protein corresponds to the viral capsid. Molecular studies of the HEV life cycle have been hampered by the lack of robust and sensitive cell culture systems. Hence, the main receptor for HEV cell entry is still elusive and there are no specific antiviral drugs against HEV so far. Here, we aimed to develop a convenient, quantitative and potentially scalable reporter system for HEV infection and replication.

**Methods:** Transposon-mediated random insertion was exploited to identify functional insertion sites within the HEV ORF2 protein. Full-length viral genomes with in-frame insertions of a split luciferase (HiBiT) tag in the capsid protein were characterized by immunofluorescence and immunoblot analyses as well as functional assays. Luciferase activity was quantified by luminometry.

Results: Transposon-mediated random insertion and sequencing of viable genomes identified functional insertion sites in the HEV capsid protein. HEV harboring a HiBiT tag in C-terminal sites remained infectious and functional in terms of RNA replication and capsid secretion, allowing for antibody-free detection and quantitation of capsid protein by luciferase assay. Ribavirin and sofosbuvir inhibited the replication of tagged HEV in a dose-dependent manner. Neutralization experiments using specific monoclonal antibodies and convalescent sera are ongoing.

Conclusion: Identification of functional insertion sites enabled tagging of the HEV capsid protein with a highly sensitive and quantitative miniaturized luciferase reporter. Tagged HEV allowed for convenient read-out of infection and replication, with a potential for development of large-scale screening assays for entry inhibitors and other antiviral agents. In addition, the tagged HEV represent a valuable tool for studies aimed at identifying the receptor(s) for HEV cell entry.

# Canagliflozin and Non-Alcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus (CaNAFLD) – A Secondary Analysis of Two Randomized Controlled Trials

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**Background:** Non-alcoholic fatty liver disease (NAFLD) is highly prevalent among patients with type 2 diabetes (T2DM), however no approved pharmacological treatment exists. While sodium glucose cotransporter 2 inhibitors (SGLT2i) have shown to decrease glycemia, blood pressure, body weight, and albuminuria in patients with T2DM, data from large randomized clinical trials on liver-related outcomes are lacking

**Methods:** This is a secondary analysis of two randomized controlled cardiovascular and renal outcome trials: CANVAS (NCT01032629) and CANVAS-R (NCT01989754). Patients with T2DM and high cardiovascular risk were randomly assigned to receive canagliflozin or placebo and were followed for a duration of up to 6 years. The primary endpoint of this study was a composite of a reduction of alanine aminotransferase (ALT) levels more than 30% or ALT normalization (decrease <30IU/L). Secondary outcomes included achievement of weight reduction of 5% or 10%, and improvement of non-invasive fibrosis scores (NAFLD fibrosis score; FIB-4 score). Data were provided by Yale Open Data Access (Project ID 2020 4409).

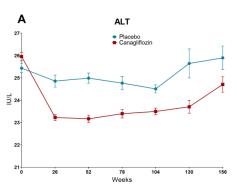
**Results:** We included 10'135 patients with T2DM. The majority of patients was male (64.2%) with a mean age of 61.8 years and a 13.5 years mean duration of diabetes. Of those, 2781 patients (27.4%) had elevated ALT levels (>30 IU/L) at baseline. These patients had a higher body weight (94.9kg vs. 88.4kg), elevated diastolic blood pressure (79.1mmHg vs. 77.2mmHg), higher glycemic indices and lipid parameters when compared to patients with normal ALT levels. The rate of the primary outcome was achieved in 39.6% of patients receiving canagliflozin compared to 30.2% with placebo, yielding an odds ratio (OR) of 1.51 (95% CI, 1.39–1.64; p <0.001). Treatment with canagliflozin was associated with lower NAFLD fibrosis and FIB-4 scores (p <0.001). Weight reduction of more than 10% was achieved in 80.5% of patients with canagliflozin compared to 4.2% with placebo (OR 3.41; 95% CI, 2.89–4.04; p <0.001).

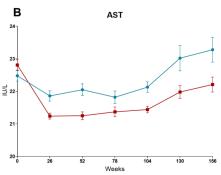
**Conclusion:** In two large randomized controlled trials involving patients with T2DM and risk of metabolic liver disease, treatment with canagliflozin resulted in a significant improvement of liver- related outcomes when compared to placebo.

Table 2 - Canagliflozin effects on liver-related Primary and Secondary outcomes

	Placebo (n=4'344)	Canagliflozin (n=5'791)	Univariate analysis, OR, regression coefficient (95% CI)	p value	Multivariate analysis, OR, regression coefficient (95% CI)	p value
Primary endpoint						
Improvement of ALT >30% or ALT normalization °	1'311 (30.18)	2'295 (39.63)	1.52 (1.40-1.65)	P < 0.001	1.51 (1.39-1.64)	P < 0.001
Secondary endpoints						
Improvement of ALT >30% b	1'027 (23.64)	1'933(33.38)	1.62 (1.48-1.77)	P < 0.001	1.61 (1.47-1.76)	P < 0.001
ALT normalization b	695 (64.59)	1'180 (77.17)	1.72 (1.47-2.01)	P < 0.001	1.74 (1.49-2.06)	P < 0.001
Weight reduction >5% 1	738 (16.99)	2365 (40.84)	3.37 (3.07-3.71)	P < 0.001	3.39 (3.08-3.73)	P < 0.001
Weight reduction >10%	181 (4.17)	747(80.50)	3.41 (2.88-4.03)	P < 0.001	3.41 (2.89-4.04)	P < 0.001
Normalization of Blood pressure <sup>b</sup>	185 (4.26)	327(5.65)	1.35(1.12-1.62)	0.002	1.41 (1.16-1.71)	0.001
Normalization of HbA1c <sup>b</sup>	966(39.08)	1969(60.45)	2.38(2.14-2.65)	P < 0.001	2.41 (2.16-2.68)	P < 0.001

Data are median (IQR) or n (%) unless otherwise stated and adjusted for age, gender, race, smoking status, hypertension, hypertipidaemia, congestive hear failure, diabetes mellitus (nephropathy & eletinopathy), coronary heart disease, peripheral artery disease, cerebrovascular incident, and renal insufficiency. \*\*
Becression confliction! \*\* Odde train.





#### Real-Life Effectiveness of DAA in Chronic Hepatitis C – the Swiss Experience

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**Background and Aim:** Directly acting antivirals (DAA) have revolutionized the management of chronic hepatitis C. We analyzed the Swiss experience with different DAA generations over time and investigated factors predictive of treatment failure.

Patients and Methods: This retrospective study, pursued within the framework of the Swiss Association for the Study of the Liver (SASL Study 44) and the Swiss Hepatitis C Cohort Study, included all patients treated with DAA between January 2015 and December 2019 in 8 Swiss tertiary referral centers.

**Results:** A total of 3088 patients were included of which 58% were male with a median age of 54 years. 24% had liver cirrhosis, of which 88% were compensated (Child-Pugh A). The overall SVR rate was 96% and increased over time. The rate of treatment failures dropped from 8.3% in 2015 to 2.5% in 2019. On multivariate analysis, female sex, caucasian origin, genotype (gt) 1 and the use of latest generation pangenotypic DAA were as-

sociated with SVR, while gt 3, the presence of active hepatocellular carcinoma (HCC) and increasing liver stiffness were associated with treatment failure. Importantly, the presence of HCC increased the risk of DAA failure by a factor of eight.

**Conclusions:** SVR rates increased over time, with highest success rates after the introduction of latest generation pangenotypic DAA. HCC and gt 3 were associated with DAA failure. Based on multivariate analysis, a predictive tool to stratify DAA failure risk, with a 85% discriminative power, will be proposed. In parallel, analyses of resistance-associated substitutions and rare subtypes are underway.

#### In vitro treatment of hepatocellular carcinoma organoids reveals additive rather than synergistic effects of doxorubicin and hypoxia

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**Introduction** Transarterial chemoembolization (TACE) is considered the first-line treatment for intermediate-stage HCC. About half the patients show an objective response. TACE combines the cytotoxic effect of chemotherapeutic agents such as doxorubicin with the ischemic effect of arterial embolization. The relative contribution of embolization and doxorubicin is poorly understood. It is also not known if the combination is synergistic or just additive. In the present work we made use of a large collection of HCC organoids (HCCO) to investigate molecular mechanisms of response and non-response to doxorubicin and to study if hypoxia enhances the efficacy of doxorubicin.

**Methods** We generated and cultured 20 HCCOs. Proliferation rates of HCCOs and their response to doxorubicin during a 6 day treatment period were assessed with CTG3D (Promega) under normoxic (20%O2) and hypoxic (1%O2) culture conditions. The effect of hypoxia and/or doxorubicin on the cell cycle of each HCCO was assessed by FACS analysis of Edu and Hoechst staining. All HCCOs were molecularly characterized by transcriptome and proteome analysis.

Results Sensitivity to doxorubicin varied by more than 50-fold between HCCO lines under normoxia and was not correlated with their proliferation rates. When cultured in hypoxic conditions, proliferation rate of HCCOs was reduced. Hypoxia did not increase doxorubicin sensitivity and even decreased sensitivity in some HCCO lines. Cell cycle analysis revealed that doxorubicin and hypoxia independently led to an increase in the percentage of cells in the subG1 and G2 phases and a decrease in the S phase. Analysis of transcriptome and proteome data with the aim to identify molecular mechanisms of response to doxorubicin is ongoing.

**Conclusion** Doxorubicin efficacy on HCCOs is not increased by hypoxia. The combination of doxorubicin and hypoxia is not synergistic, but rather additive. The clinically observed variability of response to TACE is reflected by the heterogeneous response of HCCOs to doxorubicin in vitro. HCCOs are promising models to elucidate tumor cell intrinsic properties that determine sensitivity to doxorubicin. Analysis of transcriptome and proteome profiles of the HCCOs can reveal potential predictive biomarkers of response to doxorubicin.

# Intrahepatic and extrahepatic congenital portosystemic shunts differ in clinical presentation and outcomes in children

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**Background:** Congenital portosystemic shunts (CPSS) are associated with severe systemic complications. However, it is both unclear which patients develop systemic complications and which shunts close spontaneously, consequently which patients require shunt closure. Therefore, we aimed to identify predictors of complications or spontaneous closure using data from 15/37 centers participating in the International Registry of Congenital Porto-Systemic Shunts (IRCPSS).

**Methods:** Restrospective data collection in compliance with local institutional ethics. Intrahepatic (IH) was defined as porto-hepatic and extrahepatic (EH) as a porto-systemic communication occurring either upstream of the portal vein or originating at the portal vein, or a persistent ductus venosus. Early symptoms included hypoglycemia and cholestasis, while liver nodules, cardiopulmonary complications and neurocognitive impairment were considered late symptoms. Cardiopulmonary symptoms were defined as high-output heart failure, hepatopulmonary syndrome of pulmonary hypertension. Neurocognitive deficits were defined as cognitive delay, seizures or other. The presence of any liver nodule in an otherwise healthy appearing liver on imaging was considered a positive finding. An early diagnosis occurred at < 2 years of age.

**Results:** 246 children were identified. 3 patients with both IH and EH were excluded from analysis. The main findings are summarized in Table 1. Symptoms: The presence of 1 or more symptom(s) increased with age at diagnosis reaching >80% beyond 2 years of age. Hypoglycemia or cholestasis were more frequent in patients with IH CPSS but not predictive of spontaneous closure (p = 0.038). Among patients with an early diagnosis, patients with IH shunts were more likely to experience spontaneous closure (p <.001). Patients with EH CPSS were more likely to have several symptoms than patients with IH CPSS. They were also more ikely to have liver nodules on imaging. Closure: 45% of IH CPSS and 5% of EH CPSS closed spontaneously. 35% of IH CPSS required endovascular or surgical closure of which nearly 40% for a preventive indication. 70% of patients with EH CPSS were closed through a procedure, of which 41% were preventive.

**Conclusion:** IH and EH shunts were equally frequent in this multicenter retrospective cohort of CPSS in children. IH CPSS diagnosed before the age of 2 years have a high likelihood of closing spontaneously. In older children, they CPSS be considered in the differential diagnosis of liver nodules, cardiopulmonary symptoms or neurocognitive deficits. CPSS are a cause of severe symptoms in children and should be sought in infants with hypoglycemia or cholestasis. Given the potential severity of complications, preventative closure should be considered, although timing and approach need further study, something which the IRCPSS aims to address.

Variable	IH%	EH"	p value
Diagnosis	n = 122	n = 120	<0.001
– prenatal	35	12	
– postnatal	65	88	
Ace at diagnosis (mo)	n = 79	n = 106	<0.001
– median (QI; Q3)	3 (1; 72)	36 (7; 102)	
Early diagnosis	79	47	<0.001
Incidental finding	73	41	<0.001
Symptoms	52	73	<0.001
– early	29	17	0.028
– late	30	70	<0.001
Closure (%)	81	74	
– spontaneous	47	4	p < 0.001
- surgery	11	33	
IR	20	26	
LT	1	7	

#### FIB-4 outperforms other serum non-invasive fibrosis tests in MAFLD

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**Background:** Metabolic associated fatty liver disease (MAFLD) is a recently proposed terminology to replace NAFLD. Non-invasive fibrosis tests (NITs) that are used to assess liver fibrosis are not yet validated in MAFLD patients. We therefore aimed to determine the diagnostic performance of NITs in MAFLD and whether the co-existence of alcohol abuse affects their performance.

**Methods:** We retrospectively included 409 MAFLD patients with liver biopsy and we stratified them by alcohol abuse (> 20/ 30 g/day in females/males) in: a) MAFLD-ALD and b) pure MAFLD. We calculated the following NITs: NFS, FIB-4, APRI and BARD, and assessed their diagnostic performance by ROC curve analysis.

**Results:** Among 409 patients, 277 (66.4%) had pure MAFLD and 132 (31.7%) had MAFLD-ALD. In pure MAFLD, the AUROCs of FIB-

4, NFS, APRI, and BARD for predicting advanced fibrosis ( $\geq$ F3) were 0.88, 0.74, 0.78 and 0.73, while for cirrhosis (F4) were 0.94, 0.82, 0.8 and 0.79, respectively. In pure MAFLD FIB-4 performed significantly better than the other NITs for the prediction of both  $\geq$  F3 and F4 (p <0.001). In MAFLD-ALD FIB-4 performed less well for the prediction of F4 compared to pure MAFLD (AUROC 0.83 vs 0.94, p = 0.005), while the other scores performed similarly.

**Conclusions:** FIB- 4 performs better than other serum non-invasive tests for the prediction of advanced fibrosis and cirrhosis in MAFLD patients, however its performance for the prediction of cirrhosis is reduced in the presence of alcohol abuse.

## A trajectomics approach to predict hospital admission in patients with Advanced Chronic Liver Disease

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**Background.** Patients with Advanced Chronic Liver Disease (ACLD) may develop complications characterized by high mortality rates and hospitalization costs if not early recognized and treated. It is therefore essential to identify signs and symptoms of complications as soon as possible. However, each patient may experience a different progression of the disease.

**Methods.** We developed a new methodology to longitudinally monitor patients with ACLD, with the final objective of identifying complications before their manifestation. This is achieved by recording several parameters using an Apple Watch, and by analyzing changes in these parameters

over time using artificial intelligence methods for trajectory analysis (trajectomics).

**Results.** Our methodology can continuously monitor heart rate, blood oxygen, heart rate variability, and physical activity. Moreover, it allows the execution of standardized examinations by the patients themselves such as single-lead ECG, and specifically developed assays for tremors, cognitive function (connect the numbers and tap speed tests), and quality of life.

We tested such a system on 8 healthy individuals and 3 patients with ACLD. Despite this initial number of subjects, our approach already identified distinct types of trajectories characterized by either the presence or absence of flapping tremor.

**Conclusion.** Our approach is now being used in a pilot study with patients with ACLD for extended periods of time. This will provide new insights on ACLD trajectory and the data necessary to develop patient-specific predictive models.

#### **SESSION HEPATOLOGY II**

# Enzymatic liver function assessment by <sup>13</sup>C-methacetin test before and after placement of a transjugular intrahepatic portosystemic shunt (TIPS): A prospective non-interventional pilot study

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**Background and Aims:** Transjugular intrahepatic portosystemic shunt (TIPS) placement can lead to severe complications such as hepatic encephalopathy or acute-on-chronic liver failure. Risk factors for the development of such post-TIPS complications are ill-defined. A point-of-care diagnostic <sup>13</sup>C-methacetin test for the determination of maximal liver function capacity (LiMAx\*) has been developed and validated by predicting adequately post-operative liver failure after liver resection (Stockmann M et al. J Hepatol 2012 & Annals of Surgery 2009). The aim of this prospective study is to evaluate the performance of LiMAx\* before and after TIPS placement and to ideally correlate pre-TIPS measurements to post-TIPS outcomes.

**Method:** Patients undergoing TIPS for refractory ascites, secondary prevention of variceal bleeding and/or for partial portal vein thrombosis on imaging with the danger of complete thrombosis were included. Patients undergoing TIPS placement were tested before (-1 day) and after (+1, +7, + 28, +72 and +180 days) the intervention for: LiMAx\*, hepatic encephalopathy (HE; critical flicker frequency, Stroop & connect the numbers test), laboratory (MELD score) as well as imaging of the TIPS flow by Doppler ultrasound. Patients with TIPS indication for acute bleeding (< 72h), presence of HCC, CHILD > 12, or overt HE or right heart failure were excluded.

**Results:** 15 patients (13 male / 2 female, mean age 63 (33-72 range) years) with a mean CHILD 7.8 (5-11) and MELD 9.0 (6-14) were included (TIPS indications: ascites n = 9, varices n = 3, portal vein thrombosis n = 3). Mean HVPG prior TIPS was 16 mmHg (4-30 mmHg).  $^{13}$ C-methacetin test showed a rapid, persistent and significant decline after TIPS placement (day 0: 255 ug/kg/h (range 61-753) vs. day 7: 157 ug/kg/h (43-559), p = 0.0024). This drop was paralleled by worsening of liver function assessed by MELD score (day 0: 9 (6-14) vs. day 7: 11 (8-16), p = 0.0019). LiMAx\* deterioration correlated with absolute porto-atrial pressure reduction by TIPS (day 0: 21 (12-31) vs. day 7: 9 (3-18) mmHg,  $R^2 = 0.35395$ , figure). In contrast, HE testing did not correlate with decrease in of LiMAx\*.

Conclusion: Our results indicate that the <sup>13</sup>C-methacetin (LiMAx\*) test is a sensitive method for capturing decrease in liver function after TIPS placement. LiMAx\* decrease correlates with absolute pressure reduction of

portal hypertension and is paralleled by increase in MELD score after TIPS placement. A larger study is needed to assess the value of LiMAx\* testing as predictor for post-TIPS complications.

## Clinical course of secondary sclerosing cholangitis as a sequel of severe COVID-19 – a cohort study

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**Background:** Bile duct injury leading to secondary sclerosing cholangitis (SSC) has been reported as a complication in critically ill patients with coronavirus disease 19 (COVID-19). Hence, we aimed to characterize risk factors, disease course and outcome in a larger cohort of patients developing SSC after severe Sars-CoV-2-Infection.

**Methods:** We conducted a retrospective multi-center cohort study of patients diagnosed with SSC following severe COVID- 19 from March 2020 to May 2022. Bile duct injury was identified by abnormal findings on magnetic resonance cholangiopancreatography (MRCP).

**Results:** In total, 25 patients (68% male, median age 60 y) treated at the ICU (median stay 56.5 d) were included. All but one patient required mechanical ventilation for a median period of 47.5 days. Alkaline phosphatase (AP) was first

documented >1.5 ULN after a median of 25 days, peak median values of AP were 1671.5 U/l and peak bilirubin levels 69 umol/l. Bile duct abnormalities were mostly intrahepatic. During follow up five patients died (20%) and nine patients were evaluated for liver transplantation (35%), four (16%) of which underwent successful liver transplantation.

**Conclusions:** SSC is a late complication of severe COVID-19 of significant morbidity, including the need for liver transplantation.

## Expansion of MDSC in the liver in a CCl<sub>4</sub> mouse model of cirrhosis

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**Background:** Previously, we identified immunosuppressive M- MDSC in the circulation of patients with cirrhosis and liver failure. These cells were accumulating in relation to disease severity and associated with impaired innate and adaptive immune responses, increased infection susceptibility and mortality. Impaired immune responses and expansion of M-MDSC were reversed by TLR3 agonism, i.e. poly(I:C) *in vitro*. In this project we aim to identify MDSC occurrence and distribution in murine models of chronic liver injury. Subsequently, the safety and efficacy of poly(I:C) administration will be explored *in vivo*.

**Methods:** C57BL/6C mice were administered CCl<sub>4</sub> (0.4ml/kg, i.p.) for 6 weeks. To mimic an acute insult, a group was treated with additional injection of LPS 24 hours prior to sacrifice. Poly(I:C) (1.6 mg/kg, i.p.) was administered 4 times over 7 days prior to sacrifice in the CCl<sub>4</sub>-alone model. Myeloid cells from both blood and livers were isolated and analysed via flow cytometry. Phenotyping identified PMN- & M-MDSC. Activation of T cell proliferation and cytokine responses will be assessed. Histopathological analysis of liver sections was done by H&E- and SiriusRed-staining. Plasma ALT, bilirubin and albumin were quantified.

**Results:** Both PMN- & M-MDSC expanded in the circulation and liver of  $CCl_4$  and  $CCl_4$ +LPS models compared to controls. Poly(I:C) administration did not reduce the number of MDSC in a  $CCl_4$  model. Plasma markers for liver damage and function were unvaried following poly(I:C) administration compared to  $CCl_4$  alone, underlining its safety as a potential immunomodulatory therapy.

**Conclusions:** We identified MDSC in the circulation and liver in two models of chronic liver injury. Next, we aim to assess varying dosages and administration schedules of poly(I:C) to investigate its potential to reduce MDSC expansion and restore immune homeostasis.

#### Diagnostic performance of two-dimensional shear wave elastography and transient elastography compared to liver histology for staging liver fibrosis in patients with chronic liver diseases

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**Background:** Staging of liver fibrosis traditionally relied on liver biopsy, however transient elastography (TE) and two- dimensional shear wave elastography (2D-SWE) evolved to major non-invasive alternatives. Therefore, we aimed to determine the diagnostic accuracy of 2D-SWE assessed by the recently developed Canon Aplio i800 ultrasound system using liver biopsy as reference and compare the accuracy to TE.

**Methods:** 108 patients with chronic liver disease receiving liver biopsy, 2D-SWE and TE at the University Hospital Zurich were prospectively included. Diagnostic accuracies were assessed by area under the receiver operating characteristic (AUROC) analysis and optimal cutoff values by Youden's index.

Results: 2D-SWE exhibited a good diagnostic accuracy for determining significant (≥F2; AUROC 85.2%, 95% confidence interval (95% CI): 76.2-91.2%) as well as severe fibrosis (≥F3; AUROC 86.8%, 95% CI: 78.1-92.4%) and was excellent for cirrhosis (AUROC 95.6%, 95% CI: 89.9-98.1%), as compared to liver histology. TE performed equally well with no statistically difference of diagnostic accuracy compared to 2D-SWE. The optimal 2D-SWE cutoff values were 6.5, 9.8 and 13.1 kPa for significant fibrosis, severe fibrosis, and cirrhosis, respectively.

**Conclusions:** The diagnostic accuracy of 2D-SWE was good to excellent for staging liver fibrosis with histopathology as reference standard and was well comparable with TE.

#### Mixed-reality technology for ultrasound-guided biopsies and ablations of liver tumors: Proof of concept using HoloLens as head-mounted display during liver interventions

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**Background and Aims:** Improving visualization is an important component of facilitating a safe procedure during hepatological interventions. In this context, we have explored whether addition of a mixed-reality headmounted display is feasible and useful in interventions such as liver biopsy, biopsy of focal liver lesions and procedures such as ultrasound-guided ablation of liver tumors.

**Methods:** A latest generation mixed-reality device was used as a head-mounted display for projection of the imagery from the connected conventional ultrasound screen in front of the physician's visual field (HoloLens 2 (Microsoft\*) in combination with SonoEyes\* (Incremed).

**Results:** This novel imaging technique was used in the clinical setting of biopsies (liver, focal liver lesions) as well as hepatic interventions such as US-guided microwave ablations of liver tumors (figure) and drainage of liver abscesses (3 hepatologists/1 interventional radiologist, 12/2021



through 03/2022, single center, 400+ biopsies, 50+ ablations annually). To increase visibility of liver lesions (i.e. HCC) contrast- enhanced ultrasound imaging was used if needed. Use of this mixed-reality technology was immediate and self-explanatory. Addition of a head-mounted display for the procedures allowed reduced movements of the operating physicians and led to increased focus on the intervention since the examiner remained *in situ* while having the patient, the operating field and the needle in one visual field.

**Conclusions:** This pilot study showed that using mixed-reality technology in ultrasound-guided liver interventions is feasible, easy to apply and associated with advantages such reduced movement during interventions, improved ergonomic position of the physician, improved focus on the intervention and most probably lower risk of contamination of the sterile field

## Etiologies and outcome of acute liver failure listed for liver transplantation in Switzerland

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**Background and Aim:** Acute liver failure is associated with high mortality, unless patients receive urgent liver transplantation. The etiologies of liver injury vary from country to country and data are lacking for Switzerland. The study analysed the underlying causes in patients listed for urgent liver transplantation in Switzerland from May 2008 to December 2020.

Patients and Methods: Retrospective cohort study of patients with acute liver failure listed for urgent transplantation in Switzerland, excluding those listed due to primary graft nonfunction. Data were collected from the Swiss Organg Allocation System (SOAS), the Swiss Transplant cohort study (STCS) as well as review of patient charts. Analysis included anthropomorphic data, etiology of liver injury, liver and kidney function parameters, use of organ replacement therapy at time of listing, transplantation or withdrawal from the waiting list.

**Results:** A total of 64 patients listed for urgent transplantation could be analyzed. Only 2 were not transplanted due to spontaneous recovery. No deaths occurred on the waiting list. Time to listing as well as waiting-time were on average very short (median 5d and 1d). Patients were predominantely female, mean age was 48 years. Leading etiology was non-acetaminophen DILI. Vasopressors, mechanical ventilation and dialysis at time of listing were reported in 28.1%, 21.9% and 25%. 1- and 5-year survival was 86%. There were no differences in baseline characteristics or post transplant survival between different etiologies.

**Conclusions:** Non-acetaminophen DILI is the most frequent indication for urgent liver transplantation in Switzerland. Overall patients survival is excellent.

# Mortality and morbidity related to the Hepatitis C Virus: a propensity score matching analysis using routinely collected data from a large, tertiary hospital in Switzerland

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**Background:** The WHO aims to reduce HCV mortality by 65% until 2030, but mortality estimates are difficult to obtain.

**Methods:** health records analysis applying electronic phenotyping strategies on routinely collected data from patients hospitalized at a tertiary referral hospital in Switzerland between 2009 and 2017. Controls selection using propensity score methods (matching by age, sex, intravenous drug use, alcohol abuse, and HIV co-infection).Outcomes: in-hospital mortality, attributable mortality, ICU admission, and length of stay.

Results: The non-matched dataset included records from 165972 individuals (287255 hospital stays). Applying electronic phenotyping strategies (i.e. searching by ICD-10 codes, HCV- specific prescriptions and laboratory data) resulted in the identification of 1677 individuals with evidence of HCV infection (2285 stays). After matching, the final dataset corresponded to 6855 hospital stays (2285 with evidence of HCV, 4570 controls). In-hospital mortality was higher in HCV cases (RR 2.10, 95% CI 1.64 to 2.70) despite matching and additional adjustment for confounders. Among those infected, 52.5% of the deaths were attributable to HCV (95% CI 38.9 to 63.1). HCV cases had a higher risk of ICU admission (RR 1.49, 95% CI 1.34 to 1.66) and 38% longer hospital stays.

**Conclusion:** In this study, HCV infection was strongly associated with increased morbidity and mortality. Our findings may be used to monitor the efforts made to meet the WHO elimination targets, and underline the importance of electronic cohorts as a basis for national longitudinal surveillance.

## The Swiss Primary Biliary Cholangitis Cohort Study: Report on the first five years 2017–2021

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**Background:** The Swiss Primary Biliary Cholangitis (PBC) cohort study was initiated in 2017, designed to collect high-quality data and sequential biosamples from PBC patients.

**Methods:** Inclusion criteria: subjects diagnosed with PBC or with isolated positive PBC-specific autoantibodies, aged at least 18 years and living in Switzerland are eligible. Clinical data and biosamples were collected at the time of diagnosis, at inclusion (if > 12 months after diagnosis), and at yearly follow-up visits

**Results**: 332 included by 31.12.2021, 281 female, 56% diagnosed at age 40-59 years, 32% diagnosed aged > 59 years, 12% diagnosed < 40 years. 202 (61%) were diagnosed before initiation of the study. BMI at diagnosis: 48% normal, 28% overweight, 20% obese. 51 had concomitant autoimmune hepatitis. 81% anti-mitochondrial antibody positive at diagnosis. 47% had a liver biopsy at diagnosis. 10% had liver stiffness > 15 kPa at diagnosis. 91 had concomitant extrahepatic autoimmune diseases. 277 (83%) are treated by ursodeoxycholic acid (UDCA), 38 (11%) by fibrates (of whom 37 with UDCA), and 11 (3.3%) have been exposed to obeticholic acid, of whom only one was still on this drug at 31.12.2021. Nine underwent liver transplantation

**Conclusions:** This study provides the first description of the PBC population in Switzerland.

#### **SESSION LARGIADÈR**

# Comparison of surgical outcomes in elective sigmoid resection for diverticulitis in different indication-specific strategies

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**Background:** Comparing different surgical guidelines for recurrent uncomplicated diverticulitis, a careful benefit-risk assessment is recommended. The purpose of this study was to evaluate the impact of indications-specific strategies on surgical outcomes allowing adequate benefit-risk consulting.

**Methods:** All patients undergoing elective colonic resection for diverticulitis between 2011 and 2020 in our institution were included. They were divided into two groups based on the strategy for surgical indication: relative surgery indication group (RSI; CDD (classification of diverticula disease) Type IIa, IIIa and IIIb, n=585) and absolute surgery indication group (ASI; CDD Type IIb and IIIc, n=318). Propensity score-matching (PSM) was applied at a ratio of 1:1 to compare the RSI and the ASI group.

Results: In the univariate analysis, RSI patients were younger (62 vs. 68, p <0.05), had a higher physical status (ASA score 1 or 2 in 80% vs. 61%, p <0.05), were less immunosuppressed (3% vs. 7%, p <0.05) and suffered less from coronary heart disease (4% vs. 7%, p <0.05). After PSM, 318 vs. 318 patients were selected and baseline characteristics resulted comparable. The conversion rate to open surgery for laparoscopic resection was 5.0% in RSI and 13.8% in ASI (p <0.05). Intraoperative complications were rare in both groups (3.1% vs. 5.3%, p = 0.24). Mean operation time was shorter in RSI (211 vs. 229, p <0.05). Major morbidity (Clavien/Dindo ≥3b) occurred less frequently in RSI (3.8% vs. 10%, p <0.05). Anastomotic leaks occurred in 0.9% in RSI and in 2.5% in ASI (p = 0.22). A defunctioning stoma was received by 0.9% in RSI and 10.7% in ASI (p <0.05).

**Conclusions:** These data should be considered when counselling patients with an equivocal indication for surgery for diverticular disease.

# Shorter residual IMA stump length on objective CT measurement is associated with improved oncological outcomes in rectal cancer surgery: a propensity score matched analysis.

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**Background** Studies have suggested little oncological benefit to 'high-tie' resection of the inferior mesenteric artery pedicle in rectal cancer surgery but have been based on subjective surgical intent rather than objective, quantifiable measurements. In this study we aimed to assess the level of transection objectively and investigate its influence on long-term oncological outcomes.

Methods All patients undergoing elective resection for rectal cancer with curative intent between 2012 and 2020 in a tertiary referral centre were included. IMA stump length was measured on post-operative CT scan and patients categorized as having undergone "high-tie" (left colic artery absent and stump <40 mm) resection or "low-tie" (left colic artery preserved or IMA stump >40 mm) resection. Propensity score matching was undertaken to produce comparable groups using multivariable regression modelling pre- and post-matching. Principle outcome parameters were overall survival and local recurrence free survival assessed by log-rank testing.

**Results** 450 patients (mean 65.3 years, 33% female) were analysed. Mean (SD) IMA stump length was 19 (10) mm in the high-tie group and 45 (15)

mm in the low-tie group respectively. After propensity score matching, two groups of 136 patients were compared. Multivariable survival analysis showed a significantly better overall (HR 1.85 [1.15- 2.99], p = 0.012) and local recurrence free (HR 3.96 [1.44-10.86], p = 0.007) survival for patients in the high-tie group.

**Conclusions** In contrast to other studies, our study has used objective measurements to show an association between central IMA transection and improved oncological outcomes. This association is preserved on multivariable analysis and propensity score matching.

## Novel Benchmark Values for Redo Liver Transplantation. Does the outcome justify the effort?

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**Background:** In the era of organ shortage, redo liver transplan- tation (redo-LT) is frequently discussed in terms of expected poor outcome and wasteful resources. However, there is a lack of benchmark data to reliably evaluate outcomes after redo-LT. The aim of this study was to define benchmark cutoffs for redo-LT.

Methods: We collected data on redo-LT between January 2010 and December 2018 from 22 high-volume transplant centers. Benchmark cases were defined as recipients with MELD score ≤25, absence of portal vein thrombosis, no mechanical ventilation at the time of surgery, receiving a graft from a donor after brain death. Also, high-urgent priority and early redo-LT including those for primary non-function (PNF) or hepatic artery thrombosis were excluded. Benchmark cutoffs were derived from the 75<sup>th</sup> percentile of the medians of all benchmark centers.

**Results:** Out of 1110 redo-LT, 373 (34%) cases qualified as benchmark cases. Among these cases, the rate of postoperative complications until discharge was 76%, and increased up to 87% at 1- year, respectively. One-year overall survival rate was excellent with 90%. Benchmark cutoffs included Comprehensive Complication Index (CCI®) at 1-year of  $\leq$ 72, and inhospital and 1-year mortality rates of  $\leq$ 13% and  $\leq$ 15%, respectively. In contrast, patients who received a redo-LT for PNF showed worse outcomes with some values dramatically outside the redo-LT benchmarks.

**Conclusion:** This study shows that redo-LT achieves good out- come when looking at benchmark scenarios. However, this figure changes in high-risk redo-LT, as for example in PNF. This major analysis objectifies for the first-time results and efforts for redo- LT and can serve as a basis for discussion about the use of scarce resources.

# Long-term outcomes of ruptured hepatocellular carcinoma: an international multicentric propensity scorematched study

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**Introduction** Long-term outcomes of patients with ruptured hepatocellular carcinoma (rHCC) remain scant. This study aimed to assess diseasefree survival (DFS) and overall survival (OS) after surgical resection of rHCC compared to non-ruptured HCC (nrHCC).

**Methods** Patients with rHCC and nrHCC were collected from 8 centers in Europe, Asia, and North America. Resected rHCC patients were matched 1:1 to patients undergoing surgery for nrHCC using propensity score and

nearest-neighbor method (matching criteria: age, tumor size, cirrhosis, Child-Pugh score, BCLC stage, resection status, grade, and microvascular invasion). Survival rates were calculated using Kaplan-Meier method.

Results A total of 2033 patients were included: 226 rHCC patients (172 operated: 68 with upfront surgery and 104 after embolization) and 1807 nrHCC patients. Median DFS and OS of rHCC patients (all treatments confounded) were 10 (95% CI 7-13) and 22 months (95% CI 13-31). Prognostic factors for worse OS among rHCC patients were absence of preoperative arterial embolization (HR 2.3, 95% CI 1.2-4.6, p = 0.016), cirrhosis Child B/C (HR 2.4, 95% CI 1.1-5.4, p = 0.040), and R1/R2 margins (HR 2, 95% CI 1-5, p = 0.049). Survivals were similar between Western and Eastern rHCC patients. After propensity score matching, 106 rHCC patients and 106 nrHCC patients displayed similar characteristics. Patients with rHCC had shorter median DFS (12, 95% CI 7-17 vs. 22 months, 95% CI 12-32, p = 0.011), but similar median OS compared to nrHCC patients (43, 95% CI 21-65 vs. 63 months, 95% CI 21-105, p = 0.060).

**Conclusion** In this large dataset including Eastern and Western patients, rHCC was associated with shorter DFS compared to nrHCC, while OS was similar.

#### Prospective data analysis of 1307 ventral hernia patients: Emergency hernia repair and smoking predict recurrence

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**Purpose:** Ventral hernias are frequent and hernia repair is regularly performed by general surgeons. Emergency repair is less frequent and can be challenging. Long term data comparing outcomes of emergency- vs. elective ventral hernia repair are scarce.

**Methods:** Consecutive patients undergoing emergency and elective ventral hernia repair at our institution were prospectively entered in our HerniaMed database between August 2013 and February 2020. Patients were contacted after one-, five- and ten years to assess long-term complications. Risk factors for emergency repair and hernia recurrence were assessed by univariate and multivariate analysis.

**Results:** We included 1307 patients. Emergency and elective hernia repair were performed in 11% and 89% of patients with one- year follow-op rates of 94% and 92%. Female gender, BMI >40 kg/m², ASA class 3 and 4, large size umbilical herniation (>4 cm) and epigastric herniation were more frequent in emergency hernia repair. Binary logistic regression analysis identified emergency repair and smoking as predictors of recurrence (Odds ratio: 4.04 and 95% confidence interval: 1.67–14.21, p = 0.004; Odds ratio:

2.94 and 95% confidence interval: 1.33–9.15, p = 0.011). Furthermore, female gender and significant comorbidity (ASA class 3 and 4) were risk factors for emergency repair (Odds ratio: 1.98 and 95% confidence interval: 01.05 – 3.74, p = 0.034; Odds ratio: 3.54 and 95% confidence interval: 1.79 – 6.98, p < 0.001).

**Conclusion:** Emergency repair and smoking predicted hernia recurrence. Females and highly comorbid patients are at increased risk for emergency repair and should be prioritized for early elective hernia repair.

## How can we reduce the use of antibiotics in acute uncomplicated diverticulitis – a multifactorial intervention

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**Objective:** Current evidence suggests that uncomplicated acute diverticulitis of the colon may be a self-limiting condition that can be managed without antibiotics. With the support of a multidisciplinary team, we developed an intervention to reduce the use of antibiotics for patients with left-sided uncomplicated diverticulitis.

**Methods:** The multifactorial intervention consisted of a clinical pathway with predefined criteria to select patients suitable for treatment without antibiotics, an educational intervention for both clinicians and patients, and regular auditing and feedback to clinicians in case of non-adherence to the pathway. Patients were recruited from May 2021 to April 2022.

**Results:** Adherence to the clinical pathway was 68%. 17 out of 83 patients (20.5%) with acute uncomplicated diverticulitis were successfully treated without antibiotics. None of them received antibiotics as rescue therapy. The complication rate was higher in the group with antibiotics (6% vs. 0%).

**Conclusion:** Treatment of uncomplicated diverticulitis without antibiotics can successfully be offered to a selected group of patients without a higher risk of complications. Further efforts are needed in order to overcome existing barriers to rational antimicrobial use and to risk-stratify patients with uncomplicated diverticulitis to tailor treatment.

# Coffee Is More Than Just Caffeine – Effect of Caffeine on Time to First Bowel Movement after Elective Laparoscopic Colectomy: A Randomized Clinical Trial (CaCo Trial)

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**Background**: Postoperative caffeine consumption appears to be a promising strategy to prevent postoperative bowel paralysis. The aim of this study was to assess whether postoperative oral caffeine intake shortens bowel hypomotility after elective laparoscopic col- orectal surgery.

Methods: This was a single-center, randomized, double-blinded, placebo-controlled superiority trial conducted from October 2015 to August 2020. Patients aged ≥18 years undergoing elective laparoscopic colectomy were included and assigned ran-domly to receive 3x daily either 100 mg caffeine or 200 mg caffeine or 250 mg corn starch (placebo) after the procedure. The primary endpoint was time to first bowel movement. Secondary endpoints included colonic transit time, time to tolerance of solid food, length of hospital stay and perioperative morbidity.

**Results:** 60 patients were randomly assigned to either the caffeine 200 mg group (n = 20), the caffeine 100 mg group (n = 20) or the placebo group (n = 20). 27 patients were included in the per-protocol-analysis. Baseline char- acteristics were similarly distributed among the groups. In the intention-to-treat-analysis, the time to first bowel movement was 67.9h (SD 19.2) in the caffeine 200 mg group, 68.2 h (SD 32.2) in the caffeine 100 mg group and 67.3 h (SD 22.7) in the placebo group (p = 0.887). The per-protocol-analysis and measurement of colonic transit time confirmed the lack of efficacy. No deaths or serious ad- verse events related to the trial were observed during the study.

**Conclusions:** Although caffeine intake during the first days after elective laparoscopic colorectal surgery is safe, in the present in- vestigation, its administration was not associated with a reduced time to first bowel movement.

## Prevention and management of anastomotic leakage after colorectal surgery: a Swiss national consensus

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**Background:** Anastomotic leakage (AL) is one of the most feared complications of colorectal surgery. Guidance on its prevention and management is lacking. The aim of the study was to achieve a Swiss nationwide consensus on AL management.

Methods: A three-step Delphi consensus meeting was performed in 2020 involving 78 Swiss surgeons from 40 centers. Consensus was defined as ≥70% of agreement.

Results: Consensus was reached on routine use of preoperative nutritional screening (100%) using nutritional scores (88%) and >10% weight loss (95%). Consensus was reached for no bowel preparation (BP) prior to right colectomy (RC) (76%) and for mechanical BP with oral antibiotics prior rectal resections (RR) (70%). No consensus was found on BP prior left colectomy (LC). Respondents favored a side-to-side anastomosis (76%) after RC, without consensus on the anastomosis being stapled or hand-sewn; an end-to-end (73%), stapled (80%) anastomosis after LC and a stapled anastomosis (86%) after AR irrespective of the anastomosis configuration. Anastomotic control with transanal leak-test was supported by 92%. After TME, routine diversion was favored (73%), irrespective of neoadjuvant therapy (94%) or not (70%). Consensus was reached on routine postoperative CRP monitoring (94%).

**Conclusions:** Consensus was reached on several clinical aspects providing national guidance. Further data is required on intraoperative anastomosis aspects to ensure broader consensus.

## Meta-analysis of randomized controlled trials comparing minimal-Invasive versus open pancreatic surgery

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**Objective:** To compare perioperative outcomes of minimal- invasive pancreatic surgery (MIPS) to open pancreatic surgery (OPS) using data obtained from randomised controlled trials (RCTs).

**Methods:** Literature search was done in CENTRAL, Medline and Web of Science; all currently available RCTs comparing MIPS and OPS in adult patients requiring elective distal pancreatectomy (DP) or partial pancreatoduodenectomy (PD) were included in the analysis. Outcomes were mortality, general and pancreatic surgery specific morbidity and length of hospital stay (LOS).

**Results:** A total of 166 patients for DP (80 MIPS vs. 86 OPS) in two RCTs and 856 for PD (429 MIPS vs. 427 OPS) in five RCTs were analysed. Meta-analysis showed a reduction of LOS by 1.2 days (-2 to -0.3, p <0.01) and intraoperative blood loss by 143 ml (-186 to -101, p <0.01) in MIPS. In the subgroup analysis reduction of LOS was only present for minimal-invasive DP (-2 days, -2.3 to -1.7, p <0.01). A minimal-invasive approach showed reduction of surgical site infections (odds ratio 0.4, 0.1 to 0.96, p = 0.04) and intraoperative blood loss (-141 ml, -181 to -101, p <0.01) only in PD. Duration of surgery was about 96 min longer in minimal-invasive PD (56 to 137 min, p <0.01), but not in DP. Certainty of evidence according to the GRADE approach was moderate to low.

**Conclusions:** This meta-analysis of level 1 evidence shows reduced LOS and intraoperative blood loss in MIPS compared to OPS. Morbidity and mortality did not differ between MIPS and OPS. Patients undergoing minimal-invasive PD seem to benefit from lower surgical site infections and less intraoperative blood loss.

#### **POSTER GASTROENTERLOGY**

## Natural history of patients lost to follow-up after esophageal food impaction

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**Background:** Esophageal food impaction (EFI) is a gastrointestinal emergency with an increasing incidence. As EFI may be the first manifestation of eosinophilic esophagitis (EoE), correct diagnosis with adequate follow-up is important.

**Methods:** We retrospectively identified 125 patients treated for EFI between 2015 and 2021. 25 (20%) were lost to follow-up. For these, real-world-data via a retrospective chart review as well as a prospective telephone consultation and follow-up upper endoscopies (whenever possible) were gathered.

Results: 19 (76%) patients were successfully contacted (median follow-up = 58 months). 53% of patients reported persisting dysphagia and 58% restrictive eating behavior. 16% had one further EFI each. 7 patients (37%) had a follow-up endoscopy, resulting in the diagnosis of EoE and the initiation of a specific therapy in 5 (71%). After a review of all available information, 7 (28%) were diagnosed with EoE and 1 (4%) with lymphocytic esophagitis. In 5 (20%) EoE was clinically and endoscopically suspected, but did not fulfill all diagnostic criteria (missing biopsies). 10 (40%) patients were found to have gastro-esophageal reflux disease and in 2 (8%) no diagnosis was established. Reasons for no follow-up were most often patient-dependent.

**Conclusion:** More than half of patients have ongoing esophageal symptoms after EFI, but only the minority will have further EFIs. However, follow-up will result in a diagnosis of EoE in the majority of patients. Considering that EoE is a chronic and progressive disease, almost inevitably leading to fibrotic structuring of the esophagus, this has therapeutic consequences. Thus, actively scheduled follow-up after EFI is essential and of critical importance.

## Endoscopic treatment of post-surgical esophageal fistulas, retrospective analysis of a single tertiary center cohort

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**Background:** Anastomotic fistulas are a frequent and dreaded complication of esophagectomy. Endoscopic therapy using different techniques is now a well-established first line treatment option. The aim of our study was to evaluate the efficacy of such endoscopic treatments.

**Methods:** 73 patients with post-operative esophageal fistulas were retrospectively analyzed after being treated with different endoscopic techniques at CHUV. The primary endpoint was to evaluate technical and clinical efficacy of endoscopic treatments. The secondary endpoint was to evaluate the endoscopic treatments-related complications.

**Results:** In 94.5% (n = 69) of patients, the intervention was effectively carried out from a technical point of view. In 82.2% (n = 60) of patients, treatment led to successful complete closure of the fistula. Minor complications related to the procedure occurred in 21.9% (n = 16) of patients and major complications in 6.8% (n = 5). The mortality rate related to the procedure was 2.7% (n = 2).

**Conclusions:** Endoscopic treatment is a technically achievable, highly effective way of treating post-operative esophageal fistulas. It allows patients with high risk of rapid deterioration to safely recover from their condition, avoiding severe and fatal complications without having to resort to invasive surgical solutions.

## Aufbau eines Endoskopie-Zentrums in Nepal – Fortschrittsbericht nach 10 Jahren

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Hintergrund: Nepal ist eines der ärmsten Länder der Erde. Die medizinische Versorgung der Bevölkerung ist katastrophal. Im Jahr 2010 gründeten wir die Nepal-Gruppe (GFNG) der Gastrofoundation e.V. (www.gastro-foundation.org) mit dem Ziel, im Dhulikhel Hospital bei Kathmandu ein endoskopisches Trainingszentrum (ETC) aufzubauen und nachhaltig zu fördern. Die Nepal-Gruppe (GFNG) besteht derzeit aus 13 Gastroenterologen und einem Gastro-Pathologen.

Methoden (2010-2022): 1. Aufbau einer modernen und funktional gut organisierten Endoskopie-Abteilung durch Versorgung mit Endoskopen (Gastroskope, Koloskope, Duodenoskope, EUS), endoskopischem Zubehör, SpyGlass- Cholangioskopen, EHL, Mobiliar, Röntgen-C-Bögen, Ultraschall-Geräten, EDV-Installation. 2. Ausbildung und Training von Ärzten und Assistenzpersonal des ETC in Nepal (50 Einsätze von Mitgliedern der GFNG) und in der Schweiz/Deutschland. 3. Akademische Hilfe durch gemeinsame Entwicklung und Implementierung von Ausbildungsplänen, Hygieneplänen sowie Covid-Schutzmaßnahmen und Covid- Therapieplänen.4. Ausbildung von mehreren Hundert Ärztinnen und Ärzten aus ganz Nepal bei bisher zwölf Hands-on-Workshops für Endoskopie, Ultraschall und Gastro-Pathologie vor Ort. Wegen der Corona-Pandemie wurde im November 2021 ein Kurs online durchgeführt. 5. Fundraising der GFNG für das ETC 2010-2022: ca. 1.000.000 SFr (80% als Sach- und 20% als Geldspenden), zusätzlich Erdbeben-Sammlung der GFNG 2015 mit einer Spendensumme von ca. SFr 500.000.

**Ergebnisse:** Das ETC ist das landesweit anerkannte Referenz-Zentrum für moderne diagnostische und interventionelle Endoskopie. Aus allen Distrikten von Nepal werden Patienten zur Behandlung eingewiesen. Die Zahl der therapeutischen ERCPs ist inzwischen auf über 1.400 Eingriffe pro Jahr gestiegen (2010-2022 über 7.000 ERCPs). In der ETC-Gastro-Ambulanz wurden 2019 m13.000 Patienten ambulant betreut.

**Zusammenfassung:** Der Aufbau des endoskopischen Trainingszentrums ETC ist erfolgreich und und nachhaltig. Voraussetzungen waren und sind das über Jahre anhaltende Engagement des GFNG-Teams, die großzügige Unterstützung durch zahlreiche Firmen und Spendern und vor allem die ständige vertrauensvolle Zusammenarbeit mit dem ETC-Team im Dhulikhel Hospital.

## Complete efficient endoscopic reduction of a gastric volvulus: a case report

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**Background** Gastric volvulus is a rare condition consisting of a rotation of rotation of a stomach with possible serious clinical outcomes [1]. There are only few cases of gastric volvulus with successful endoscopic reduction reported [2, 3, 4].

**Results:** We present a case of a 54 years old female patient presenting with sudden abdominal pain and vomiting. The abdominal CT- scan performed showed a voluminous type 2 hiatal hernia with cardia malposition and features of possible gastric volvulus. An urgent upper GI endoscopy was performed to evaluate the mucosa and rule out ischemia and necrosis. During the procedure, the mucosa of esophagus and stomach appeared normal. The pylorus was not primarily visualized therefore a catheter was passed through the operative channel into the hernia collar. The hiatal hernia could only be visualized with the means of X-ray. A stiff guide wire was then positioned into the hiatal hernia. The endoscope was then

gently pushed on the guide wire under endoscopic and radiological guidance into the excluded gastric part. This maneuver allowed a complete immediate reduction of the gastric volvulus. An elective fundoplication by robotic surgery was performed 7 days after endoscopy and the patient was discharged 3 days after surgery.

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- 4 Kulkarni K, Nagler J. Emergency endoscopic reduction of a gastric volvulus. Endoscopy 2007; 39(S01): 173 -173. doi:10.1055/s-2007-966584.

# Polymicrobial infection of the spine and central nervous system due to a fistula between the rectosigmoid and lumbosacral joint

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**Background**: The majority of spinal infections are caused by haematogenous spread of bacteria and seldom by direct extension of a contiguous soft tissue focus. The recovery of the anaerobic bacteria, parvimonas micra from spinal biopsies as cause of spondylodiscitis is very rare. Even rarer is to find parvimonas micra, concomitantly with actinomyces funkei also in the in cerebrospinal fluid (CSF). The additional growth of prevotella nigrescens in a blood culture raised suspicion of an intestinal infection.

Case: A 40-year-old male presented with progressive pain in the sacral region for several weeks, and headache and chills for few days. The physical examination revealed percussion pain in the sacral region and mild meningism. Laboratory findings showed leukocytosis with 14.5 G/I and increased CRP 348 mg/l. The MRI showed a spondylodiscitis at L5-S1 and a diffuse inflammatory reaction of the subarachnoid space. The cerebrospinal fluid was purulent with a pleocytosis of 8400 cells/ul (88% polymorphonuclear leukocytes) and showed a high protein of 1900 mg/l. The gram staining of the CSF showed gram positive cocci and gram negative bacilli. Accordingly to these findings an empiric antibiotic treatment with ceftriaxone and vancomycin was started. A day later a percutaneous CT-guided biopsy of L5-S1 was performed. The culture of the CSF revealed growth of actinomyces funkei and parvimonas micras. The latest grew also in the biopsy of L5-S1. Additionally one blood culturewas positive with prevotella migrescens. By review of the medical records we learned that several years ago the patient had undergone several endoscopies and even a laparotomy to extract self-introduced foreign bodies from the colon. Therefore we performed a diagnostic colonoscopy, which detected suppurative ulcerative lesions in the rectum and rectosigmoid. An MRI of the pelvis demonstrated a fistula between the inflamed rectosigmoid and L5-S1. Due to its small size a conservative management of the fistula with ceftriaxone and metronidazol for at least six weeks was decided. However a follow-up MRI showed persistency of the fistula. Therefore a resection of the rectosigmoid with excurettage of the fistula and colostomy were performed to control the intestinal source of infection. The antibiotic treatment was continued for six weeks after surgery. We will follow-up the patient in surgery, orthopedic and infectious disease consultations.

**Conclusion:** A polymicrobial infection with anaerobic bacteria of the spine and central nervous system (CNS) in an immunocompetent patient is extremely rare. A comprehensive anamneses combined with an extended focus search according to the isolated germs guided us to the diagnosis of a fistula between the recto sigmoid and L5-S1 as focus of the infection.

Colonoscopy: ulcerative lesions in the rectum and rectosigmoid with a fistula entry

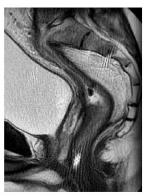




MRI lumbar spine: spondylodiscitis at L5-S1 and a diffuse inflammatory reaction of the subarachnoid space



MRI pelvis: a fistula between rectosigmoid and L5/S1



Iron isomaltoside 1000 (IIM) in patients with iron deficiency (ID) or iron deficiency anemia: a multicentric, prospective, observational study in Switzerland – Interim analysis

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**Background:** Iron deficiency (ID) with and without anemia is the most common nutritional deficiency in the world. Intravenous iron is the treatment of choice if oral iron cannot be used or is not tolerated.

**Methods:** Real-CHOICE (<u>Real</u> life study on IIM in the treatment of ID in <u>CKD</u>, <u>H</u>eart failure, <u>O</u>bGyn, <u>IBD</u>, <u>C</u>ancer and <u>E</u>lective Surgery), designed as a prospective, non-interventional longitudinal study to investigate the treatment of adult patients with ID in Switzerland with the intravenous preparation Iron isomaltoside 1000 (IIM, Monofer\*) according to the SmPC under routine conditions.

**Results:** Here we present the preliminary results of 229 patients enrolled (218 pts treated) until cutoff of interim analysis in February 2022. This analysis set shows a median age of 38.8 yrs, 94% of pts were female. Most pts had a gynecological etiology of iron deficiency (52.1%), followed by non-menstrual bleedings (5.16%) and inflammatory bowel disease

(4.23%). Treatment-emergent adverse events (including drug use in pregnancy and off label use) were documented in 14.7% of pts. Adverse drug reactions occurred in 6.9% of pts and were mostly mild infusion reactions except for one serious adverse drug reaction (bronchial obstruction).

**Conclusion:** Real-CHOICE is the first NIS to investigate real- world use of IIM in Switzerland across several medical fields. At this year's SGG Congress, the inclusion progress to date and preliminary results from interim analysis will be presented.

This study is funded by Pierre Fabre Pharma AG (Allschwil).

#### A Swiss Study to Investigate Real-world Clinical, Biochemical and Patient-reported Responses to Tofacitinib Induction Therapy for Ulcerative Colitis: Rationale and Study Design

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Background: Real-world populations in IBD differ from those in clinical trials and trial endpoints may not always capture the outcomes that matter most to patients and clinicians. Tofacitinib is an oral Janus kinase inhibitor for the treatment of moderate to severe ulcerative colitis (UC). While tofacitinib induction therapy has been associated with reductions in stool frequency and rectal bleeding, the response in terms of other patient-reported outcomes (PROs) and fecal calprotectin (fCAL) are less well characterised.

**Methods:** We present the design of KIC-START (NCT05069259), a Swiss observational study aiming to investigate a suite of PROs and fCAL during induction therapy with tofacitinib in sixty adult patients with UC.

**Results:** The primary outcome of the study is the change in partial Mayo score at week eight. Patients will report PROs daily using a research version of the Sidekick Health mobile application. Home stool CALEX\* Cap collection kits (Bühlmann Laboratories) will allow frequent fCAL testing. Intestinal ultrasound data will be collected.

**Conclusion:** Recruitment has commenced at five sites and final results are expected in 2024. KIC-START should provide important insights into how patients experience response to tofacitinib induction therapy, as well as the usefulness of and interactions between PROs, fCAL and clinical outcomes.

## Stricture prevention after circular ESD of a large LST of the rectum – a case report

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We performed successfully a circular ESD on a 14cm circular lateral spreading tumour granular mixed type (LSTgm), ranging from the linea dentata to the recto-sigmoidal junction. The lesion was classified as Paris Is/IIa, Nice 2, JNET 2a and Kudo IV. As there was no infiltration of the muscularis propria, and no enlarged lymph nodes in the endosonography we concluded a uT1, NO.

The histology of the circular specimen, which was removed en bloc, revealed an adenoma with low grade dysplasia with no signs of high-grade dysplasia or cancer.

To prevent postinterventional strictures, we administered prednisolone 40 mg orally for three days, followed by triamcinolone injections in the wound at day three after the ESD as well as budesonide rectal foam 2mg/d for 8 weeks. We continued triamcinolone injections in outpatient endoscopies after the ESD at day 14 and then every two weeks for two months.

Relative lumen-narrowing was seen but there were no signs of a relevant strictures and the patient did not complain of any symptoms.

# Use of complementary medicine in children and adolescents with inflammatory bowel disease in Switzerland

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**Background:** Complementary and alternative medicine (CAM) is considered any treatment beyond conventional medicine. Data about the use of CAM in children with inflammatory bowel disease (IBD) is lacking. Aim: To evaluate the use of CAM in pediatric IBD patients in Switzerland and to identify associated factors.

**Methods:** Prospective cohort study employing a questionnaire about the detailed use of CAM in conjunction with clinical data from the Swiss pediatric IBD cohort study.

**Results:** We analysed data of 108 patients, 58 with Crohn's Disease (CD) and 50 with Ulcerative colitis (UC) or IBD-unclassified. 42 (38.9%) patients reported to have used CAM during their disease course. Most used CAM was phytotherapy in 22%, followed by homeopathy (15%), massages (7%) and kinesiology (5%). We did not find any association between CAM use and disease activity (PUCAI or PCDAI score) (p = 0.7 resp. p = 0.8) or use of TNF-alpha inhibitor (p = 0.78) as markers of a more severe disease course. 47% of caregivers attributed a positive impact to the use of CAM. There was no significant difference seen in overall quality of life (p = 0.18) between CAM and no-CAM users.

**Conclusion:** While there is a high demand by caregivers to use CAM and a positive attribution of effects to their use, our data assumes that CAM use does not make a relevant clinical difference. Practitioners should be aware about CAM use in pediatric IBD patients to include CAM in their management strategies. Increasing knowledge about CAM will ensure a safer and more coordinated care for patient.

## Acute liver failure due to Budd-Chiari syndrome and inflammatory bowel disease flare

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**Background:** Budd-Chiari Syndrome (BCS) is defined as the obstruction of hepatic venous outflow. Most of the patients present with prothrombotic factors or myeloproliferative neoplasms but other rare causes include inflammatory bowel disease (IBD). Here, we report previously non-documented association between an acute liver failure due to BSC and IBD.

Case presentation: The patient is a 37-year-old female diagnosed with undetermined colitis for a year, under oral 5-ASA maintenance therapy and no oral contraception. She flared since two weeks with bloody diarrhea, new-onset right upper quadrant pain and ascites. Her physical examination revealed no haemodynamic instability, no hepatic encephalopathy nor jaundice.

**Investigations:** Laboratory studies showed acute liver failure and inflammatory syndrome. Fecal calprotectin was highly elevated and fecal analysis were negative for enteric pathogens. Abdominal ultrasound and CT scan showed thrombosis of the hepatic veins with significant hepatic perfusion disorders and indirect signs of portal hypertension. The bi-directions was accordingly to the properties of the pro

tional endoscopy confirmed active Crohn's disease (CD). A thorough investigation into potential alternative causes showed no hypercoagulability, nor myeloproliferative diseases, neither paroxysmal nocturnal hemoglobulinuria.

Treatment and follow-up: The hepatic veins thrombosis was treated by intravenous heparin, transitioned to oral acenocoumarol for long-term anticoagulation therapy, combined with angioplasty of left and right hepatic veins. Anasarca was treated with intravenous furosemide and oral spironolactone. CD was managed with infliximab. Rapid improvement of hypervolemic and digestive status, allowed us not to resort to a TIPS or liver transplantation.

## Power spiral enteroscopy-assisted therapeutic ERCP in patients with Roux-en-Y bilioenteric reconstruction

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**Background:** In patients with Roux-en-Y bilioenteric reconstruction, endoscopic retrograde cholangio- pancreatography (ERCP) is technically challenging. The optimal endoscopic strategies for these cases remain unknown.

**Aim:** To explore the feasibility and effectiveness of power spiral enteroscopy-assisted therapeutic (SEAT)-ERCP in patients with bilioenteric Roux-en-Y anastomosis.

**Methods:** This is a case series of the first 10 consecutive procedures in 8 patients, performed between September 2021 and May 2022 at a tertial referral center.

**Results:** SEAT-ERCP was performed in 5 cases with hepaticojejunostomy and Roux-en-Y reconstruction and in 5 cases with Roux-en-Y gastric bypass. The papilla/ hepaticojejunostomy was reached in 9/10 (90%) cases and successful ERCP was performed in 9/10 (90%) cases, including successful stone removal, balloon dilation and stent placement (plastic and metal). In one case a deep mucosal laceration of the gastrojejunostomy requiring transient stent therapy was seen after the examination.

**Conclusion:** SEAT-ERCP in patients with Roux-en-Y bilioenteric reconstruction is safe and effective with a high success rate. However, larger prospective studies are needed to confirm these preliminary results.

#### Intrafamilial spectrum of ABCB4 disease expression

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**Background:** ABCB4 gene deficiency leads to a clinical disease spectrum including progressive familial intrahepatic cholestasis type 3 (PFIC3), whose presentation varies significantly without clear genotype-phenotype correlations. We report here a case highlighting the marked heterogeneity within a same family of the clinical expression of an identical ABCB4 mutation.

Methods and Results: We present the long-term follow up of a patient with PFIC3 born to consanguineous parents (second degree cousins) whose disease progressed rapidly to decompensated cirrhosis by age 11, requiring a liver transplant. As the patient did not qualify for deceased donation, in the patient underwent living related liver transplant from his father in 2009. The post-operative course was uneventful, other than a persistent GGT elevation and mild ductopenia on histology. Further investigations and the advent of next-generation- sequencing would later reveal that the proband and his father carried the same homozygous c.572A>G ABCB4 nonsense gene mutation. The most recent liver biopsy available at 8 years post-LT revealed a mild, partial non-inflammatory slowly evolving ductopenia without clinical repercussions.

**Conclusions:** This case describes the phenotypic expression of a single patient transplanted with a liver containing an identical ABCB4 mutation with an uneventful long-term follow up of 13 years after LDLT.

#### EUS-guided gastrojejunostomy: a technic to consider

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**Background:** Endoscopic ultrasound guided gastrojejunostomy (EUS-GJ) is a novel emerging technic widely described and accepted for treatment of gastric outlet obstruction. Future challenge will be to improve this technic to gain time and ease punction of the targeted enteral loop. For this purpose, we propose a case series of patients who underwent EUS-GJ procedures with an ultraslim scope orally inserted.

**Methods:** We included eleven consecutive patients who underwent EUS-GJ direct technic for gastric outlet obstruction who cannot undergo surgical procedure.

**Results:** For 10 patients, ultra slim scope could be inserted through the obstruction. Mean time procedure was 64.5 ± 18.6 minutes but usually included several procedures during the same time. Eight patients had a duodenal stent in place that was obstructed. LAMS of 20 mm were used in 82% of procedures. Technical success was achieved for all patients. No severe adverse events occurred. One minor adverse event occurred which was a misdeployment of a first LAMS and a second one was successfully deployed. After a median time of follow-up of 2.77 months (IQR 2.15-3.15) for all patients, recurrence of symptoms occurred for two patients.

**Conclusion:** An ultraslim scope could be use to improve enhancement of the targeted enteral loop and ease its punction which are the longest and hardest steps of EUS- gastroenterostomy.

## Hybrid FTRD in the upper and lower GI tract: results of a large Swiss patient cohort

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Hybrid FTRD has been described as an effective approach for large lesions in the duodenum and colorectum with non-lifting sign, as FTRD technique is limited by lesion size. Here we describe results of different hybrid FTRD approaches in a cohort of 40 patients.

**Methods:** Retrospective data analysis of 40 patients who underwent hybrid EMR-FTRD (16 Hybrid EMR, 8 CAP O Clip, 14 COL-FTRD) for a variety of lesions in the upper (n = 7), mid (n = 8) and lower GI tract (n = 25) was performed. Technical success, histological confirmation of margin-free resection and adverse advents were assessed.

**Results:** 32 of 40 (80%) lesions could be resected macroscopically complete. Full thickness resection was achieved in all cases. Histological workup of the full-thickness specimens showed free lateral margins in 37 patients (92.5%) and positive margins in three patients. One of these patients received successful EMR treatment with negative histology on index endoscopy. In the hybrid EMR group there were three cases of bleeding requiring hospitalisation and one hospitalisation due to periprocedurally closed perforation while n = 4 patients were prophylactically hospitalized in the CAP O CLIP and COL FTRD collective due to old age and comorbidities.

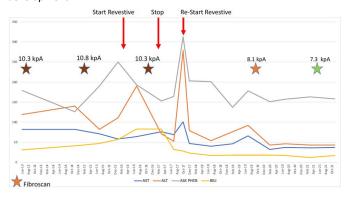
**Conclusions:** Hybrid EMR-EFTR and associated techniques seems to be safe and effective for lesions across the GI tract.

#### Pushing boundaries: improvement of IAFLD under teduglutide in a patient with familiary adenomatous polyposis (FAP) and short bowel syndrome

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We report the case of a 53-year-old male patient diagnosed with FAP in his adolescence. Shortly after diagnosis the patient underwent proctocolectomy temporary ileostomy. After ileostomy reversal the patient required multiple small bowel resections over a course of seven years ending in definitive enterostomy due repetitive small bowel obstructions caused by adhesions and development of desmoid tumours in the small bowel mesenterium. Consequently, the patient developed short bowel syndrome with malnutrition and requirement for parenteral nutrition. Elevated liver enzymes and cholestatic parameters were first noted in 2013 with elevated fibroscan values and a diagnosis of intestinal failure associated liver disease was made. Liver biopsy was avoided to not trigger desmoid growth. The patient suffered multiple port infections requiring hospitalisation and liver parameters as well as fibroscan values remained high despite adaption of parenteral nutrition protocols. In 2016 an interdisciplinary decision was made to start off label revestive in order to avoid progression of IAFLD. Figure 1 Summarizes liver and fibroscan values showing a marked drop in bilirubin, liver and cholestasis parameters as well as fibroscan values. The patient was able to reduce and completely stop parenteral nutrition in 2018. He regularly underwent enteroscopies with removal of small bowel adenomas - none of them showing malignancy. Repetitive imaging studies were able to rule out tumor or desmoid development.



Revestive is a Glucagon like petide 2 analogon applied in patients with short bowel syndrome in order to increase resorptive capacity of the remaining small bowel. It is formally contraindicated in patients with a history of malignant disease within the last 5 years as it seems to induce bowel mucosa malignancy. However, there is little data on adequate treatment of patients with short bowel syndrome after surgery for hereditary colon cancer syndromes. Small bowel transplantation is a high-risk procedure which is not ubiquitary available and would have required immunosuppression with added risk of further desmoid development. To best of our knowledge this is the first case of a patient with FAP, short bowel syndrome and associated IAFLD treated successfully under consequent endoscopic and radiologic surveillance with Revestive in the literature.

## The potential of D-lactate as a biomarker for inflammatory bowel disease in paediatric patients

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Background: In the inflamed tissue, the permeability of the epithelium increases and causes the D-lactate produced by the bacteria to be released into the blood. This in turn results in an increase in the serum D-lactate level in patients. Since the D-lactate concentration in the blood reflects the permeability of the intestinal mucosa, its increase in serum could serves as a biomarker reflecting the activity of the chronic intestinal disease in patients. The aim of this work is to assess the potential of D-lactate as a non-invasive biomarker for pediatric patients with inflammatory bowel disease.

Material and methods: Serum samples of 44 pediatric patients with inflammatory bowel disease and 49 healthy patients were included into this study. PicoProbe™ D-Lactate test kits from BioVision were used to measure D-lactate and the results correlated with the clinical profile of the patient.

Results: Serum D-lactate level of pediatric IBD patients is significantly increased compared to non-IBD subjects. The serum D- lactate level of pediatric IBD patients during an active phase of the disease is not significantly different from the serum D-lactate level of pediatric IBD patients who are in remission.

**Conclusion:** The hypothesis that D-lactate is elevated in patients with inflammatory bowel disease was clearly confirmed. The extent to which D-lactate can be used as a biomarker as a diagnostic marker to distinguish disease activity remains to be clearly answered.

#### **POSTER HEPATOLOGY**

# Clinical outcome of patients with severe alcoholic hepatitis (AH) responders (R) and non responders (NR) to steroids: the Geneva experience

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Patients with severe AH and steroid non response have a poor reported survival rate of 25% after 6 months (*Louvet, Hepatology 2007*) without liver transplantation (LT). We aim to study the clinical outcome of such patients with AH from our local community.

**Methods:** From 12/2015 to 1/2022, 59 patients (M/F: 40/19, mean age 56.7 years, MELD 21, Maddrey 56.3) with biopsy-proven severe AH, and steroid-guided therapy (Lille score day 7) and 6 months follow-up available were included. Complications, alcohol relapse and survival without LT was obtained.

**Results:** n =, (%)

	Steroid R			Steroid NR			p value
	1 mo	3 mo	6 mo	1 mo	3 mo	6 mo	
Total pts	35	35	33	22	21	21	
Infection	12(34)	12(34)	12(36)	7(31)	9(42)	10(47)	0.41
Bleeding	4(11)	5(14)	7(21)	6(27)	7(33)	7(33)	0.32
Renal failure	3(9)	3(9)	4(12)	7(31)	7(33)	9(42)	0.01
6 mo survival	27 (81%)			11 (52%)			0.02

Forty percent (40%) of patients were steroid NR. At 6 months of followup, 52% of patients in the NR group were alive. Alcohol relapse was reported in 11 (31%) and 7 patients (29%) in the Responders and Non Responders groups, respectively (p = 0.8).

**Conclusion:** The expected difference in survival between steroids R and NR is observed in our cohort, but mortality is much less elevated than previously published.

# Early liver transplantation (ELT) for severe alcoholic hepatitis (AH): a case series from the Centre Univ. Romand de Transplantation (CURT)

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 ${\it Gastroenterology/Hepatology, Transplantation, HUG, Gastroenterology/Hepatology} \ {\it CHUV}$ 

Liver transplantation (LT) performed early after the first episode of decompensation in patients with severe AH and non response (NR) to steroids is an effective treatment, although it remains a controversial issue with regards to alcohol relapse and associated liver-related complications. We studied the clinical characteristics and outcome of carefully selected patients who received ELT for AH.

**Methods:** From March 2009 to April 2021, 5 patients with severe AH resistant to medical treatment who underwent ELT were included in this retrospective study. Eligibility for ELT was assessed using criteria from the seminal study (*NEJM 2011*), including: first admission for alcoholic liver disease, biopsy-proven severe AH and non response to steroids, supportive family members, no severe comorbidities and agreement between all care givers. Time interval between listing and LT, Maddrey and MELD scores, clinical outcome, and return to alcohol consumption were reviewed.

Time NR to listing	Time listing to LT			Alcohol re- lapse
29.8 [21-51]	44.5 [11-83]	33.4 [28-40]	72.7 [13.2-126]	n = 1 (20%)
days	days			

**Results:** There were 4 males and 1 female, with a mean age of 55.6 years [53-61], mean Maddrey score 74 [40-94], and a mean Lille score 0.88

[0.74-0.98]. Relevant comorbid conditions included obesity (n = 2), ischemic heart disease (n = 1) and renal failure (n = 3). Note: time expressed in days, mean [range]Survival at 6 months and 2 years was 100%. During follow-up, 1 patient developed cirrhosis on liver graft, and 1 had oesophageal carcinoma, both conditions were the cause of death.

**Conclusion:** Early LT in highly selected patients with severe AH and steroid NR is an effective treatment with excellent short and mid-term survival. Post LT alcohol relapse may affect outcome.

## Loss to Follow-up after treatment of hepatitis C virus infection with direct-acting antivirals

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**Background:** Direct-acting antivirals (DAA) result in high cure rates in hepatitis C virus (HCV) infection but loss to follow up (LTFU) is frequent in the cascade of care. We assessed the proportion of patients with LTFU after DAA prescription and to determine factors related to LTFUs.

**Methods:** We retrospectively included patients infected with HCV who received a DAAs prescription at our center between January  $1^{\text{st}}$ , 2014 and December  $31^{\text{st}}$ , 2021. LTFU was defined as lack of confirmation of sustained virologic response assessed

12 weeks (SVR12) after the end of the treatment. We then identified factors associated with a LTFU.

**Results:** LTFU occurred in 70/447 patients (15.7%, 95% CI 12.6 - 19.3). Among them, 21 (4.7%) were never tested for HCV RNA during treatment, while 49 (11%) were on-therapy complete virologic responders but never showed up to confirm SVR12. Being under psychiatric treatment was the only factor associated with increased risk of LTFU (OR 2.00, 95% CI 1.09 - 3.64), while a prior antiviral therapy was associated with a lower risk of LTFU (OR 0.32, 95% CI 0.13 - 0.77). Illegal residency, marital status and history of intravenous drug use were not significantly associated with LTFU.

**Conclusions:** We report a high prevalence of LTFU after initiating treatment with DAAs. An ongoing treatment for a psychiatric comorbidity was associated with LTFU but prior exposure to antiviral therapy was associated with a lower risk of LTFU. These data suggest the importance of an accrued integrated management of patients with chronic hepatitis C affected by comorbidities limiting antiviral therapy adherence.

#### Ribociclib-induced liver injury: A case report

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**Background:** Idiosyncratic drug-induced liver injury (DILI) is a rare, unpredictable hepatic adverse event and the most common cause for acute liver failure in Europe and the US. Ribociclib is a potent Cyclin-dependent kinases 4 and 6 (CDK4/6)-inhibitor admitted for advanced hormone-receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer. Ribociclib has been associated with hepatotoxicity without liver necrosis in previous reports.

**Methods:** We report the case of a 41-year-old female patient with primarily metastatic HR-positive, HER2-negative breast cancer who developed grade 3 DILI (International DILI Expert Working Group) due to ribociclib.

**Results:** Ribociclib was withdrawn 8 weeks after initiation due to liver enzyme elevation. Liver biopsy, performed due to further enzyme elevation

(peak ALT 2836 U/I), onset of jaundice (peak bilirubin 353 µmol/I) and coagulopathy (INR 1.8), revealed acute hepatitis with 30% parenchymal necrosis. Roussel Uclaf Causality Assessment Method (RUCAM) score was 7 points (probable). Under treatment with prednisone (60 mg), initiated 2 weeks after withdrawal, and subsequently N-acetylcystein (Prescott) liver enzymes normalized within 8 weeks with tapered- off prednisone.

**Conclusion:** This case illustrates development of idiosyncratic severe mixed pattern of DILI grade 3 induced by ribociclib. Routine liver enzyme testing during therapy, immediate hepatologic work-up and treatment interruption are highly recommended.

## A case of liver failure after *Bacillus cereus* food poisoning: an under-recognized entity?

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Background: Bacillus cereus (B. cereus) is known to cause 2 types of food poisoning: diarrheal and emetic syndromes. Usually, these diseases are

self-limiting. Rare cases of liver failure and rhabdomyolysis due to mitochondrial dysfunction induced by cereulid toxin have been reported in children

Case report: A 48-year old female patient presented gastrointestinal symptoms 30 minutes after eating a rice salad. In the emergency department, she received acetaminophen (1g) and became lethargic and tachycardic. Blood analysis showed elevated transaminase (ASAT: 3'536U/I, ALAT: 3'248U/I) with a low prothrombin activity (32%) and factor V (15%), acute renal failure (Creatininemia: 124mcmol/I) and rhabdomyolysis (Creatinine Kinase: 1'525U/I). Liver ultrasound showed no hepatomegaly nor signs of chronic hepatopathy. She received N- acetylcysteine (NAC) treatment and was hospitalized in Intensive Care Unit. A liver disease screen found no viral nor autoimmune aetiology. Stools culture were positive for *B. cereus spp* which was also found in the rice salad. Ciprofloxacin was administered for five days due to persistence of diarrhea suggesting the presence of intestinal vegetative *B. cereus*. At day 2, liver function and psychomotor activity improved, and she went back home on day 9.

**Conclusion:** We report the first documented case of hepatocellular dysfunction in an adult patient after *B. cereus* food poisoning. Severity of liver dysfunction reported suggests that acetaminophen should be avoided in case of food poisoning and NAC could be a potential therapy.

#### **POSTER SURGERY**

#### Small bowel diverticulitis: a case report

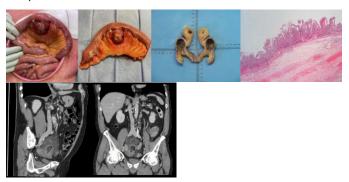
Ismael Turk<sup>1</sup>, Tiago Varella-Cid Maldonado Santos<sup>1</sup>, Sonaz Malekzadehlashkariani<sup>2</sup>, Jolanta Gourmaud<sup>3</sup>, Boumediene Guendil<sup>1</sup>, Carlos Apestegui<sup>1</sup>

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**Background:** Small bowel diverticulitis is a rare pathology with a higher prevalence amongst patients in the 6th and 7th decade of age. It is most often considered an incidental finding, but complications such as diverticulitis, perforation, abscess, generalized peritonitis, fistula, obstruction and bleeding can still occur. Here we present the case of a small bowel diverticulitis with associated abscess.

**Methods:** A 72 year-old male patient presented to our Emergency Department with a 2 day diffuse lower abdominal and right iliac fossa pain, with no other symptoms. The physical examination showed a dilated abdomen with right flank and periumbilical pain without rigidity or rebound tenderness. The laboratorial tests indicated an elevated leucocyte count of 12 G/L with a C-reactive protein at 56 mg/L and a haemoglobin level at 96 g/L. An abdominal CT-scan revealed small bowel diverticulitis with associated abscess of 36 mm.

**Results:** An exploratory laparotomy was performed and revealed a small bowel diverticulitis with associated abscess 120 cm distal to the Treitz angle. A 20 cm segmental resection was done, followed by a side-toside manual anastomosis. The pathology results showed 2 pseudodiverticula with intestinal type mucosa, one of which showing signs of inflammation. The postoperative course was uneventful and the patient was discharged at day 7.



**Conclusion:** Small bowel diverticulitis is a rare pathology which needs to be taken into account as a differential diagnosis in the case of acute and unspecific abdominal pain. Diagnosis is often made at emergency surgical exploration with high morbidity and mortality rate

## Mid-term outcome of Percutaneous Posterior Tibial Nerve stimulation treating faecal incontinence

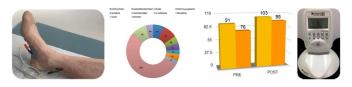
Xavier Delgadillo<sup>1</sup>, Tunde Gaspar<sup>1</sup>, Lena Beurret <sup>2</sup>, Philippe Wüthrich<sup>1</sup> Centre Médico Chirurgical Volta, La Chaux-de-Fonds, Switzerland

**Background**: Our objective was to establish the efficacy of *percutaneous*-PTNS for the treatment of gaz, passive & urgent faecal incontinence.

**Methods:** We stablished a prospective study including patients with FI. Anamnesis, complete proctologic examination, Jorge-Wexner score, ASCRS's quality of life score & Miller's Visual Analogic Incontinence Scale (*VAIS*) were registered during 24 months. Patients underwent one weekly session for 12 consecutive weeks of *p*-PTNS. 3-D anal manometry, 3-D endo-anal ultrasound were performed prior to the procedure. Finally the intention-to-treat analysis has been developed.

**Results:** 84 patients (72 females; mean age 61.84 ± 10.02 years) with FI were treated with *p*PTNS. Ethiology: 52.99% obstetric injuries, 44.4%

proctological surgery. For the universe, median Jorge-Wexner baseline was 11.0 at the begining of the treatment, 5.0 at the end. Three patients, were excluded due to lack of confidence on the procedure. 24 months follow-up demonstrated a Miller's VAIS scale improvement from 3.88 to 7.10 (p < 0.001). All included patients, presented a significant enhancement in their QoL, less depressive access & better self-perception scores. Embarrassment scores were not significant. According to the FI to gaz, it was improved in more than 35%, passive FI was improved in 31.3% & urgency FI presented improvement of 38% (even in mixed FI there were significative recovery 28%) on Jorge-Wexner Score evaluation.



**Conclusions:** *Percutaneous*-PTNS is an effective treatment for gaz, passive and urgent FI, mid-term follow—up demonstrates efficacy and remaining benefits on FI. Patients with urinary & FI benefit from this therapy evolving in therms of less accidents, better QoL & improvemment on their self-perception in the society were definetly positives.

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#### An unusual cause of pneumoscrotum

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**Background:** Pneumoscrotum is a rare condition. Etiology varies from gas forming bacteria, direct air introduction from scrotal injuries to thoracic or abdominal related conditions.

**Methods:** We present the case of a 52 years old male with progressive right testicular pain for one week, nausea and diarrhoea. On clinical examination we found an enlarged, painful and thickened right scrotum. Laboratory examination showed a CRP of 384 mg/l, WBC of 14 G/l and microhematuria. Sonography of the scrotum was inconclusive due to huge amount of air artifacts. CT scan then illustrated the picture of a right pneumoscrotum secondary to a retroperitoneal perforation. After attempted laparoscopy we performed an open ileocecal resection and right semicastration. Histology revealed a locally advanced cecum cancer with retroperitoneal perforation. One week later we completed the right hemicolectomy with wedge resection of segment VI and placed a port a cath system. Definitive TNM was pT4a pN2a (6/20) pM1a (HEP) L1 V1 Pn1 G3 according a stadium IV A

Results and Discussion: Retroperitoneal intestinal tumor perforation can be one rare reason of pneumoscrotum. Embryologically the testicles develop intraabdominally and perform a so called descensus testis later on. Due to this, testicular pain can cause abdominal symptoms and vice versa. In our case the leading symptom of the patient was painful swelling of the scrotum. A good clinical examination not only includes the scrotum but also the total abdomen. As the air was trapped in the retroperitoneum abdominal symptoms were mild and not obvious for the patient. Thus, although radiologic diagnostic tools get better, we should never neglect training young doctors' clinical skills.

#### Bowel recovery after intra vs extracorporeal anastomosis for oncologic laparoscopic right hemicolectomy within an ERAS protocol: a retrospective study

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**Objective:** Restoring bowel continuity after laparoscopic right hemicolectomy (LRH) by intracorporeal (IC) vs. extracorporeal (EC) ileocolic anastomosis, may offer advantages in post- operative recovery. We compared bowel function recovery between IC/EC after LRH within an enhanced recovery after surgery (ERAS) protocol.

**Methods:** All consecutive patients underwent LRH in January 2012 – February 2021 in our institution were included. Data were gathered from the prospectively maintained official ERAS (EIAS) database. The primary endpoint was Prolonged Postoperative Ileus (PPOI). Propensity score matching was used to mitigate the risk of bias.

**Results:** 108 patients with 36 (30%) IC and 72 (70%) EC were included. Characteristics were similar except for more epidural analgesia in EC group (62 (72.9%) vs. 17 (47.2), p = 0.007). Operative time was longer in IC group (197 min (176-223) vs. 160 (140-189), p < 0.001). PPOI was similar (2 (5.6%) patients in IC vs. 10 (11.6%) in EC group (p = 0.306), but time to first passage of flatus and stool was shorter in IC group. Morbidity was similar but patients after IC anastomosis had less pain (VAS) at 24h (p = 0.004) and a trend to shorter LoS (6 (5-8) days vs 7 (5-10) in EC group, p = 0.054). After PSM, there were 36 patients per group. PPOI, time to first flatus/stool, morbidity, LoS were similar despite a trend to better recovery in IC group. IC group had longer operative times but less 24h pain.

**Conclusions:** Although IC anastomosis was not significantly associated to shorter PPOI, it showed trends to faster recovery and significantly less post-operative pain at the expense of longer operating times.

# Introducing minimally invasive liver surgery in a tertiary center of Southern Switzerland: reappraisal of the first 100 cases

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**Background:** Laparoscopic liver resection (LLR) is the standard approach in selected patients affected by localized liver tumors. LLR program was implemented in January 2015 at our center.

**Methods:** Post-operative results of consecutive LLRs were retrospectively compared to consecutive open liver resections (OLRs) performed in January 2015 – September 2021. LLRs were stratified by difficulty level (low, intermediate, advanced, expert) according the IWATE criteria.

**Results:** 200 consecutive patients (LLR = 100; OLR = 100) were included. Mean age (65.4 vs. 64; p = 0.40), male sex (53% vs. 58%; p = 0.70), median ASA score (3 vs. 3; p = 0.83) as well as previous abdominal surgery (72% vs. 82%; p = 0.54) were similar between the two groups. Incidence of chronic liver disease was higher in LLR group (29% vs. 13%; p = 0.024). LLRs had shorter operative time (315 vs. 475 min; p <0.01), less blood loss (IBL) (200 vs. 300 ml; p = 0.01), shorter length of hospital stays (LOS) (6 vs. 9 days; p <0.01) vs. OLRs. Morbidity and incidence of major complications (Clavien-Dindo  $\geq$ 3) were 21% vs. 43% (p = 0.02) and 6% vs. 23% (p = 0.003) in LLRs vs. OLRs respectively. 90-day mortality was 1% each. R0 was similar (95% vs. 83%; p = 0.51) in LLR and OLR. Difficult resections (advanced and expert level) accounted for 16 and 18 cases (34%) in the current series. Conversion was 12%. Operative time, IBL, conversion to open surgery and LOS increased at increasing difficulty (all p <0.05), however, morbidity and major morbidity did not. R0 rate was similar among the four groups.

**Conclusions:** LLR was safely implemented with favorable short-term outcomes compared to OLR. Difficulty level of LLRs correlated with intra-operative but not post- operative outcomes.

#### Sigmoid Perforation: an endoscopic alternative to surgery

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**Introduction:** Sigmoid perforation is often an indication for surgical exploration, which can be risky in polymorbid patients. In colorectal endoscopy however, OTSC (over-the-scope-clip) technique is mostly described in the context of iatrogenic perforation and only 2 case reports from 2012 of perforation secondary to enemas are described using OTSC closure (1).

**Method:** The relevance of this case report is to discuss and illustrate the place of conservative/endoscopic therapy in the case of "typical" surgical pathology, such as a perforated colon.

Observation: A 87-year-old woman was admitted with acute abdomen. Brutal abdominal pain has appeared a few hours earlier, following a rectal enema. Daily enemas are performed due to incomplete C4 tetraplegia, following a C5 fracture. A CT- scan showed a perforated sigmoid colon associated with free fluid. Due to the patient's important comorbidities an endoscopic management is initially preferred. A coloscopy is performed and a 1.5-centimer-wide hole is found at 23 centimeters from the anal margin. The perforation is completely closed with 2 OTSCs. A radiological control with contrast product is immediately performed, showing no leak. Surgery was therefore avoided. Initial postoperative management consisted of wide-spectrum antibiotherapy. A week later, a control CT-scan was performed showing the development of peri-colonic fluid collection which was successfully drained percutaneously under CT-guidance. The drain was removed after 4 days and the patient was discharged a further 2 days later.

**Conclusion:** With polymorbid patients unfit to undergo an operation, it is worthy to consider alternative options such as endoscopic therapy. A multidisciplinary approach and thorough clinical evalution are essential in this respect.

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#### Ectopic intravagal adenoma causing persistent severe hyperparathyroidism

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**Background:** Persistent hyperparathyroidism after surgical management occurs in about 3-6% of cases and failure to cure are usually due to an unidentified ectopic or supernumerary gland. Intravagal parathyroid adenoma are rare and can lead to unsuccessful surgical treatment.

**Methods:** We present the surgical management of an intravagal parathyroid adenoma in a 49 yo woman with persistent primary hyperparathyroidism after multiple ineffective attempts of parathyroidectomy.

Results: The patient was diagnosed with primary hyperparathyroidism at the age of 22. Between 1994 and 2004 she underwent two cervical explorations with resection of the thyrothymic ligaments however with persistent hyperparathyroidism; a mediastinoscopy followed by a thoracoscopic thymectomy were performed without identification of pathological parathyroid tissue. As complications of the persistent hyperparathyroidism, she developed severe hypercalcemia, recurrent nephrolithiasis, chronic pancreatitis, osteoporosis, gastric ulcer, depres-

sion, and musculoskeletal pains. 15 years after the last surgery, radiological studies (cervical ultrasound, 99m-Tc-Sestamibi scan and 18F- fluorocholine PET/ CT) were repeated and were concordant for a suspected right paratracheal adenoma which was resected. The fresh frozen section turned positive for a lymphnode. Intraoperative study of the F-choline PET CT imaging showed an additional zone of high uptake 2cm cranially to the left carotid bifurcation. A left submandibular latero-cervical exploration was carried out and an intravagal autofluorescent parathyroid adenoma was evidenced. We performed a microsurgical dissection of the vagal nerve to resect the adenoma. The PTH value at the first postoperative day came back to normal and the patient went home with a left recurrent nerve palsy. The histopathological analysis confirmed a hyperplastic parathyroid gland.

**Conclusion:** The high accuracy of 18F-fluorocholine in detecting parathyroid adenoma together with the use of intraoperative autofluorescence provide the opportunity to improve the surgical management of patients with persistent hyperparathyroidism due to ectopic localization.

# Long-term Outcome after Biliopancreatic Diversion with Duodenal Switch: A Single-Center Experience with up to 20 Years Follow-up

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**Background** Biliopancreatic diversion with duodenal switch (BPD-DS) is the most effective bariatric procedure in terms of weight loss and remission of comorbidities but carries the risk of severe long-term side effects. The aim of this study was to analyze the long-term effects of BPD-DS on weight loss, comorbidities and reoperation rate.

**Methods** Retrospective single-center study of prospectively collected data of all BPD-DS procedures from 1999 to 2011.

**Results** 116 patients (83.6% female) underwent BPD-DS with a mean initial body mass index (BMI) of  $47 \pm 6.5 \text{ kg/m}^2$ . Mean follow-up time was  $14 \pm 4.4$  years and follow-up rate at 5, 10 and 14 years was 95.6% (n = 108), 90% (n = 98) and 75.3% (n = 70). Mean excess BMI loss (%EBMIL) at 5, 10 and 14 years was  $78\% \pm 24.1$ ,  $76.5\% \pm 26.7$  and  $77.8\% \pm 33.8$ , respectively. The highest % EBMIL was reached two years postoperatively with  $84\% \pm 23.6$ . Complete (n = 22) or partial remission (n = 4) of type 2 diabetes mellitus was observed in 92.8% of patients. Reoperation was necessary in 33 patients (28.4%) due to malnutrition or refractory diarrhea (10), insufficient weight loss or weight rebound (7), reflux or stenosis (7) and various/combined indications (9). Mean time to reoperation was  $7.7 \pm 5$  years. The predominant deficiencies were vitamin D (99.1%), zinc (86.9%), iron (83.5%) and calcium (71.3%).

**Conclusion** BPD-DS leads to sustainable long-term weight loss with an acceptable reoperation rate. Nevertheless, regular follow-up is necessary to detect and treat malnutrition and vitamin deficiencies.

#### Feasibility and safety of intraoperative bile duct clearance by sphincter of Oddi balloon dilatation: A prospective observational pilot study

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**Background:** Concomitant cholecysto- and choledocholithiasis is common. Standard treatments are ERCP followed by cholecystectomy or laparoendoscopic rendez-vous. ERCP has drawbacks such as post- ERCP-pancreatitis (5%) or -bleeding (5%) and potentially more than one intervention to address common bile duct (CBD) stones. Safety and fea- sibility of an intraoperative antegrade transcystic single-stage approach during

cholecystectomy with papillary balloon dilation and pushing of concrements to the duodenum has not been evaluated prospectively. The aim of the study was to evaluate this procedure regarding safety and stone clearance rate.

Methods: Prospective single centre intervention study. 80 consecutive patients admitted to our institution between 1/2021 and 4/2022 with suspected or confirmed choledocholithiasis (stones ≤ 6 mm) and known cholecystolithiasis were included. Success of the procedure was defined as lack of filling defects in the intraoperative control cholangiography and absence of symptoms at 6 weeks follow up. Simon's two stage design was used to determine sample size. Aiming for 95% positive outcomes (no pancreatitis) and tolerating at most 15% negative outcomes, power analysis revealed 57 participants (80% power, alpha 0.05).

Results: 57/80 patients (71%) fulfilled the inclusion criteria. Mild pancreatitis or cholangitis were present at admission in 15 (26%) and 15 (26%) patients, respectively. While there was no postoperative pancreatitis, 2 patients (3.5%) had asymptomatic amylasemia 4h postoperatively. Stone clearance was achieved in 54 patients (94%). The main reason for failed stone clearance was the inability to push the guide wire along the concrement into the duodenum resulting in the impossibility to insert the dilation balloon. Median number of CBD-stones was 1 (1-6). Median stone diameter was 4 mm (0.1-6 mm). Median intervention time was 28 min (14-129 min).

**Conclusions:** Intraoperative bile duct clearance by balloon dilation of the sphincter of Oddi appears to be safe and highly feasible. Its overall superiority to the current standards requires evaluation in a randomized controlled trial.

## Endoscopic surveillance after bariatric surgery: Results from a large, single-institution cohort

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**Objective:** Sleeve gastrectomy (SG) and Roux-en-Y-gastric bypass (RYGB) are common bariatric procedures associated with long- term abnormalities of the upper gastrointestinal tract, including erosive esophagitis (EE), hiatal hernia (HH), gastritis, Barrett's esophagus and ulcers. The aim of this study is to assess the prevalence of abnormal endoscopic and histologic findings after SG and RYGB in a large cohort.

**Methods:** This is a retrospective analysis of 720 consecutive patients who underwent esophagogastro-duodenoscopy (EGD) after primary SG or RYGB. Patients were invited for a control EGD after two years of follow-up. EGD was also performed in order to evaluate postoperative symptoms, such as nausea, vomiting or reflux. If revisional surgery was planned, an EGD was included in the pre-revisional work up.

Results:3 04 post-SG patients (64.1% female) and 416 post-RYGB patients (85% female) were included. The mean age at the time of operation was 43.9 years (95% confidence intervals (CI) 42.5-43.3 years) for the post-SG group and 40.5 years (95% CI 39.4-41.6 years) for the post-RYGB group (p<0.001). The mean preoperative body mass index (BMI) was 44.2kg/m² (95% CI 43.4-44.9) and 41.1kg/m² (95% CI 40.7-41.5) for the post-SG and the post-RYGB group respectively (p <0.001). EE, gastritis and HH were more prevalent after SG than RYGB (38.8% vs 8.9%, 62.5% vs 27.6% and 28% vs 2.6% respectively, p <0.001). RYGB was associated with more post-operative ulcers than SG (14.4% vs 0.7%, p <0.001). The incidence of anastomotic strictures requiring anastomotic dilatation after RYGB was 4.6%. No significant difference was found in the prevalence of Barrett's esophagus (4.3% post SG vs. 4.1 post RYGB, p = 1.000) and Helicobacter pylori (3.3% post SG vs. 1.2% post RYGB, p = 0.065) between the two groups.

**Conclusion:** SG is associated with higher rates of EE, gastritis and HH, while the prevalence of ulcers is higher post RYGB. There is a low risk of anastomotic stricture post RYGB. The incidence of Barrett's oesophagus

is low after both procedures. Endoscopic surveillance after bariatric surgery is a useful diagnostic tool and its routine use should be evaluated.

# Anterograde biliary stenting during laparoscopic cholecystectomy as a rescue maneuver in extensive choledocholithiasis

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**Introduction:** In case of choledocholithiasis therapeutic gold standard is endoscopic retrograde cholangiography (ERC) with stone extraction  $\pm$  stent placement followed by laparoscopic cholecystectomy (lap CHE). When unnoticed choledocholithiasis is diagnosed by intraoperative cholangiography (IOC) during lap CHE and biliary decompression is required, anterograde stent placement via the cystic duct may be a rescue maneuver avoiding the necessity of intraoperative ERC.

**Methods:** Case report of a patient with extensive cholecysto- and choledocholithiasis diagnosed by IOC during lap CHE.

Results: An 85 years old female patient admitted with acute onset of abdominal pain and cholestasis diagnosed by blood test. Preoperative ultrasound revealed a moderately widened common bile duct (CBD) of 9mm. The patient was taken to the operating room to perform lap CHE. IOC revealed a large prepapillary biliary stone of 15 mm with widened CBD proximally. Laparoscopic biliary stone clearance was not feasible due to the size of the stone. Moreover, intraoperative ERC was not possible due to unavailable ERC resources. Therefore, for biliary decompression, a 10cm, 7 Fr., double-pigtail cholangiocatheter was trans-cystically inserted over a guide-wire into the CBD along the stone and across the papilla into the duodenum. The procedure was completed by CHE. Postoperatively, cholestasis rapidly improved and the patient was discharged at the third postoperative day. ERCP with stent and stone removal ± lithotripsy will follow in 3 months.

**Conclusion:** Intraoperative anterograde trans-cystic CBD-stenting is a rescue maneuver to be considered in case of extensive choledocholithiasis and unavailable intraoperative ERC. It should be regarded as a bridging therapy to definitive treatment of choledocholithiasis by ERCP and eventually lithotripsy.

## Interdisciplinary combined sacrocolporectopexy: Results after one-year follow-up

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**Background:** The aim of this study was to access postoperative quality of life and complications as well as outcome after one-year follow-up after operation of multicompartmental pelvic floor prolapse (POP).

**Methods:** The study is a retrospective cohort study of all patients undergoing combined ventral mesh rectopexy and anterior mesh sacrocolpopexy between 2015 and 2020 in our institution. Follow-up was scheduled at 6 weeks, 6, and 12 months. It consisted of clinical examination and questionnaires. Quality of life and patients' satisfaction were evaluated at each consultation.

Results: 27 patients were included. All patients were seen at 1-year follow-up. Preoperatively, all patients suffered from severe multicompartment descensus, 81.5% of these had a POP-Q stage of II or III. Laparoscopic surgery was performed in 92.5% of cases and intraoperative conversion rate was 7.4%. We used in 55% of cases a Dynamesh® Visible, in 41% a Gynamesh®, and in 4% a Surgipro™ Mesh. 30-day morbidity and 90-day mortality was 0%. At 1 year, patients reported a high level of satisfaction (8.5 Pt. VAS Scale) and massive improvement of QoL. A tension free vaginal tape (TVT) had to be inserted in 4 patients (15%) due to new onset

of urinary incontinence. Symptomatic recurrence of prolapse did not occur.

**Conclusion:** Combined sacrocolporectopexy is an effective therapy of multicompartmental POP. It is a safe procedure with low perioperative morbidity and high patients' satisfaction.

## Outcome of revisional procedures up to 14 years after sleeve gastrectomy: a single-center experience

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**Background:** In the long-term, laparoscopic sleeve gastrectomy (SG) may be associated with insufficient weight loss (IWL), development of gastroesophageal reflux disease (GERD) as well as persistence or relapse of comorbidities.

**Methods:** Retrospective single-center analysis of a prospective database on patients who had a minimal follow-up of two years after conversion from SG.

Results: During 14 years 549 SGs were performed. 84 patients (15.3%) underwent a conversion from SG and 71 fulfilled inclusion criteria. They were converted to short biliopancreatic limb Roux-en-Y gastric bypass (short BPL RYGB) (n = 28, 39.4%), biliopancreatic diversion type duodenal switch (BPD/DS) (n = 19, 26.8%), long biliopancreatic limb Roux-en-Y gastric bypass (long BPL RYGB) (n = 17, 23.9%) and re-sleeve gastrectomy (RSG) (n = 7, 9.9%). Indications for conversion were GERD (33.8%), IWL (32.4%), a combination of both (31.0%) or stenosis/kinking of the sleeve (2.8%). Mean time to conversion was 5.2 years and the mean follow-up was 5.1 years. The overall percentage of total weight loss (%TWL) was greatest after BPD/DS (36.6%) and long BPL RYGB (32.9%) compared to RSG (20.0%; p = 0.004; p = 0.049). Patients with BPD/DS had higher %TWL at three years (27.3%) after conversion compared to short BPL RYGB (13.8%, p = 0.007) and RSG (8.7%, p = 0.004). In case of GERD, reoperation led to a resolution of symptoms in 82.2% after RYGB. 16.9% of patients underwent an additional revisional procedure.

**Conclusion:** In the event of IWL after SG, conversion to BPD/DS provides a significant post-conversional weight loss. RYGB leads to good symptom control in patients suffering from GERD.

## Systematic review of enhanced recovery after pancreatic surgery

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**Background:** The concept of "fast track surgery" was first implemented in the 90's. Later enhanced recovery after surgery (ERAS) concepts were established also for pancreatic surgery. These contain specific preoperative counselling, nutritional therapy, epidural analgesia, perioperative iv-fluid

restriction, avoidance or early removal of tubes, drains and catheters, early mobilization and early oral feeding. The aim of this systematic review was to summarize the evidence for the potential benefit regarding

postoperative outcomes in pancreatic surgery.

**Methods:** Systematic literature search was performed in CENTRAL, Medline and Web of Science without language restrictions. Randomized controlled trials (RCT) investigating any kind of enhanced recovery program in pancreatic surgery were included. Postoperative outcomes were analysed with a random- effects model by either the Mantel-Haenzsel or inverse variance method. Cochrane RoB 2.0 tool and GRADE approach was used for assessment of risk of bias and certainty of evidence.

**Results:** Finally, six randomized controlled trials (RCT) with 646 patients were included. The risk of delayed gastric emptying was significantly reduced in the ERAS group (odds ratio 0.44; 95%- CI: 0.28 to 0.69; p<0.01; certainty of evidence: moderate). Likewise length of hospital stay was shortened by about 3 days (95%-CI: -5.7 to -0.2 day; p = 0.03; certainty of evidence: low). Mortality, postoperative complications like pancreatic fistula, intra-abdominal fluid collections, bile leak or post- pancreatectomy hemorrhage were not altered by the ERAS concept (certainty of evidence: moderate to low).

**Conclusions:** After pancreatic surgery, the ERAS protocol results in shortened length of hospital stay and less delayed gastric emptying. Mortality or postoperative morbidity were not affected by the ERAS concept.

## Finding the best available evidence in pancreatic surgery – the EVIglance randomised controlled trial

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**Objective:** Profound and thorough literature search is a vital element of evidence-based medicine. However, increasing number of publications and limited time make it hard to find the best available evidence. The objective of this randomised controlled trial (RCT) was to demonstrate superiority of the ISGPS Evidence Map of Pancreatic Surgery (via EVIglance on www.evidencemap.surgery) compared to a conventional literature search via PubMed for answering clinically relevant questions in pancreatic surgery.

**Methods:** A single-centre, blinded, cross-over RCT was performed. Participants conducted literature searches with two predefined PICO questions, one with PubMed and the other with EVIglance. The order of the search tools and the PICO questions were assigned by randomisation. Primary endpoint was time in minutes until a synopsis was made regarding the PICO question. The synopsis was characterised by the direction of the effect and the certainty of evidence.

**Results:** 84 participants were randomised and analysed. A synopsis for the PICO question was found with PubMed after

10.8 minutes and with EVIglance after 1.7 minutes (95%-CI for difference: 9.9 to 8.3 minutes; p<0.001Participants were able to guess both the direction of the effect (95% vs 48%; p<0.001) and the certainty of evidence (99% vs 30%, p<0.001) better with EVIglance than with PubMed.

**Conclusion:** Pancreatic surgeons find best available evidence faster via EVIglance on www.evidencemap.surgery. Furthermore, a synopsis made from EVIglance is more concise regarding direction of effect and certainty of evidence. Given the advantages of EVIglance it may be considered the new gold standard for finding best available evidence in pancreatic surgery.

# Does the change from conventional circular to linear stapling in proximal gastric bypass surgery affect quality of life in the follow up?

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**Background:** The continuous desire to improve bariatric surgery outcomes and therefore patient's satisfaction leads to a constant search for new surgical approaches. Long-term effect on quality of life has not yet been studied. We analysed quality of life scores and clinical outcomes at a single bariatric centre transitioning from circular to a linear bypass protocol.

**Methods:** Between June 2012 and March 2016, 235 patients were included in this retrospective study from a prospectively collected database. Group CBP included those patients treated by the circular stapling bypass protocol (n = 117). This protocol was primarily used in 2012. Between 2013 and 2015 a transition period occurred. Thereafter, the linear stapling bypass protocol (Group LBP, n = 118) was primarily utilized. Quality of life (QoL) was assessed with the Moorehead-Ardelt QoL score, which was gathered preoperatively, and at 1, 2 and 5 years after surgery.

**Results:** Quality of life scores improved significantly after intervention in both groups. The most prominent improvement was seen within the first year after intervention. No statistically significant differences were seen between groups. During the first two years, quality of life score improvement occurred independently of achieved weight loss, whereas a correlation between QoL-improvement and reported weight loss was identified between 24 and 60 months (r2 0.112, p<0.001).

**Conclusion:** Quality of life scores assessed by the Moorehead-Ardelt QoL questionnaire were significantly improved after gastric bypass surgery, independently of operative technique and postoperative weight loss in the first two years after surgery. Thereafter QoL scores improved in correlation with further weight loss.

# Functional and radiological evaluation of the pancreatic anastomosis one year after pancreatoduodenectomy: a pilot prospective study

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**Background** While short-term complications after pancreatoduodenectomy (PD) are well described, long-term evolution of the pancreatic anastomosis remains poorly studied. This study aimed to assess the functional and radiological aspects of the pancreatic anastomosis 1 year after PD.

**Methods** Consecutive patients undergoing PD were prospectively included (2017-2020). Inclusion criteria were adult patients with PD indication for benign or malignant etiologies. Chronic pancreatitis or language barrier were exclusion criteria. Questionnaires on pancreas insufficiency and elastase stool tests were perfomed before and 1 year after PD. A secretin-MRI was realized 1 year after PD.

Results Twenty-one patients were included. The only difference between pre- and postoperative questionnaires was constipation (less frequent 1 year after PD). Median pre- and postoperative elastase level in the stools were 96 ug/g (IQR 15-196, N>15) and 15 ug/g (IQR 15-26, p = 0.042). On the 1-year MRI, median main pancreatic duct (MPD) size was not different before and after secretin injection (4, IQR 3-5 vs. 4 mm, IQR 3-5, p = 0.892). There were no differences before and after secretin injection in terms of MPD border regularity, stenosis, visibility, image improvement, and secondary pancreatic duct dilation (p>0.05). One patient was judged to have no permeability of the pancreaticojejunal anastomosis. No significant correlation was found between jejunal filling on 1-year MRI and 1-year elastase dosage (rho: 0.16, p = 0.660) and between jejunal filling on 1-year MRI and steatorrhea presence on questionnaire (rho: 0.235, p = 0.488).

**Conclusions:** This prospective cohort found a high patency rate of the pancreatic anastomosis after PD on 1-year secretin MRI, while median 1-year fecal elastase was low, suggesting that pancreatic exocrine secretion is altered.

#### Hypocortisolemia following unilateral adrenalectomy

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Unilateral adrenalectomy (UA) is the best option for unilateral functioning and non-functioning adrenal adenomas, localized primary or metastatic carcinomas. Post-operative hypocortisolemia (HC) in Cushing Syndrome is well known, but several studies reported HC after UA for other indications. A systematic full endocrine investigation for all adrenal mass is not systematic and dexamethasone suppression test (DST) is not recommended in non-Cushing functioning tumours. Double secretion (autonomous cortisol co-secretion) is a rare phenomenon. The purpose of the study was to review incidence of postoperative HC in a tertiary centre.

Retrospective study (2012-2020) looking for hypocortisolemia after UA in patients operated for Cushing Syndrome and other endocrine tumours. Pre- and postoperative laboratory findings were reviewed in a total of 115 patients with UA. Patients receiving perioperative dexamethasone (DEX) for nausea and vomiting prophylaxis were included as well.

UA (51 right and 64 left) were performed in 47 women and 68 men (mean age 53.5 y.), laparoscopically in 97 (84.3%, 3 converted). UA indications included: Cushing (8), autonomous cortisol secretion (10, in 2 with combined Conn), Conn syndrome (37), pheochromocytoma (24), non-functioning adenoma (10, adrenal carcinoma (3), adrenal metastasis (19) and other diagnosis (4). 18 patients had a preoperative DST (15.7%). Anaesthesia reports revealed that 53/115 patients received DEX. 51/115 patients had a control of postoperative cortisol level. Hypocortisolemia was observed overall in 28/51 patients, by excluding Cushing patients in 24/45, in 19/53 patients who received DEX and in 7/48 in those without DEX. Confusion comes when patients receiving DEX had normal postoperative cortisolemia.

The fact that some patients received DEX (ERAS pathway), complicated the interpretation of cortisol levels at postoperative day one (D1). DEX is known to supress the hypothalamic-pituitary-adrenal axis (HPA axis) at D1. Thus, claiming that hypocortisolemia is the result of cortisol co-secretion (adenoma with double secretion), also able to supress the HPA axis, is not possible in patients who received DEX. These results suggests 1) to fully investigate all hormone functions in case of adrenal mass and 2) not administrating DEX in patients undergoing UA, for adequately assessing the HPA axis function postoperatively.

#### Robotic-assisted Right Colectomy with CME and D3 Lymphadenectomy for Colon Cancer

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**Background:** There is increasing scientific evidence that complete mesocolic excision (CME) and D3 lymphadenectomy (D3LN) improve the oncological outcome of surgical resection for right-sided colon cancer. We introduced robotic-assisted laparoscopic right colectomy in our institution and standardized it for CME and D3LN for curative resection of right-sided colon cancer.

**Methods:** We started robotic-assisted (daVinci Xi, Intuitive) right colectomy for colon cancer in March 2016. After a learning period with standard right colectomy we changed to routine CME and D3LN with a suprapubic approach in October 2019. We collected all patient data in a prospective database (AQC), classifying postoperative complications according to Clavien-Dindo. We performed a retrospective analysis of our data comparing the operations with CME + D3LN versus the earlier cohort. Endpoints were number of lymph nodes in the specimen and postoperative complications.

**Results:** We performed 65 robotic-assisted right colectomies (RARC) in our institution from March 2016 until May 2022. The patients were 69 years old on average, 35 (53.8%) males and 30 (46.2%) females. The number of lymph nodes in the specimen were significantly higher in the group

with CME and D3LN (n = 25.1) as compared to the earlier cohort (n = 17.7), p = 0.003. There was no statistically significant difference in postoperative complication rates.

**Conclusions:** Standardized robotic-assisted right colectomy with CME and D3 lymphadenectomy for curative resection of colon cancer is feasible and safe. It allows extended lymphadenectomy without comprising patient safety.

Clavien-Dindo	Standard	CME + D3LN
0	59.5%	56.5%
1/2	28.6%	34.8%
3a/b	4.8%	8.7%
4a/b	2.4%	0.0%
5	4.8%	0.0%

## Intraabdominal complication after splenectomy – a paradigm shift in routinely performed inflammatory markers

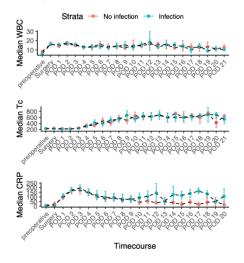
Laetitia Zoë Hampe, Suna Erdem, Rosita Sortino, Markus von Flüe, Martin Bolli, Christoph Kümmerli

**Background:** Patients with resectable tumors in the body or the tail of the pancreas undergo splenectomy as a standard procedure. In order to identify postoperative complications, peripheral blood inflammatory markers, such as white blood cell count (WBC), are routinely assessed knowing that an elevated WBC count is also considered a physiologic process after splenectomy. The aim of this study was to determine if routine inflammatory markers (i.e., WBC, platelet count (PCT) and C- reactive protein (CRP)) can be used effectively to predict postoperative intraabdominal infection.

**Methods:** This retrospective study included all patients who underwent surgery for distal and total pancreatectomy with splenectomy between 2014 and 2021. Postoperative peripheral blood draws assessing CRP, WBC and PCT were performed beginning on day one after surgery and were continued until discharge or day 21. Patients were screened for intraabdominal infection, determined as intraabdominal fluid collection on imaging studies.

**Results:** 63 patients were included, of which 38 (60,3%) were treated with a left/distal pancreatectomy. In 40 of the 63 patients (63.5%), postoperative inflammation occurred, 15 (37.5%) of these presented with intraabdominal infection. Postoperative CRP elevation on day 10 was most indicative for intraabdominal infection, while elevation of WBC and PCT was not significant.

**Conclusion:** WBC and PCT are not reliable markers to identify postoperative complications. CRP elevation on postoperative day 10 is the only indicative parameter to detect intraabdominal infection.



## Osteopenia resistent to therapy: Phosphaturic mesenchymal tumor as a rare cause

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Background: Phosphaturic mesenchymal tumor (PMT) is a rare neoplasm of bone and/or soft tissue origins which ectopically secretes a fibroblast growth factor 23 (FGF23), responsible for the phosphate homeostasis. The high blood levels of FGF23 causes hypophosphatemia and hypovitaminosis D. The compensatory mobilization of calcium and phosphate from bones manifests clinically as widespread osteomalacia which can lead to pathological fractures.

**Methods:** We report a case of a 44-year-old man with more than a year history of progressive immobilizing back pain. Laboratory blood results showed hypophosphatemia, high bone-specific alkaline phosphatase and high levels of FGF23. X-Ray and MRI revealed diffuse osteopenia, older sacral fracture and bone edema in femoral neck. The previous attempts to manage osteomalacia with vitamin D and phosphate supplementation were consequently useless. The PET CT showed a tumor in left thigh adductor region. The core needle biopsy confirmed the suspected diagnosis of PMT.

**Results:** The patient underwent a surgical resection. Thereafter, we noted a sharply decreased level of FGF23 associated with an improved phosphatemia and a complete relief of systemic pain.

**Conclusions:** The diagnosis of PMT can be delayed even for years due to non-specific symptoms. The measurement of serum level of FGF23 is a straightforward diagnostic way. Complete surgical removal of the PMT is the treatment of choice and results in the resolution of the osteomalacia, blood abnormalities and pain.

#### Swiss consensus on the management of acute diverticulitis

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**Background:** Management of acute diverticulitis (AD) has changed in the last years, with notably recent guidelines published by international medical societies. The aim of the study was to reach a consensus on AD management.

Methods: A 3-round Delphi process was performed in Switzerland, including surgeons from 40 hospitals. Agreement of ≥70% was considered to indicate consensus.

Results: On initial workup, leucocytes count (87%), CRP (98%) and imaging (98%) were parameters that reached consensus for the diagnosis, but no AD classification was retained. Signs of generalized peritonitis (100%), requiring intravenous pain medication (98%), inability to tolerate oral intake (95%), lack of adequate social network (86%), immunosuppression (96%), and complicated AD on CT (84%) were criteria for hospitalization. Persisting symptoms (95%) and immunosuppression (89%) were criteria for elective colonic resection. In case of abscess, a size  $\geq$  4 cm reached consensus for percutaneous drainage (88%). No consensus were reached for surgical approach and technique in emergency settings, apart from damage control surgery which was an option for unstable patients (70%).

**Conclusion:** Consensus was reached for several diagnosis, hospitalization, and elective surgery criteria. Emergency surgical management and follow-up seemed however less standardized. These variations should be further assessed, and particularly their evolution in the context of the latest published recommendations.

#### Inhibition of SUMOylation Modulates the Immunosuppressive Microenvironment of Pancreatic Cancer

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**Introduction:** Pancreatic cancer (PC) has been poorly responsive to immunotherapy so far. The Small Ubiquitin-like MOdifier (SUMO) pathway is upregulated in PC and correlates with poor survival.

TAK-981 is an inhibitor of SUMO and has demonstrated induction of antitumor immune responses in preclinical models. Our hypothesis is that TAK-981 will modulate the tumor microenvironment and increase antitumor immunity in PC.

**Methods:** A 3-dimensional organoid cell line derived from a genetically-engineered "KPC" mouse was injected orthotopically into the head of the pancreas. Once tumors reached 5 mm in diameter, mice were randomized to the control vs. TAK-981 (15mg/kg daily, i.p.) group. Tumors were harvested on day 14 for further analysis.

**Results:** Tumor growth (Fig. 1) in the TAK-981 group (mean  $\pm$  SD volume = 207  $\pm$  109 mm³) was significantly inhibited compared to the control group (595  $\pm$  141 mm³, p < 0.01). Immunohistochemical staining for CD 31 (Fig. 2) and Caspase 3 indicated a reduction of angiogenesis and increased apoptosis of tumor cells. Gene expression analysis showed a 26-fold increase in Interferon beta (p<0.05), and an almost 2- fold increase in CD80 (p<0.05) and CD86 (p = 0.14) in the TAK-981 group.

**Conclusion:** Our results suggest that the inhibition of SUMOylation with TAK- 981 is associated with improved local tumor control and changes in the immunosuppressive tumor microenvironment. We expect that TAK- 981 will improve PC responsiveness to immunotherapy, such as with checkpoint inhibitors.

Fig. 1 Tumor growth

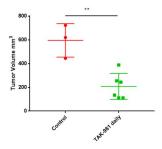
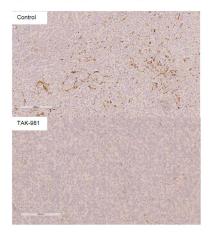


Fig. 2 Immunohistochemistry - CD 31



## Mechanical colonic obstruction as a rare manifestation of pancreas cancer metastasis

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**Background:** Pancreatic cancer is the 4th leading cause of cancer-related mortality in Switzerland, with a relative 5-year survival of 13%. Diagnosis is often delayed, with metastatic cancer at the time of diagnosis, typically in the liver, peritoneum, lungs and more rarely in bones. Colon metastases are rare, with only less than 10 cases described in the literature.

We describe the case of a sigmoidal metastasis from pancreatic cancer presenting as a mechanical obstruction.

**Method:** Female, 55 years old, known for a history of ductal adenocarcinoma of the pancreas body staged IA 3 years ago treated by caudal spleno-pancreatectomy followed by chemo- therapy, a well-differentiated hepatocellular carcinoma of seg-ment III treated by wedge resection at the same time, and a di- verticular disease with a normal colonoscopy 4 years ago, came to the emergency with sigmoid obstruction confirmed by CT-scan.

Results: Obstructive sigmoid tumor was confirmed by emergency endoscopy. Next day, due to clinical deterioration, an emergency oncological sigmoidectomy and terminal colostomy were performed. Surgical exploration did not find peritoneal carcinosis or hepatic metastasis. Pathological analyses were entirely consistent with a metastasis of known ductal-type adenocarcinoma of the pancreas, staged yM1 (sigmoid, lymph nodes 3/24) R0. Work-up was completed by a PET-CT, which was negative. Adjuvant palliative chemotherapy with Gemcitabine and Capecitabine was started.

**Conclusion:** Although colonic metastases from pancreatic cancer are extremely rare, they have been described few times in the literature. Based on literature, risk factors for this particular event cannot be identified for this clinical case. Although rare, colonic metastasis should be considered in obstructive colonic tumors in patients with a history of pancreatic cancer.

## Combined expression of fascin-1 and MAP17 in colorectal cancer: A group of patients in high risk

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**Background:** Fascin and MAP17 are two well-known stem cell markers that have been previously shown to be associated with aggresive clinical features in cancer. This study aimed to assess their expression patterns and clinical significance in colorectal cancer.

**Methods:** Immunohistochemistry was used to assess the expression of fascin-1 and MAP17 in 111 specimens from patients with primary resectable colorectal cancer. Results were correlated with clinicopathological characteristics and survival data.

**Results:** Fascin-1 and MAP17 expression levels were associated with progressive anatomic disease extent (p = 0.005), higher T classification (p = 0.033), lymph node metastasis (p = 0.002), high grade tumors (p = 0.002), and vascular invasion (p = 0.021). All patients with combined high fascin-1 and MAP17 expression died within 46 months after surgery, whereas patients with low fascin-1 and MAP17 expression had an excellent 5-year overall survival rate of 92.8% (95% CI: 83-98). Concerning 3-year PFS, only 14.3% (95% CI: 11-30) of patients with combined high expression of both biomarkers did not experience recurrence or death within 30 months of surgery.

**Conclusions:** Conclusions; Combined high expression of fascin-1 and MAP17 identifies a group of patients with poor early overall survival, indicating therefore targeted therapy's necessity.

## Are positive resection margins a bad prognosis factor in patients with locally advanced diffuse gastric cancer?

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**Background:** Some authors suggested that microscopic involvement of the proximal margin (R1 resection) might not influence overall survival (OS) in case of advanced gastric cancer. However, these results were shown in small series with large heterogeneity of patients and gastric cancer types. Diffuse cancers appear to have a very poor prognosis in comparison with intestinal type. This study aimed to assess OS of patients with R0 and R1 gastric margin resections in patients with diffuse gastric cancers after gastrectomy.

**Methods:** All consecutive patients from 2 international tertiary centers operated with curative intent for diffuse gastric cancer between January 2000 and December 2018 were collected. Lymph node involvement was based on pathology. Kaplan-meier curves with log-rank test for comparison were used to evaluate survival between groups.

**Results:** A total of 108 patients with diffuse gastric cancer were included. No difference in terms of preoperative data and intraoperative characteristics was found between the R0 and R1 groups. Median OS was better in the R0 group (27 months, 95% CI 17-37) compared to R1 group (7 months, 95% CI 3-11, p<0.001). Similar results were found with RFS (25 vs. 6 months, p = 0.002). On multivariable analysis, T stage and resection margin (R status) were independent factors predicting OS (T stage: HR 4.5, p<0.001, R status: HR 4.2, p<0.001) and DFS (T stage: HR 2.9, p = 0.004, R status: HR 3.5, p = 0.001) in the cohort of patients with lymph node involvement.

**Conclusion:** Even though gastric cancer with diffuse type has extremely poor prognosis, the present results suggest that patients with negative surgical margins have better OS compared to patients with positive margins in case of locally advanced diffuse gastric cancer.

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