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ABSTRACTS WITH ORAL PRESENTATION BEST ABSTRACT AWARD

HEPATITIS E SEROPREVALENCE IN SOLID ORGAN TRANSPLANT RECIPIENTS IN CROATIA

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Introduction. Hepatitis E virus (HEV) is an emerging infectious disease and growing concern in Europe. After solid organ transplantation (SOT), patients are at a greater risk of developing acute and chronic graft hepatitis with progression to cirrhosis. Consumption of undercooked or raw pig meat is the main route of HEV infection in developed countries. However, risk factors for the acquisition of HEV among SOT recipients are incompletely understood. This study aimed to determine HEV exposure in a SOT cohort.

Materials and methods. In this cross-sectional study, 639 SOT recipients were screened for anti-HEV IgG seroprevalence on routine post-transplant outpatient visits during the 2002-2017 period. There were 420 patients after liver transplantation (LT) and 219 patients after kidney transplantation (KT). Serum samples were tested for anti-HEV IgG using an enzyme immunoassay (Mikrogen, Neuried, Germany). All participants completed a risk factor assessment questionnaire.

Results. Anti-HEV IgG seroprevalence was 21% in LT recipients and 16.4% in KT recipients. The majority of the recipients were male (68.4%), median age 58 (range 18-80) years. Anti-HEV IgG positive recipients were older (p=0.029) and more often lived in a rural area (p=0.045) as compared with anti-HEV negative recipients. There was no significant difference in HEV seroprevalence according to the type of transplanted organ, gender, level of education, number of household members, having a farm within a household, type of sewage system, or type of drinking water supply. Contrary to initial assumptions, production and/or consumption of cured meat and occupational exposure had no statistically significant strength of association with anti-HEV IgG seropositivity.

Conclusion. Our results show that anti-HEV IgG seroprevalence is high among SOT recipients (19.4%). Socio-demographic factors for exposure to HEV are the basis for further research of sources and routes of transmission and clinical significance of HEV infection after SOT.

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COMPUTED TOMOGRAPHY FOR THE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA IN ADULTS WITH CHRONIC LIVER DISEASE – A COCHRANE SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction and objective. Hepatocellular carcinoma (HCC) occurs mostly in people with chronic liver disease and its global incidence and mortality is on a rise[1]. Computed tomography (CT) represents a second-line imaging test to confirm HCC suspected on prior diagnostic tests and to assess the potential for resectability. According to current guidelines, imaging alone is sufficient to diagnose HCC, however, a significant number of HCCs are missed due to the absence of typical imaging features[2,3]. Conflicting results exist on the benefits of surveillance programs, which may be due to inaccurate detection. Objectives of this review are to assess diagnostic accuracy of CT for diagnosing HCC at any size and stage and diagnosing HCC as being resectable.

Methods. We searched the Cochrane Hepato-Biliary Trials Register, the Cochrane Library, MEDLINE, Embase, LILACS, Science Citation Index Expanded, and Conference Proceedings Citation Index-Science until May 4, 2021, for the studies assessing diagnostic accuracy of CT for the diagnosis of HCC using pathology of the explanted liver and histology of resected or biopsied focal liver lesion with follow-up as a reference standard. We screened studies, extracted data, and assessed the risk of bias and applicability concerns, using the QUADAS-2 checklist.

Results. We included 21 studies with a total of 3101 participants. We judged all studies to be at a high risk of bias due to the use of different and inappropriate reference standards and absence of time interval between CT and reference standard. Regarding applicability, we judged 86% (18/21) of the studies to be at high concern mainly due to the participants being patients on liver transplant list. The sensitivity and specificity of CT for detecting HCC were 77.5% (95% CI 70.9% to 82.9%) and 91.3% (95% CI 86.5% to 94.5%), respectively. The sensitivity and specificity of CT for detecting resectable HCC were 71.4% (95% CI 60.3% to 80.4%) and 92.0% (95% CI 86.3% to 95.5%), respectively. The observed heterogeneity in the results remains mostly unexplained.

Conclusion. We found that using CT in detecting HCC, 22.5% of people with HCC would be missed, and 8.7% of people without HCC would be unnecessarily treated. Also, 28.6% of people with resectable HCC would improperly not be submitted to resection, while 8% of people without HCC would undergo inappropriate surgery. The high risk of bias and high applicability concerns in the included studies limit our ability to confidently draw conclusions based on our results.

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References

1. Bray F, Ferlay J, Soerjomataram I, *et al*. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin, 2018;68:394-424. doi: 10.3322/caac.21492
2. Galle PR, Forner A, Llovet JM, *et al*. EASL Clinical Practice Guidelines: management of hepatocellular carcinoma. J Hepatol. 2018;69:182-236. doi: 10.1016/j.jhep.2018.03.019
3. Lee JH, Lee JM, Kim SJ, *et al*. Enhancement patterns of hepatocellular carcinomas on multiphasic multidetector row CT: comparison with pathological differentiation. Br J Radiol. 2012;85:e573-e83. doi: 10.1259/bjr/86767895

DERANGED LIVER BLOOD TESTS AT HOSPITAL ADMISSION HAVE SIGNIFICANT PREDICTIVE CAPACITY FOR 30-DAY CLINICAL OUTCOMES OF PATIENTS WITH COVID-19

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Introduction and objective. Derangement of liver blood tests (LBT) is frequent in patients with coronavirus disease 2019 (COVID-19), but their predictive capacity in terms of short-term clinical outcomes has been disputed. In this study, we aimed to analyze the prevalence of deranged LBT in patients with COVID-19 at admission to the hospital and their association with 30-day outcomes.

Methods. Consecutive patients with COVID-19 hospitalized in a single referral hospital over a 12-month period were included. Clinical severity of COVID-19 at hospital admission and 30-day outcomes (need for intensive care, mechanical ventilation, or death) were analyzed. LBTs were collected at hospital admission, and they were considered deranged if outside the reference intervals. Liver injury was considered in patients with elevated total bilirubin level in addition to deranged liver enzymes.

Results. Deranged LBTs were observed in 2854/3812 (74.9%) patients, most frequently due to elevation of aspartate transaminase (AST) (61.6%), gamma-glutamyl transferase (GGT) (46.1%) and alanine transaminase (ALT) (33.4%). Elevated AST, ALT and GGT, and low albumin were associated with a more severe disease at admission. However, in multivariate Cox regression analysis, when adjusted for age, sex, obesity and presence of chronic liver disease, only AST remained associated with the risk of dying (hazard ratio (HR) 1.5081 and 2.1315 for 1-3x upper limit of normal (ULN) and >3x ULN elevations, respectively), independently of comorbidity burden and COVID-19 severity at admission. AST at the respective cut-offs <22 U/L and >91 U/L could be used to rule out and rule in the risk of 30-day mortality in hospitalized patients with COVID-19 with >90% sensitivity and specificity. Patients with liver injury more frequently experienced the defined adverse outcomes in comparison to patients who only had elevated liver enzymes.

Conclusion. Derangement of LBTs is frequently observed among patients with COVID-19 at hospital admission. Elevated AST and presence of liver injury might be used as predictors of adverse clinical outcomes in these patients.

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ABSTRACTS WITH ORAL PRESENTATION

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN THE PREVENTION OF POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS: REAL-LIFE EXPERIENCE FROM A SINGLE TERTIARY CARE CENTER

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Introduction and objective. Endoscopic retrograde cholangiopancreatography (ERCP) is a therapeutic procedure used for treating pancreatobiliary conditions. Post-ERCP pancreatitis is a relatively common complication of the procedure and non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to reduce the incidence of post-ERCP pancreatitis[1]. The objective of this study was to analyze the incidence of post-ERCP pancreatitis and hyperamylasemia in patients in whom ERCP was performed for the first time, before and after the introduction of routine NSAID prophylaxis in everyday clinical practice.

Methods. Medical records of patients undergoing ERCP in the periods from January 2012 until December 2014 and from January 2019 until July 2021 were analyzed for general patient data, NSAID usage, and compli-

Table 1. Comparison of NSAID and non-NSAID patients

		NSAID	non-NSAID
Patients (n)		495	616
Age (years)		67±16	67±15**
Female, n (%)		257 (52%)	363 (59%)*
Indication, n (%):			
	Choledocholithiasis	331 (66.9%)	401 (65.1%)
	Cholangitis	101 (20.4%)	76 (12.3%)
	Benign biliary obstruction	21 (4.2%)	28 (4.5%)
	Malignant biliary obstruction	108 (21.8%)	101 (16.4%)
	Acute pancreatitis	42 (8.5%)	57 (9.3%)
	Chronic pancreatitis	8 (1.6%)	9 (1.5%)
	Miscellaneous	41 (8.3%)	24 (3.9%)
Periampullary diverticulum, n (%)		60 (12.1%)	73 (11.9%)**
Post-ERCP pancreatitis, n (%)		13 (2.6%)	39 (6.3%)*
Hyperamylasemia n (%)		46 (9.3%)	174 (28.2%)*

NSAID = non-steroidal anti-inflammatory drugs; ERCP = endoscopic retrograde cholangiopancreatography; χ^2-test and Mann-Whitney U test; *$p<0.05$; **nonsignificant

cations. Post-ERCP pancreatitis is defined as the occurrence of pain with elevated amylase concentrations at least three times above the upper limit of normal, more than 24 hours after ERCP. The χ^2-test and Mann-Whitney U test were used to compare discrete and continuous variables, with the level of statistical significance set at $p<0.05$.

Results. A total of 1111 ERCP-naïve patients were analyzed. Patients were split in two groups, one receiving and the other not receiving NSAID prophylaxis (495 *vs*. 616 patients, respectively). There was no difference in age (NSAID 67±16 yrs *vs*. non-NSAID 67±15 yrs, p=0.49). The group of patients that did not receive NSAID prophylaxis had a higher proportion of females (52% *vs*. 59%, p=0.02) and lower ASA class ($p<0.05$). The group of patients that received NSAID prophylaxis had lower rates of post-ERCP pancreatitis (2.6% *vs*. 7.2%, $p<0.05$) and transient hyperamylasemia (9.3% *vs*. 28.2%, $p<0.05$) (Table 1).

Conclusion. Data from real-life experience demonstrated the introduction of NSAID prophylaxis in routine clinical practice to have resulted in a significant decrease in post-ERCP pancreatitis.

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Reference

1. Pekgöz M. Post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review for prevention and treatment. World J Gastroenterol. 2019;25:4019-42. DOI: 10.3748/wjg.v25.i29.4019

ACCURACY OF SERUM BIOMARKERS IN THE DIAGNOSIS OF STEATOSIS, FIBROSIS, AND INFLAMMATION IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE IN COMPARISON TO LIVER BIOPSY

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Introduction and objective. The diagnosis of nonalcoholic fatty liver disease (NAFLD) represents a clinical challenge in everyday practice since most patients are asymptomatic. In the last decade, numerous laboratory tests and biomarkers for steatosis, inflammation, and fibrosis detection, as well as imaging methods have been intensively investigated. The aim of this study was to evaluate diagnostic performance of various biomarkers of steatosis, fibrosis and inflammation in comparison to liver biopsy in patients with NAFLD.

Methods. This was a cross-sectional study that included 135 patients with biopsy proven NAFLD. Fatty liver index (FLI), hepatic steatosis index (HSI), cell death markers (CK-18 M30 and CK-18 M65), FIB-4 index, NAFLD fibrosis score (NFS), BARD and AST to Platelet Ratio Index (APRI) were calculated and analyzed. Liver biopsy was performed under ultrasound guidance and according to a standardized protocol using the 16G Temno needle. By using the NASH CRN scoring system and NAFLD activity score (NAS), steatosis (0-3), ballooning (0-2), lobular inflammation (0-3) and fibrosis (0-4) were evaluated

Results. FLI, HSI scores and cell death biomarkers showed poor diagnostic accuracy for steatosis detection and quantification with an area under the curve (AUC) <0.70. Cell death biomarkers did not perform well for detection of nonalcoholic steatohepatitis (NASH) (AUC <0.7) either. As for fibrosis staging, only APRI and cell death biomarkers showed moderate accuracy (AUC >0.7) for advanced fibrosis, whereas FIB-4, BARD and NFS score demonstrated poor performance (AUC <0.70). However, a combination of FIB-4 and NFS with cell death biomarkers had moderate accuracy for advanced (≥F3) fibrosis detection with AUC >0.70.

Conclusion. In this first study on Croatian patients with NAFLD, serum biomarkers demonstrated poor diagnostic performance for noninvasive diagnosis of liver steatosis and NASH. APRI and cell death biomarkers had only moderate accuracy for advanced fibrosis, as well as the combination of FIB-4 and NFS with cell death biomarkers. Further studies regarding serum biomarkers for all NAFLD stages are needed.

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COMPARING QUADRUPLE CONCOMITANT AND TAILORED THERAPY FOR ERADICATION OF *HELICOBACTER PYLORI* INFECTION

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Introduction and aim. Given the high resistance to clarithromycin in the Split-Dalmatia County, the primary aim of this study was to compare the empirical quadruple concomitant and personalized therapy for eradication of *Helicobacter pylori* (*H. pylori*) infection based on the previous antibiotic sensitivity test as a potential first-line treatment[1-3].

Methods. As part of an open-label, randomized clinical trial, 80 treatment-naïve patients with *H. pylori* infection were randomized to either concomitant quadruple therapy (esomeprazole 40 mg, amoxicillin 1 g, metronidazole 500 mg, clarithromycin 500 mg BID for 14 days) or personalized therapy based on the previous antibiotic sensitivity test. The eradication rate was assessed 4 weeks after treatment.

Results. The eradication rate was significantly higher in the personalized treatment *vs*. quadruple concomitant treatment arm, both in the intention-to-treat (70% *vs*. 92.5%, p=0.010) and in the per-protocol (87.5% *vs*. 100%, p=0.030) analysis. We also verified an increasing rate of antibiotic resistance among strains (clarithromycin 37.5%, metronidazole 17.5%, dual resistance 10%). Adverse reactions were more frequent in the concomitant quadruple treatment arm (32.5% *vs*. 7.5%, p=0.006).

Conclusion. Personalized therapy achieves better efficiency in *H. pylori* eradication with a lower rate of adverse reactions. In the times of the increasing issue of bacterial resistance, an eradication approach with these characteristics should be considered as a potential first-line treatment.

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References

1. Perkovic N, Mestrovic A, Bozic J, Ivelja MP, Vukovic J, Kardum G, *et al*. Randomized clinical trial comparing concomitant and tailored therapy for eradication of *Helicobacter pylori* infection. J Pers Med. 2021 Jun 9;11(6):534. doi: 10.3390/jpm11060534.1
2. Graham DY. Transitioning of *Helicobacter pylori* therapy from trial and error to antimicrobial stewardship. Antibiotics. 2020;9:671. doi:10.3390/antibiotics9100671
3. Megraud F, Coenen S, Versporten A, Kist M, Lopez-Brea M, Hirschl AM, Glupczynski Y. *Helicobacter pylori* resistance to antibiotics in Europe and its relationship to antibiotic consumption. Gut. 2012;62:34-42.

ABSTRACTS – POSTER PRESENTATIONS

A YOUNG PATIENT WITH DYSPHAGIA: EOSINOPHILIC ESOPHAGITIS, ACHALASIA, OR ATYPICAL COURSE OF GASTROESOPHAGEAL REFLUX DISEASE: A CASE REPORT

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Introduction and aim. Differential diagnosis of esophageal symptoms, especially dysphagia with suspicion of esophageal obstruction in young patients may represent a challenge to clinical practice.

Methods. A 19-year-old female patient presented with symptoms of dysphagia, esophageal retention, and endoscopic suspicion of esophageal stricture. This initial evaluation was performed at another institution and the patient was advised to undergo peroral endoscopic myotomy because of the diagnosis of achalasia. Due to long-lasting symptoms, loss of weight and anxiety, and facing the complex endoscopic procedure, the young patient and her family decided to seek second evaluation and opinion at our institution. The evaluation included upper gastrointestinal endoscopy with narrow-band imaging and histology of esophageal mucosa, magnetic resonance imaging of the thorax and abdomen, 24-h esophageal impedance pH monitoring, and esophageal high-resolution monitoring. The results of diagnostic work-up excluded the presence of eosinophilic esophagitis and achalasia, indicating the atypical course of gastroesophageal reflux disease (GERD). The patient underwent intense and combined pharmacological (proton pump inhibitors, H2 blockers, antacids) and endoscopic (repeated balloon-dilatation of esophagogastric junction stricture) therapy over a period of two years. With this combined and long-lasting therapy, the patient significantly improved, clinically. The esophageal peristaltic activity was also recovered, yet incompletely. The patient remained well and gaining weight with minimal symptoms.

Conclusion. In the case of a young female patient presented, we witnessed the overlapping nature of different criteria denoting distinct entities, linked to esophageal dysphagia and esophageal motility disorder, such as achalasia, eosinophilic esophagitis and GERD. The complex diagnostic approach including esophageal functional testing pointed to the presence of GERD as the underlying condition for this complex clinical situation. The combined therapeutic approach, including antisecretory agents and repeated balloon dilatations, led to significant clinical improvement.

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References

1. Vissagi P, Savarino E, Sciume G, Di Chio T, Bronzini F, Tolone S, *et al*. Eosinophilic esophagitis: clinical, endoscopic, histologic and therapeutic differences and similarities between children and adults. Ther Adv Gastroenterol. 2020;14:1-17. doi: 10.1177/17562 84820980860.
2. Nijhuis RAB, Zaninoto G, Roman S, *et al*. European guidelines on achalasia: United European Gastroenterology and European Society of Neurogastroenterology and Motility recommendations. United Eur Gastroenterol J. 2020;8(1):13-33.
3. Herbella FA, Patti MG. Gastroesophageal reflux disease: from pathophysiology to treatment. World J Gastroenterol. 2010 Aug 14;16(30):3745-9. doi: 10.3748/wjg.v16.i30.3745.

COVID-19 MANIFESTATIONS ON SMALL INTESTINE: A CASE REPORT

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Introduction and aim. The acute COVID-19 infection can cause changes, not only on respiratory system, but on many other organs[1,2]. According to recent findings, it is reasonable to assume that endothelial dysfunction contributes to COVID-19-associated vascular inflammation, particularly endotheliitis, in the lung, heart, kidney and intestine, as well as COVID-19-associated coagulopathy, particularly pulmonary fibrinous microthrombi in alveolar capillaries[3], and in our case also in the intestine (ACE2 receptor is expressed on endothelial cells (ECs) in the lung, heart, kidney, and intestine). The aim of this case report is to present a clinical case that could combine the relationship of COVID-19 infection and changes of small intestine integrity during the infection period[1-3].

Case report. We present an 81-year-old female patient who had severe form of COVID-19 infection. During previous hospitalization at another hospital, she underwent upper gastrointestinal endoscopy and colonoscopy on several occasions due to suspected gastrointestinal bleeding. They performed three upper gastrointestinal endoscopies and one colonoscopy (without terminal ileum intubation). At that hospital, she was suspected to have bleeding from the small intestine. Because of the severe form of clinical infection, she was transmitted to our university hospital, ICU-COVID department. After the patient was stable, we continued with endoscopic gastrointestinal investigations that included three upper endoscopy procedures and push small intestine endoscopy procedure (enteroscopy, Olympus). There were no findings of gastrointestinal bleeding, but multi-slice computed tomography angiography performed at our Radiology Department was highly suggestive of jejunum bleeding. Therefore, we decided to use the Olympus video endo-capsule system.

Results. On video endo-capsule procedure, we detected multiple submucosal hematomas and bleeding erosions in the middle part of the small intestine, which resolved the diagnostic problem. Two selected photos are presented in Figure 1.

Conclusion. This case indicated the possible influence of SARS-CoV-2 infection on small intestine mucosa integrity and coagulation. Further research is needed to confirm the preliminary results and elucidate the possible mechanisms.

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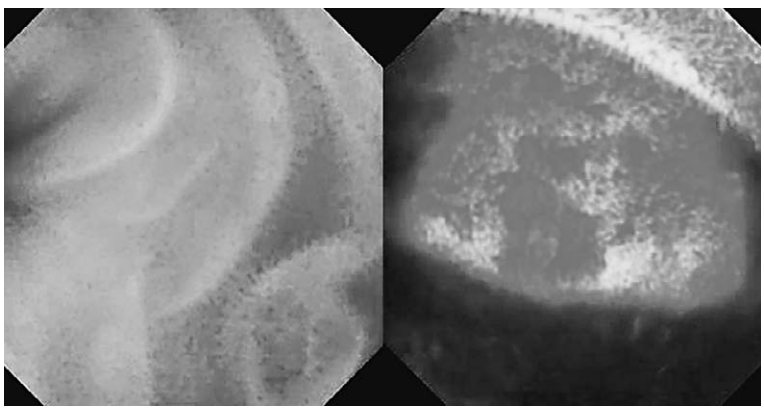


Fig. 1. Video endo-capsule image of small intestine: submucosal hematoma of jejunum (left) and vascular mucosal defects of jejunum (right).

References

1. Gupta A, Madhaven MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, *et al*. Extrapulmonary manifestations of COVID-19. Nature Med. 2020;26:1017-32.
2. Leal T, Costa E, Arroja B, Goncalves R, Alves J. Gastrointestinal manifestations of COVID-19: results from a European centre. Eur J Gastroenterol Hepatol. 2021;33(5):691691.
3. Zhang J, Tecson KM, McCullough AP. Endothelial dysfunction contributes to COVID-19-associated vascular inflammation and coagulopathy. Rev Cardiovasc Med. 2020 Sep 30;21(3):315-9. PMID: 33070537; doi: 10.31083/j.rcm.2020.03.126.S

INFLAMMATORY BOWEL DISEASE AND HEMATOLOGIC TUMORS

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Introduction and aim. Gastrointestinal and extraintestinal malignancies are long-term complications in patients with inflammatory bowel disease (IBD), likely as a result of chronic inflammation and immunomodulatory medications used to control inflammation[1,2]. Here, we assessed the occurrence of malignancies in two patients that were treated with azathioprine (AZA), in a large tertiary IBD center at Dubrava University Hospital in Zagreb. Patients with IBD are at a higher risk of intestinal and extraintestinal malignancies than the general population due to therapy with thiopurines[3]. Immunomodulatory therapy used to treat inflammation in IBD patients, such as AZA, 6-mercaptopurine (6-MP), also increases the risk of different types of extraintestinal malignancies such as non-Hodgkin lymphoma, non-melanotic skin cancer, or melanoma and urothelial carcinoma[1-3]. Since there are only scarce data from previous literature and those conclusions were quite contradictory, we decided to present two patients with IBD and extraintestinal malignancies due to immunomodulatory therapy.

Methods. Both patients were diagnosed with IBD/ulcerative colitis and treated with AZA. While treated with immunomodulatory therapy and continuous monitoring due to basic clinical course, both of them developed hematologic malignancies. During his therapeutic procedures and therapy, the male patient (aged 27 years, 10 years with IBD, total duration of intermittent therapy with AZA of 3 years) developed acute monocytic leukemia. The female patient (aged 79 years, 40 years with IBD, total duration of intermittent therapy with AZA of 5 years) developed plasmacytoma/multiple myeloma, diagnosed by standard procedure.

Conclusion. Our data support the assumption of other authors that a long-standing disease course and immunosuppressive therapy increase the risk of developing malignancies in IBD patients. Wide use of immunomodulatory therapy in treating IBD patients raises actually big concerns because of the potential risks of developing malignancies. Since the data from different sources were quite contradictory, we suggest closer and longer clinical monitoring.

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References

1. Medanchi M, Zeits J, Barthel C, Samaras P, Scharl S, Sulz MC. Malignancies in patients with inflammatory bowel disease: a single-centre experience. Digestion. 2016;94(1):1-8. doi: 10.1159/000447259. PMID: 27318857
2. Biancone L, Onali S, Petruzziello C, Calabrese E, Pallone F. Cancer and immunomodulators in inflammatory bowel diseases. Inflamm Bowel Dis. 2015 Mar;21(3):674-98. doi: 10.1097/MIB.0000000000000243. PMID: 25545375
3. Kotlyar DS, Lewis JD, Beaugerie L, Tierney A, Brensinger CB, Gisbert JP. Risk of lymphoma in patients with inflammatory bowel disease treated with azathioprine and 6-mercaptopurine: a meta-analysis. Clin Gastroenterol Hepatol. 2015 May;13(5):847-58.e4; quiz e48-50.; doi: 10.1016/j.cgh.2014.05.015.

POST COVID-19 COLON AND ANORECTAL MANIFESTATIONS: A CASE REPORT

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Introduction and aim. The COVID-19 infection can cause changes on many organs during acute period[1,2]. The post-COVID gastrointestinal manifestations are still under observation and evaluation. The aim of this case report is to present a case of the relationship of COVID-19 infection with changes in bowel and anorectum peristaltic activity in the post COVID-19 infection period.

Methods. We present a 70-year-old male patient who had a mild form of COVID-19 infection. About 1 month after acute infection, the patient presented with diarrheal syndrome and fecal incontinence. Microbiological samples were negative for bacterial, parasitic, viral and mycotic infection. Fecal calprotectin and C-reactive protein were within the normal range. Colonoscopy with histologic analysis excluded microscopic colitis. After that, the patient underwent anorectal manometry by use of the MMS Solar HRM-360° system with 24-channel perfusion catheter. The anorectal manometry procedure and results were performed and analyzed according to London protocol[3].

Results. We detected normal resting pressure of 45 mm Hg, normal anal canal length, anal squeeze under lower limit of normal value of 70 mm Hg; rectoanal inhibitory reflex test yielded 64% of relaxation; balloon expulsion test was negative with anal pressure decrease during push test. Sensation test had 3 of 4 sensory parameters above the upper limit.

Conclusion. This case indicated the possible influence of SARS-CoV-2 infection on colon and anorectal function integrity. Further research is needed to confirm the preliminary results and elucidate the possible mechanisms.

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References

1. Gupta A, Madhaven MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, *et al*. Extrapulmonary manifestations of COVID-19. Nature Medicine. 2020;26:1017-32.
2. Leal T, Costa E, Arroja B, Goncalves R, Alves J. Gastrointestinal manifestations of COVID-19: results from a European centre. Eur J Gastroenterol Hepatol. 2021;33(5):691691.
3. Scott SM, Carington EV. The London Classification: Improving characterization and classification of anorectal function with anorectal manometry. Curr Gastroenterol Rep. 2020;22:55.

POST COVID-19 MANIFESTATIONS ON ESOPHAGEAL MOTILITY – REALITY OR SPECULATION

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Introduction and aim. Acute COVID-19 infection can cause changes on many organs, but changes in the post infection period are not uncommon either[1,2]. The aim of this study was to assess the relationship of this infection and changes in esophageal motility (manometry parameters) in the post COVID-19 infection period.

Methods. We repeatedly evaluated 21 patients after clinical recovery from COVID-19 infection, who had been diagnosed with ineffective esophageal motility before infection with SARS-CoV-2 virus. All patients enrolled were submitted to re-evaluation because of chest discomfort, swallowing problems, and dysphagia. The potential coexistence of gastroesophageal reflux disease was excluded clinically and on 24-h impedance monitoring. Measurements were performed on the MMS HRM 360° system using 36 channel water perfused catheters according to Chicago 3 protocol[3].

Results. Using high-resolution esophageal manometry and comparing the results to previous functional evaluation before COVID-19 infection, we detected significant lowering of distal contractile integral (321.2±111.5 mm Hg-s-cm *vs*. 212.85±115.08 mm Hg-s-cm) and prolongation of distal latency (5.81±0.91 s vs. 9.75±4.66 s) according to Chicago 3.0 Classification in all study patients ($p<0.05$). In the peristaltic break 2.78±0.59 cm *vs*. 5.21±6.16 cm we detected borderline significance ($p<0.48$). In the contractile front velocity (cm/s), upper esophageal sphincter pressure (mm Hg) and lower esophageal sphincter pressure (mm Hg) there was no significant difference ($p>0.05$).

Conclusion. As part of an ongoing study, these preliminary results on the first 21 patients indicated the possible effect of SARS-CoV-2 infection on esophageal motility. Further research is needed to confirm these results and elucidate the possible mechanisms.

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References

1. Gupta A, Madhaven MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, *et al*. Extrapulmonary manifestations of COVID-19. Nature Med. 2020;26:1017-32. DOI: 10.1038/s41591-020-0968-3
2. Leal T, Costa E, Arroja B, Goncalves R, Alves J. Gastrointestinal manifestations of COVID-19: results from a European centre. Eur J Gastroenterol Hepatol. 2021;33:691-1. DOI: 10.1097/MEG.0000000000002152
3. Herbela FA, Armijo PR, Pastti MG. A pictorial presentation of 3.0 Chicago classification for esophageal motility disorder. Einstein. 2016;14(3):439-42. DOI: 10.1590/S1679-45082016MD3444

PNPLA3 AND NOTCH3 GENE POLYMORPHISMS AS RISK FACTORS FOR ALCOHOLIC CIRRHOSIS DEVELOPMENT AND ITS PROGRESSION TO HEPATOCELLULAR CARCINOMA

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Introduction and aim. Alcohol consumption is a risk factor for the development of alcoholic cirrhosis (AC) and hepatocellular carcinoma (HCC), with 5%-15% of AC patients developing HCC. In the study, we investigated the association between PNPLA3 (rs738409) and Notch3 (rs1043996) single gene polymorphisms (SNP) and the development of AC and its progression to HCC.

Methods. The study included 245 patients transplanted at a single institution due to AC (124 with HCC and 121 without HCC), and 70 patients with no liver conditions. Five-mL blood samples were collected from all study subjects and stored at -80 °C until DNA isolation, after which polymerase chain reaction (PCR) using commercially available kits (TaqMan SNP) helped determine the PNPLA3 (rs738409) and Notch3 (rs1043996) gene polymorphisms[1,2]. The association between the studied polymorphisms and AC and HCC was examined in the dominant, recessive, co-dominant, overdominant and log-additive model[3].

Results. Genotypes were in Hardy-Weinberg equilibrium (p>0.05). Minor allele frequency (MAF) was 41% for PNPLA3 and 27% for Notch3 gene. PNPLA3 (rs738409) gene was associated with an increased risk of AC in the co-dominant (OR 95%CI=6.15 (2.28-16.60) for GG *vs*. CC genotype and 2.78 (1.55-4.97) for GC *vs*. CC genotype), dominant (OR 95%CI=3.36 (1.94-5.82) for GG/GC *vs*. CC genotype), recessive (OR 95%CI=3.71 (1.42-9.69) for GG *vs*. GC/CC genotype), and log-additive model (OR 95%CI=2.60 (1.69-3.99) for G allele). This polymorphism was also responsible for an increased risk of HCC in AC patients in the co-dominant (OR 95%CI=2.88 (1.37-6.03) for GC *vs*. CC genotype), recessive (OR 95%CI=2.72 (1.43-5.17) for GG *vs*. GC/CC genotype), and log-additive model (OR 95%CI=1.63 (1.14-2.34) for G allele). Notch3 (rs1043996) gene polymorphism was associated with a lower risk of AC in the co-dominant (OR 95%CI=0.30 (0.13-0.70) for GG *vs*. AA genotype), recessive (OR 95%CI=0.32 (0.14-0.72) for GG *vs*. GA/AA genotype), and log-additive model (OR 95%CI=0.63 (0.43-0.94) for G allele). On the other hand, no statistically significant correlation was found between the Notch3 gene and the risk of HCC in any of the studied models (p>0.05).

Conclusion. This study demonstrated that PNPLA3 (rs738409) gene polymorphism is a risk factor for AC and for disease progression and development of HCC. On the other hand, Notch3 (rs1043996) gene polymorphism was associated with a lower risk of AC and showed no statistically significant correlation with the risk of HCC.

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References

1. Stickel F, Buch S, Nischalke HD, *et al*. Genetic variants in PNPLA3 and TM6SF2 predispose to the development of hepatocellular carcinoma in individuals with alcohol-related cirrhosis. Am J Gastroenterol. 2018;113:1475-83.
2. Trépo E, Nahon P, Bontempi G, *et al*. Association between the PNPLA3 (rs738409 C>G) variant and hepatocellular carcinoma: evidence from a meta-analysis of individual participant data. Hepatology. 2014;59:2170-7.
3. Zhang Y, Li D, Feng F, *et al*. Progressive and prognosis value of Notch receptors and ligands in hepatocellular carcinoma: a systematic review and meta-analysis. Sci Rep. 2017;7:14809.

DRUG INDUCED GINGIVAL OVERGROWTH IN A PATIENT AFTER LIVER TRANSPLANTATION

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Introduction. Drug induced gingival overgrowth (DIGO) is proliferation of gingival tissue which occurs as a side effect of certain drugs. Immunosuppressants, most commonly cyclosporine, and calcium channel blockers (CCBs) such as nifedipine and diltiazem, are the most important DIGO-inducing drugs. Combining these drugs leads to an even higher risk of developing DIGO. DIGO can be reversed after discontinuation of the drug, although severe cases require surgical treatment. Here we present a case of a patient with DIGO after liver transplantation (LT).

Case report. Twelve months after LT due to alcoholic cirrhosis, a 62-year-old patient noticed enlargement of gingival tissue. He reported the side effect a year and a half after the initial signs. Inspection of the oral cavity revealed generalized gingival hyperplasia, most prominent at the anterior mandible, firm and painless to touch, which caused nodding and dislocation of the lower canines and incisors. Chronic therapy consisted of cyclosporine, mycophenolate mofetil, diltiazem, and simvastatin. After diagnosing DIGO, cyclosporine was replaced with tacrolimus, and diltiazem was discontinued. Resection of the hypertrophied gingival fold was performed with tooth extraction. Complete recovery was achieved two months after the procedure.

Conclusion. Calcineurin inhibitors and CCBs carry a risk of developing DIGO, which in addition to aesthetic changes, significantly impairs the quality of life, affecting speech, feeding, and oral hygiene. Inadequate hygiene favors the development of infection and additional complications. If possible, treatment of choice should be discontinuation of the drug, whereas resistant cases require surgical treatment. An interdisciplinary approach, cooperation of physicians with dentists is necessary for achieving optimal results.

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ABDOMINAL ULTRASOUND – THE LEADING METHOD IN THE DIAGNOSIS OF BLEEDING *CORPUS LUTEUM/RUBRUM*

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Introduction. Ovulation can be a cause of abdominal pain and intra-abdominal bleeding. Bleeding of the *corpus luteum/rubrum* during ovulation can, in some cases, lead to hypovolemic shock. In the case of hypovolemic shock in combination with pain in lower abdomen, it is always necessary to consider ovarian bleeding as a differential diagnosis and perform abdominal ultrasound and consultation with a gynecologist as part of treatment[1,2].

Case report. A 23-year-old female patient was referred *via* Emergency Department due to diffuse abdominal pain persisting for two days. The patient had no major comorbidities and was free of dysuric problems upon arrival. The patient was in the 20th day of menstrual cycle. Palpation revealed abdominal periumbilical pain (predominant in the lower left quadrant), without signs of peritonitis. On arrival, mild leukocytosis was the only significant deviation in laboratory findings. Pregnancy test was negative, and abdominal ultrasound was performed immediately which showed free fluid in the Morrison space, as well as at the medial border of the spleen and in the pelvis. The left ovary was enlarged by a cystic inhomogeneous structure of about 4 cm in size, with no clear flow on color Doppler (Fig. 1). Intra-abdominal bleeding was suspected, and a gynecologist was consulted. Immediately, transvaginal ultrasound was performed and doubt about bleeding of the *corpus luteum/rubrum* was confirmed. Emergency laparoscopy was performed. During the operation, bleeding of the *corpus luteum* with a total of 500 mL of free intra-abdominal hemorrhagic fluid was verified. The bleeding was treated intraoperatively, and the patient was discharged from the hospital in good general condition on postoperative day six.

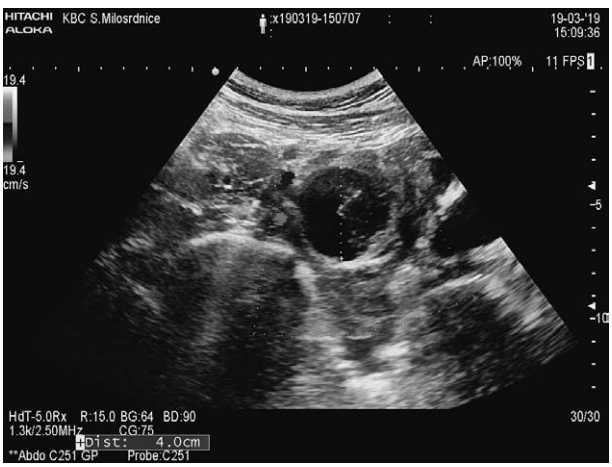


Fig. 1. Enlarged and cystically altered left ovary with an inhomogeneous structure, 4 cm in diameter, without flow recorded on color Doppler.

Conclusion. Abdominal ultrasound may be the leading method in the diagnosis of bleeding *corpus luteum/rubrum*.

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References

1. Bouwman LH, Schmidt GB. Diagnostic image. A woman with peracute abdominal pain in the right lower quadrant. Ned Tijdschr Geneeskd. 2007 Mar 3;151(9):535.
2. de Rooij T, Luttmer R, Tiersma S, Dzelili M. Hypovolemic shock due to ovarian bleeding. Ned Tijdschr Geneeskd. 2021 Aug 5;165:D5276.

EXTRAHEPATIC MANIFESTATION OF HEPATITIS E VIRUS INFECTION – NEUROINVASIVE INFECTION

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Introduction and aim. Hepatitis E virus (HEV) is the most common cause of acute hepatitis worldwide. In the majority of patients, it causes acute, self-limiting disease, but its course can include a broad spectrum of extra-hepatic manifestations, the most common being neurological, occurring in 16.5%-31% of patients. Furthermore, acute HEV infection has been proven in 2.4%-6.9% of patients with neurological disorders. The prevalence of extrahepatic HEV manifestations in Croatia in unknown. In this study, we analyzed the prevalence of HEV infection in patients with a neuroinvasive disease of unproven etiology.

Methods. In the period from 2017 to 2020, 105 adult immunocompromised patients with a neuroinvasive infection from inland Croatia were tested for HEV antibodies using an enzyme immunoassay (ELISA, Euroimmun, Lübeck, Germany). Cerebrospinal fluid (CSF) results suggested viral etiology of the neuroinvasive disease, with exclusion of arboviruses (tick-borne encephalitis, West Nile virus, Usutu virus, Toscana virus and Tahyna virus), lymphocytic choriomeningitis virus, herpes simplex virus, varicella-zoster virus, *Borrelia burgdorferi* and *Listeria monocytogenes*. All samples were initially tested for HEV IgG antibodies. The samples with proven IgG antibodies were additionally tested for the presence of IgM antibodies in order to confirm acute/recent HEV infection.

Results. The study group consisted of 60.9% of male and 39.1% of female subjects, mean age 51.39±19.63 years. HEV IgG antibodies were proven in 16/15.2% of serum samples, while one sample had proven HEV IgM and IgG antibodies, which suggested an acute/recent HEV infection. Furthermore, IgG antibodies were proven in 4/16 (3.8%) CSF samples, while IgM antibodies were not proven in any of the samples.

Conclusion. Although acute neuroinvasive HEV infection of the central nervous system was not confirmed, the finding of IgG antibodies in 3.8% of CSF samples may suggest a possible prior HEV infection. In patients with neuroinvasive infection of unproven etiology, especially in the areas with high HEV infection prevalence, inclusion of HEV in the diagnostic workup should be considered.

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STRONGYLOIDES STERCORALIS HYPERINFECTION – A CASE SERIES

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Introduction and aim. Helminthic infection caused by *Strongyloides stercoralis* (*S. stercoralis*) is common in tropics and very rare in European countries. Autochthonous human infections were documented in inland northern Croatia more than half a century ago[1]. According to recent data, low-grade disease transmission still occurs in the region, while the mortality rate has risen despite a decreased disease incidence[2]. We describe a case series of our patients with hyperinfection in order to explore their demographic data and clinical burden of the disease.

Methods. Retrospective descriptive study of patients with laboratory proven *S. stercoralis* hyperinfection treated at Dr. Fran Mihaljević University Hospital for Infectious Diseases from January 2010 until June 2021.

Results. Among 79 patients with strongyloidiasis, 22 were immunocompromised, five of which developed a hyperinfection. All were males aged 37-81 (median, 64) years, four being from rural areas. The diagnosis was established after 0.5-3 (median, 1.5) months of symptom duration. All patients were cachectic and four were hypoalbuminemic (serum albumin, 13.3-27.7 g/L). Clinical presentations were as follows: recurrent sepsis caused by gastrointestinal flora in two patients, sepsis followed by meningitis, bacterial pneumonia with suspected sepsis, and chronic gastroenterocolitis in one patient each. Nonspecific gastrointestinal symptoms were present in 4/5 patients, while two of these four developed ileus. In all patients, the diagnosis was established accidentally, i.e. by microscopy of gastric/duodenal mucosa in four patients and in bronchial aspirate in one patient. Peripheral blood eosinophilia was absent in 2/5 patients, both of whom died. Despite combined antibiotic, antifungal and anthelmintic therapies (albendazole in all patients; in two additionally ivermectin), 3/5 (60%) patients died.

Conclusions. Significant diagnosis delay and lack of clinical suspicion were observed in our patients with the most severe clinical presentations of strongyloidiasis, which could have contributed to the high mortality rate. Early upper gastrointestinal endoscopy and analysis of mucosal samples could accelerate the diagnosis in patients with gastrointestinal symptoms and secondary bacterial infections of blurred origin. Patients from the Zagreb region should be screened for strongyloidiasis before introducing immunosuppression. Additional education of clinicians is needed, especially those dealing with immunosuppressed individuals.

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References

1. Bezjak B, Breitenfeld V. [Strongyloidosis in northwestern Croatia. (Clinical, diagnostic and therapeutic experiences). G Mal Infett Parassit. 1969;21(1):43-7. (in Italian)
2. Balen Topić M, Marjanović E, Tomasović D, Sviben M. Is strongyloidiasis currently autochthonous in Croatia? [Published online ahead of print, 2021 Sep 14]. Trans R Soc Trop Med Hyg. 2021;trab139. doi:10.1093/trstmh/trab139

KNIFE PRECOAGULATION OF LARGE SUBMUCOSAL VESSELS USING 1-10 FORCED COAGULATION METHOD SIGNIFICANTLY REDUCES COAGULATION FORCEPS USE DURING ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) AND PERORAL ENDOSCOPIC MYOTOMY (POEM)

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Introduction and aim. Intraprocedural bleeding is a major complicating factor that prolongs third-space endoscopy procedures such as endoscopic submucosal dissection (ESD) and peroral endoscopic myotomy (POEM). Vessel recognition and adequate precoagulation is therefore crucial in preventing bleeding and reducing procedure time. Coagulation forceps are usually used for that purpose, but more recently a simpler technique of knife precoagulation using 1-10 forced coagulation has been introduced into practice by Japanese ESD experts, reducing the need for repeated accessory exchange. The aim of our single-center study was to evaluate the efficacy of 1-10 precoagulation of large vessels by ESD knife during ESD and POEM procedures and its influence on coagulation forceps use.

Methods. Analysis was performed on prospectively collected data including all consecutive patients/procedures where this novel technique was used. Upon dissection of the surrounding submucosal tissue and isolation of the vessel, it was hooked from both directions with opened ESD knife (DualKnife, Olympus, Japan) and coagulated using forced coagulation effect 1-10W on VIO200D electrosurgical unit (ERBE Elektromedizin, Germany). The method was not used on very large vessels, and vessel selection was at discretion of the endoscopist, but limited to vessels that would otherwise have required the use of coagulation forceps. Successful vessel coagulation and resection was recorded, as well as failures requiring switch to coagulation forceps.

Results. A total of 17 patients undergoing ESD and 11 patients undergoing POEM were included in the analysis, with a total of 61 vessels attempted for 1-10 knife precoagulation. Success rate of knife precoagulation was 92% (56/61), and only 5/61 vessels required switch to coagulation forceps. There was no difference in the efficacy regarding procedure type (ESD *vs*. POEM, 91% *vs*. 93%, p=1). Use of 1-10 knife precoagulation obliterated the need for coagulation forceps use completely in 11 out of 28 patients (39%, 6/17 in ESD and 5/11 in POEM group), thus reducing procedure costs.

Conclusion. Vessel precoagulation with ESD knife using the 1-10 forced coagulation method is an effective way of reducing operational time and costs during third-space endoscopic procedures. Our preliminary results clearly showed benefit of introducing this method into routine practice. Gaining more experience is expected to further reduce the proportion of procedures requiring coagulation forceps use.

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OUTCOMES OF PERORAL ENDOSCOPIC MYOTOMY (POEM): A SINGLE CENTER EXPERIENCE

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Introduction and aim. Peroral endoscopic myotomy (POEM) has become the first-line treatment for achalasia and other esophageal motility disorders, as well as esophageal epiphrenic diverticula. It has an excellent efficacy and safety profile. Increased frequency of gastroesophageal reflux is the only disadvantage when comparing POEM to surgical treatment of achalasia. The aim of our analysis was to evaluate the outcomes of POEM performed in our center since the introduction of the method in 2017.

Methods. This study represents analysis of prospectively collected data on all consecutive patients having undergone POEM between December 2017 and October 2021. All patients received a proton pump inhibitor (PPI) for one month after the procedure and were scheduled for follow-up visit and upper gastrointestinal endoscopy at 3 and 12 months, and yearly thereafter. Achalasia symptoms, treatment success (defined as Eckardt score ≤2), reflux esophagitis, reflux symptoms and use of PPI were all recorded.

Results. A total of 28 patients underwent a POEM procedure (posterior variant in all cases). Most patients had achalasia type 2 or 1, and received standard myotomy (8 cm). Three patients had achalasia type 3 and two patients had diffuse esophageal spasm, where extended myotomy of 15-18 cm in length was performed. One patient was treated with POEM for epiphrenic esophageal diverticulum. Four patients had previously been treated with dilatation or surgery. Except for the initial two cases, the procedures lasted for 45-110 minutes (mean time, 86 minutes). Intraprocedural complications included only pneumoperitoneum (in 3 of 5 initial cases and an additional one in other 23 cases), and postprocedural complications were observed in two patients (1 case of aspiration pneumonia and of prolonged chest pain with subcutaneous emphysema each). Patients were discharged 2 days after the procedure in all but the two mentioned cases with postprocedural complications. Therapeutic success was observed in all cases (Eckardt score 2 in one patient, score 0 or 1 in all other patients); none of the patients reported symptom recurrence thus far. One early patient reported persistence of proximal spasms, and was probably a misdiagnosed case of type 3 achalasia. Reflux esophagitis was observed in 47% of patients on follow-up endoscopy, and 31% of patients reported reflux symptoms 1 year after the procedure, requiring PPI use.

Conclusion. POEM is a very safe and effective procedure for a whole range of esophageal motility disorders, as well as for the treatment of distal esophageal diverticula. Introduction of the method in a new center without expert supervision was not associated with increased complication rate or reduced efficacy. Reflux disease was observed in the usual reported range of 40%-50%.

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TELEMEDICINE ACCEPTANCE BY IBD PATIENTS IN THE ERA OF COVID-19 PANDEMIC

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Background. In the face of COVID-19 pandemic, shift of clinical care to telemedicine has been advocated. Broadened availability and numerous advantages (such as reduction in disease transmission, accessibility to health care, patient convenience, and lower costs, to name a few) have increased implementation of telemedicine modalities in daily clinical practice. Little is known about the inflammatory bowel disease (IBD) patient satisfaction with telehealth services provided by gastroenterologists. Thus, we conducted a survey of patient concerns, satisfaction, and potential change in the perception of telemedicine in our cohort of IBD patients.

Methods. Adult IBD patients treated at our Centre were invited to fill-out anonymous online survey from January 17 to February 25, 2021. Participant characteristics were assessed using descriptive statistics. Normal distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables were compared with independent t-test. Categorical variables were analyzed using the χ^2-test and McNemar test.

Results. A total of 120 subjects (43.3% of female, mean age 34.5±12.3 years, 56.7% with Crohn's disease) completed the survey with a response rate of 96%. Median of disease duration was 8 years (interquartile range, 3-12 years) and 65.8% of participants were on biologics. In the pre-pandemic time, 75% of patients would have chosen personal contact with a gastroenterologist during clinic visits as a preferred way of communication. According to patients, the most desirable way of communication with health care provider during the pandemic were clinic visits (34.2%), followed by phone calls (25.8%) and e-mail (25%). Only 10.8% of patients preferred real-time communication *via* video conferencing platforms. When they were asked about the post-pandemic period, only 54.2% of patients said they would prefer clinic visits, yielding a statistically significant difference compared with the pre-pandemic period (χ^2 (1, N=120)=9.4, p<0.01). There was no age difference in the preferred way of communication. Females were more prone to personal contact with IBD specialist in the post-pandemic period (χ^2 (1, N=120)=4.6, p<0.03). Forty-eight (48%) patients expressed acceptance of telemedicine as adequate substitution for face-to-face clinic visit with IBD specialist in the future.

Conclusion. Telemedicine services provide satisfactory and acceptable methods to ensure continuity and prevent disruptions in health care of IBD patients during and post COVID-19 pandemic.

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LIVER ENZYME ALTERATION IN PATIENTS WITH COVID-19 INFECTION

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Introduction and aim. COVID-19 has been a global public health issue for almost 2 years, with about 4.500.000 fatalities reported since the beginning of the pandemic. Although SARS-CoV-2 is predominantly a respiratory virus, numerous extrapulmonary manifestations of the infection have been proven, including liver enzyme alteration. The aim of this study was to establish whether there is a correlation between liver enzyme levels and the severity of COVID-19 infection.

Methods. This was a retrospective, cohort study carried out at the Rijeka University Hospital Center in the period from February to May 2020. The study included patients aged >18 with confirmed COVID-19 infection, with no known history of liver conditions. Patients were divided into two groups, group 1 including patients hospitalized at the COVID-19 Respiratory Center (patients on noninvasive and invasive ventilation), and group 2 including patients hospitalized at the COVID-19 Patient Ward. We analyzed patient demographics, liver enzymes (aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase (GGT), bilirubin) on admission and on day 5 of hospital stay.

Results. A total of 76 patients, i.e. 30 group 1 patients and 46 group 2 patients, were analyzed. Both groups had a slightly higher number of male patients (56% and 52%, respectively). Patient mean age was 64 and 66 years in group 1 and group 2, respectively. In group 1, 76% of patients had elevated baseline liver enzymes, compared to 50% in group 2, which was a statistically significant difference ($p<0.05$). Follow-up GGT recorded on day 5 was significantly higher in group 1 patients as compared to group 2 patients ($p=0.013$). Moreover, follow-up GGT in group 1 patients was significantly higher than their baseline GGT ($p=0.038$). In group 1, follow-up bilirubin recorded on day 5 was significantly higher as as compared to their baseline level ($p=0.038$).

Conclusion. Liver enzyme alteration was present in about 70% of patients with a more severe clinical picture of the COVID-19 infection, and there was also a statistically significant difference in GGT level between the two patient groups. However, this study was conducted on a small number of patients, hence it could not be clearly established if there was a correlation of liver enzyme alteration and any liver lesion with the severity of the COVID-19 infection, even more so because the patients received different medications during treatment.

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SIGNIFICANT LIVER FIBROSIS IS INDEPENDENTLY ASSOCIATED WITH CHRONIC VASCULAR COMPLICATIONS OF TYPE 2 DIABETES: A CROATIAN MULTICENTER STUDY

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Introduction and objectives. The aim of this study was to investigate whether controlled attenuation parameter (CAP) and liver stiffness measurement (LSM), as assessed by vibration-controlled transient elastography (VCTE), are associated with chronic vascular complications of diabetes mellitus type 2 (T2DM).

Methods. We studied 442 outpatients with established T2DM, who underwent VCTE and extensive assessment of chronic vascular complications of diabetes.

Results. A quarter of analyzed patients had a previous history of myocardial infarction and/or ischemic stroke, and about half of them had at least one microvascular complication (chronic kidney disease (CKD), retinopathy or polyneuropathy). The prevalence of liver steatosis (i.e., CAP ≥238 dB/m) and significant liver fibrosis (i.e., LSM ≥7.0/6.2 kPa) was 84.2% and 46.6%, respectively. Significant liver fibrosis was associated with an increased likelihood of having myocardial infarction (adjusted-odds ratio 6.61, 95%CI 1.66-37.4), peripheral polyneuropathy (adjusted-OR 4.55, 95%CI 1.25-16.6), CKD (adjusted-OR 4.54, 95%CI 1.24-16.6) or retinopathy (adjusted-OR 1.81, 95%CI 1.62-1.97), independently of cardiometabolic risk factors, diabetes-related variables, and other potential confounders. Liver steatosis was not independently associated with any macro-/microvascular diabetic complications.

Conclusions. Significant liver fibrosis is strongly associated with the presence of macro-/microvascular complications in patients with T2DM. These results offer a new perspective on the follow-up of people with T2DM.

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EXPERIENCE WITH ENDOSCOPY IN SARS COV-2 POSITIVE PATIENTS AT THE PRIMARY RESPIRATORY INTENSIVE CARE CENTER, DUBRAVA UNIVERSITY HOSPITAL

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Introduction and aim. To describe the experience with endoscopic procedures in patients with active COVID-19.

Methods. We analyzed data on all endoscopic procedures in SARS CoV-2 positive patients performed in Dubrava University Hospital from March 2020 until July 2021.

Results. A total of 246 endoscopic procedures were performed in 174 patients (98 (56.3%) male, median age 71, and 76 (43.7 %) female, median age 70), as follows: 133 (54%) *esophagogastroduodenoscopies* (EGDs), 53 (21.5%) colonoscopies, 45 (18.3%) endoscopic retrograde cholangiopancreatographies (ERCPs), 14 (5.7%) endoscopic ultrasonography + fine needle aspiration (EUS±FNA), and one each of percutaneous endoscopic gastrostomy (PEG) and capsule endoscopy. Of the total number, 14 (5.7%) procedures (12 ERCPs and EUSs) were performed in patients referred from another institution to which they were returned following the procedure. Of the total of 133 EGDs, 17 (12.8%) were repeated or follow-up EGDs performed during the same hospitalization. Ten (8.6%) of the 116 first EGDs were performed in patients who presented on admission with signs of gastrointestinal (GI) bleeding, while the others were for GI bleeding that had developed during hospital stay or due to anemia and suspected malignancy. The majority of patients (78%) had comorbidities and received anticoagulants before and/or during hospital stay (80%), and 29 (25%) of them died during hospitalization. The mean Glasgow-Blatchford score was 7.07, Rockall score 4.18, and endoscopic hemostasis was performed during 16 (13.7%) endoscopies. At the time of endoscopy, 76 (65%) patients did not require oxygen support for COVID-19, 18 (16%) were on oxygen support at the flow rate of 1-5 L/min, three at more than 5 L/min, while 13 (11%) patients were intubated and on mechanical ventilation.

Conclusion. Endoscopic procedures are safe with good selection of patients, which should be done solely by gastroenterologists. In the first wave of the pandemic, due to many unknowns we opted for endoscopic procedures extremely rarely, whereas in the second and third waves (Fig. 1), it was easier of us to indicate endoscopy due to better understanding of the disease, possibly also owing to the increased feeling of security among the personnel after vaccination.

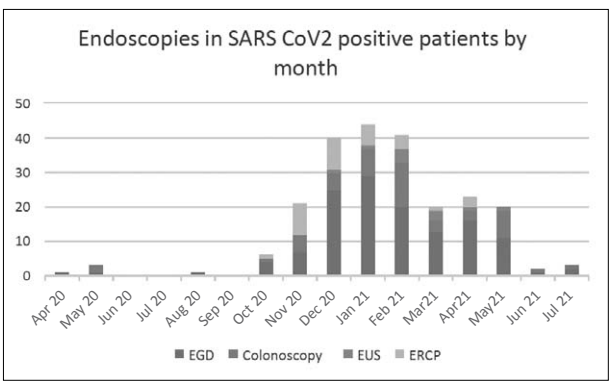


Fig. 1. Endoscopies in SARS CoV-2 positive patients by months/years.

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FIRST EXPERIENCES WITH CHOLANGIOSCOPY-GUIDED LASER LITHOTRIPSY OF BILIARY STONES

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Introduction and aim. We present our first experiences with cholangioscopy-guided laser lithotripsy (LL) of biliary stones.

Methods. We analyzed data on all LLs performed (Auriga™, holmium YAG laser, 30 W) guided by cholangioscopy (SpyGlass™, DS, Boston Scientific), performed at Dubrava University Hospital from May 2019 until October 2020.

Results. A total of 16 procedures were performed in ten patients: six (60%) men, median age 62 (29-86) years and four (40%) women, median age 61 (21-69) years, of which four had been referred from other hospitals in Croatia and neighboring countries. A mean of 1.6 procedures were performed *per* patient until complete extraction of lithiasis, with one patient undergoing four sessions (first patient with extensive intra- and extrahepatic lithiasis), two patients undergoing three and two sessions, respectively, while the rest had one LL session until complete resolution of lithiasis. The average procedure duration was 108 minutes. The patients had previously undergone three *endoscopic retrograde cholangiopancreatography* (*ERCP*) procedures on average with attempted extraction of concrements from biliary tract. In eight (80%) patients, mechanical lithotripsy had also been previously attempted (in two patients on two occasions, and in the others once). The patients had a mean of 4.6 concrements of different size; median of the largest ones was 26 (8-38) mm. Mechanical lithotripsy had not been previously attempted in one patient with a concrement of 22 mm in diameter, stuck in the distal choledochus, which could not be reached by the basket, and in one patient in whom classic basket which caught the stones in the lumen of the relatively narrow choledochus remained after wires fractured during Soehendra lithotripsy about 10 cm from the basket, and the wires remained free in the duodenal lumen. All the procedures were performed under anesthesia with endotracheal intubation. After two sessions, a transient increase in transaminases was observed with an increase in bilirubin and C-reactive protein, with no clinical correlate in terms of cholangitis (at the time of the procedure, all patients received a broad-spectrum antibiotic, i.e. ceftriaxone or ciprofloxacin), while after two procedures transient hyperamylasemia developed, with no clinical correlate. There were no periprocedural perforations or bleeding. The patients were discharged from the hospital two days after the procedure on average.

Conclusion. Cholangioscopy-guided laser lithotripsy is a safe method that should completely eliminate the need for surgical extraction of bile duct stones. The technique itself can be learned easily and our results are comparable to the results described in the literature.

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SERUM LEVELS OF ADROPIN AND INACTIVE MATRIX GLA PROTEIN IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background and aim. Matrix Gla protein (MGP) is a vitamin K dependent peptide which has an established role in suppression of vascular calcification. Recent studies have pointed to a possible link between the immunomodulatory effect of MGP and inflammatory bowel disease (IBD). Adropin is a novel peptide mostly associated with energy homeostasis and vascular protection, while recent studies have also implied its possible role in IBD pathophysiology. The aim of this study was to compare serum levels of adropin and inactive MGP form between patients with IBD and healthy controls, as well as to assess the possible correlation between these two biomarkers.

Methods. This cross-sectional study was conducted on 50 IBD patients (25 ulcerative colitis (UC) patients and 25 Crohn's disease (CD) patients) and 50 age- and gender-matched controls. Serum levels of adropin were determined by dual-ELISA of human adropin (Phoenix Pharmaceuticals, Burlingame, CA, USA). Inactive MGP serum levels were analyzed by CLIA method using IDS-iSYS InaKtif MGP (Immunodiagnostic Systems, Frankfurt, Germany). Fecal calprotectin (FC) levels were determined from stool by turbidimetric immunoassay method using Buhlmann fCAL turbo assay (Buhlmann Laboratories AG, Schonenbuch, Switzerland).

Results. In comparison with control group, IBD patients had significantly lower adropin levels (3.01±0.84 *vs.* 3.42±0.72 ng/mL, p=0.010) and significantly higher inactive MGP levels (641.91±139.11 *vs.* 571.23±112.23 pmol/mL, p=0.006). Comparison between UC and CD patients did not show any significant differences in serum levels of these biomarkers (adropin: p=0.499; dp-ucMGP: p=0.693). There was a significant negative correlation between serum adropin and inactive MGP levels (r=-0.322, p=0.022). FC showed a significant negative correlation with adropin (r=-0.283, p=0.046) and significant positive correlation with inactive MGP (r=0.396, p=0.004). Multivariable logistic regression showed that both serum adropin (OR 0.455, 95% CI 0.251-0.823, p=0.009) and inactive MGP (OR 0.575, 95% CI 0.347-0.913, p=0.009) were significant predictors of positive IBD status when estimated along with baseline characteristics of the study population.

Conclusion. Our findings imply the possible link between MGP and adropin. These outcomes suggest that both of these biomarkers could play a role in the complex pathophysiology of IBD. However, future longitudinal larger scale studies are needed to address these results.

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References

1. Brnic D, Martinovic D, Zivkovic PM, Tokic D, Vilovic M, Rusic D, Tadin Hadjina I, Libers C, Glumac S, Supe-Domic D, Tonkic A, Bozic J. Inactive matrix Gla protein is elevated in patients with inflammatory bowel disease. World J Gastroenterol. 2020;26:4866-77. DOI: 10.3748/wjg.v26.i32.4866
2. Brnic D, Martinovic D, Zivkovic PM, Tokic D, Tadin Hadjina I, Rusic D, Vilovic M, Supe-Domic D, Tonkic A, Bozic J. Serum adropin levels are reduced in patients with inflammatory bowel diseases. Sci Rep. 2020;1:9264-9.

CORRELATION BETWEEN THE DEVELOPMENT AND DEGREE OF LIVER AND PANCREAS DAMAGE IN PATIENTS SUFFERING FROM ALCOHOL ADDICTION

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Introduction and objective. Liver and pancreas damage are the most common types of alcohol-induced organ damage. It is known by experience that these lesions rarely occur simultaneously, meaning that clinically manifested liver damage is most often not followed by significant pancreatic damage and *vice versa*. The aim of this study was to determine the relationship between liver and pancreas damage caused by alcohol consumption.

Methods. Patients suffering from alcohol addiction defined by the specialized AUDIT-C questionnaire were included in the study. Target population was assessed for liver damage by biochemical analysis and abdominal ultrasound on which liver damage is defined by Hamaguchi score >2. Additionally, in order to assess liver fibrosis, serological enhanced liver fibrosis (ELF) test was performed and FIB-4 score was calculated. Patients were divided into two groups based on the presence of liver damage and will be assessed for possible pancreatic disease by fecal elastase and endoscopic ultrasound.

Results. Preliminary results on a total of 32 patients aged 35-71 years (25 males and 7 females) were included. The average AUDIT-C score was 5 (females 4-6, males 4-10). Patients with higher Hamaguchi score had higher ELF test values (7.23-12.27, mean 8.65), which was followed by FIB-4 scores. There were no statistical differences in ELF (p=0.43) and FIB-4 (p=0.31) between the groups with elastase <500 and elastase >500. Patients with higher Hamaguchi score had lower fecal elastase levels, but (for now) there is no statistical difference.

Conclusion. Preliminary results showed that there was no statistical difference between the groups, but there was a tendency to correlation between higher alcohol consumption and subclinical exocrine pancreas hypofunction and higher degree of liver stiffness.

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ENDOSCOPIC ULTRASOUND GUIDED FINE-NEEDLE BIOPSY IS ONLY SLIGHTLY SUPERIOR TO FINE-NEEDLE ASPIRATION IN PANCREATIC TUMOR DIAGNOSIS

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Introduction and aim. There is no strong evidence that endoscopic ultrasound (EUS) guided fine-needle biopsy (FNB) is superior to EUS guided fine-needle aspiration (FNA) in characterizing solid pancreatic tumors[1]. The aim of the study was comparison of sensitivity and accuracy between EUS guided FNA and FNB in the diagnosis of solid pancreatic tumors.

Methods. This prospective study included patients diagnosed with pancreatic solid tumor from January 2019 to December 2020. Included were patients over 18 years of age with pancreatic tumor on prior image findings. Exclusion criteria were cystic tumors and/or contraindications for the procedure. Patients were randomized in two groups (FNA and FNB). Procedures were performed using midazolam and fentanyl sedation with transgastric or transduodenal approach. Two passes were used either with FNA (Olympus EZ shot 3Plus) or FNB (Boston Scientific Acquire), with a 22-gauge low negative pressure needle.

Results. The study included 103 patients. Patients were mostly (52%) female, and most frequently (47.9%) aged 65 to 80. The most common tumor localization was pancreatic head (42.7%). FNB was performed in 73 and FNA in 30 patients; 94.2% of tumors were malignant (85 adenocarcinomas and 12 neuroendocrine tumors). Histopathology material was adequate in 30.1% of patients, so only cytological results were analyzed. FNB *vs*. FNA had better sensitivity (96.92%; 95%CI [89.32%-99.63%] *vs*. 96.15%; 95% CI [80.36%-99.90%]) and accuracy (94.52%; 95%CI [86.56%-98.49%] *vs*. 93.33%; 95%CI [77.93%-99.18%]), however, without statistical significance (p=0.742). One case of prolonged bleeding that resolved spontaneously was recorded in the FNB group.

Conclusion. FNB is slightly but not significantly better than FNA in the diagnostics of solid pancreatic tumors without an increased risk of complications.

Table 1. Demographic data, localization, and tumor characteristics

Age (years)	**n (%)**
<65	15 (14.6)
65-80	49 (47.9)
>80	39 (37.5)
Gender	
Male, n (%)/female, n (%)	50 (48.5)/53 (51.5)
Localization	**n (%)**
Head	44 (42.7)
Body	40 (38.8)
Tail	19 (18.5)
Method	**n (%)**
FNA	30 (29.1)
FNB	73 (70.9)
Cytology report	**n (%)**
Malignant tumors	97 (94.2)
Adenocarcinoma	85(87.6)
Neuroendocrine tumors	12 (12.4)
Other benign lesions	4 (3.8)
Other malignant lesions	2 (2)

FNA = fine-needle aspiration; FNB = fine-needle biopsy

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Reference

1. Elhanafi S, Mahmud N, Vergara N, *et al*. Comparison of endoscopic ultrasound tissue acquisition methods for genomic analysis of pancreatic cancer. J Gastroenterol Hepatol. 2019 May;34(5):907-13. doi: 10.1111/jgh.14540. Epub 2018 Dec 10

THE ROLE OF TRANSESOPHAGEAL ENDOSCOPIC ULTRASOUND IN THE DIAGNOSIS OF LUNG CANCER

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Introduction. Lung tumor is one of the leading causes of death in the world. Lesions located near the mediastinum, retrocardially, near the aorta or pulmonary vessels, and in front of the spine are difficult to access by percutaneous or bronchoscopic access. We present a case of a patient with a peripheral lung tumor where the diagnosis was made by endoscopic ultrasound-guided fine-needle aspiration/biopsy (EUS FNA/FNB)[1].

Case report. A 64-year-old patient was hospitalized for weakness, weight loss (loss of about 10 kg in the past 10 weeks), night sweats, and subfebrility. The patient was an active smoker (30 packs/year). Examination revealed decreased body mass index (18.5 kg/m^2) and slightly prolonged expiration. Laboratory findings showed chronic disease anemia, thrombocytosis, mildly elevated aminotransferase, and triple elevated alkaline phosphatase with normal tumor markers. An elongated, sharply delineated shadow suprachillary on the right contour of the upper mediastinum was verified by x-ray, while a conglomerate of enlarged paratracheal lymph nodes was visualized by computed tomography. Fiber bronchoscopy revealed no pathologic changes in the bronchial orifice, while brush and catheter aspirate did not detect tumor cells. Transesophageal EUS was performed with a 5-12 MHz linear probe, which determined an irregularly round hypoechoic expansive formation, elastographically harder consis-

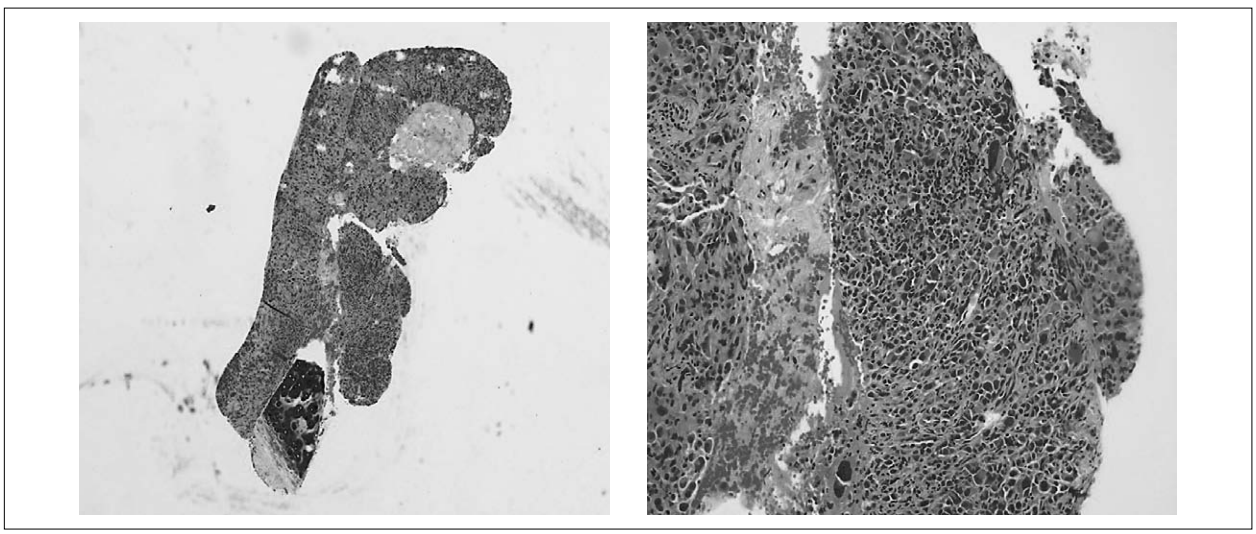


Fig. 1. Histopathology sample obtained by EUS-FNB method. Left panel: magnification x20 (cartilage tissue visible); right panel: magnification x200 (HE staining).

tency with 6.7 cm in diameter at the upper/middle mediastinum border with enlargement of mediastinal lymph nodes. In the same act, EUS FNA/FNB with needle (Boston Scientific Acquire, 22-gauge) was performed with negative pressure in three passes, without post-procedural complications. Poorly differentiated carcinoma was verified by cytologist, and pleomorphic lung cancer was confirmed by histopathology (Fig. 1). The patient was

presented at the Council for Lung Tumors, where a treatment modality in the form of radiotherapy was proposed.

Conclusion. Transesophageal EUS may be the leading diagnostic method in the diagnosis of peripheral lung tumors.

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Reference

1. Chira RI, Chira A, Ichim VA, Nagy GA, Florea A, Crisan D, Popovici B. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of paraesophageal lung tumors – diagnostic yield and added value. Med Ultrason. 2019 Nov 24;21(4):377-81. doi: 10.11152/mu-2184

CARCINOSARCOMA OF THE GALLBLADDER – AN UNUSUAL PRESENTATION OF A RARE TUMOR

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Introduction. Carcinosarcoma is an extremely rare form of gallbladder carcinoma and accounts for less than 1% of all neoplasms. It is composed of two components, epithelial and mesenchymal[1]. In 90% of cases, it affects women aged above 60[1]. Clinically, it presents with nonspecific complaints such as abdominal pain, painless palpable formation, and vomiting[1]. Imaging results are nonspecific and definite diagnosis is established by histopathology, most commonly upon autopsy[1]. The prognosis is poor, with median survival of 5.5 months[1].

Case report. A 62-year-old female patient presented for the first time in June 2020, with pain under the right costal margin, when ultrasound (US) revealed cholecystolithiasis and elective cholecystectomy was recommended but was not performed. She presented again in August 2021 with abdominal pain and elevated inflammatory markers. In addition to cholecystolithiasis and thickened wall in the gallbladder fossa, US revealed an inhomogeneous formation of 9x7 cm in size. Multi-slice computed tomography (MSCT) raised suspicion of possible abscess collection of the gallbladder with a fistula towards the pylorus of the stomach, or of a necrotizing tumor process. Explorative laparotomy was performed with evacuation of gallbladder abscess and drainage, while histopathologic analysis of the gallbladder sample and immunohistochemistry (Vimentin, EMA and CD138 positive) indicated sarcomatoid carcinoma. In September 2021, the patient presented again due to abdominal pain, hematemesis and melena, with consequently severe posthemorrhagic anemia and shock. Upper endoscopy revealed tumor infiltration of the duodenum as the cause of bleeding, and MSCT showed tumor progression, which now was of larger dimensions and infiltrating the antropyloric region of the stomach, duodenal bulb and hepatic colic flexure. Despite conservative treatment, the patient's condition worsened soon and she died.

Conclusion. In this case, we describe an unusual presentation of a rare gallbladder tumor. Literature describes one more case of carcinosarcoma manifested as an abscessing formation in the gallbladder region, which is not a common presentation of gallbladder tumor[2]. Due to nonspecific symptoms, these tumors are recognized at the advanced stage, when treatment possibilities are limited[1].

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References

1. Xiaorong C, Yuwen Z, Xinyao S, Guixia W, Meng Q. Gallbladder carcinosarcoma: current perspectives and new development. Exp Rev Gastroenterol Hepatol. 2021; 1:1-8.
2. Khurram R, KhamarR, Lunat R, *et al*. Gallbladder carcinosarcoma masquerading as a hepatic abscess. Radiol Case Rep.s 2020;16(1): 152-6.

COVID-19 PANDEMIC IMPACT ON DISABILITY AND QUALITY OF LIFE IN IBD PATIENTS

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Introduction and objective. Inflammatory bowel disease (IBD) represents a group of chronic, relapse-remitting, disabling, intestinal disorders that affect patient quality of life (QoL) significantly. Little is known about the impact of COVID-19 pandemic on QoL in this group of patients. We aimed to investigate IBD related disability and QoL in a Croatian cohort of IBD patients prior and during the COVID-19 pandemic.

Methods. QoL was assessed using a validated 10-item IBD disk questionnaire. IBD disk answers prior to the pandemic (pre-pandemic questionnaire) were collected in an anonymous questionnaire conducted from October 2019 to January 2020. An additional set of data (pandemic questionnaire) were collected *via* anonymous online questionnaire conducted from January 17 to February 17, 2021. Participants were paired according to a combination of personal data (age, sex, height, disease type and duration, time needed to diagnose IBD, accompanying comorbidities, and county they lived). Participant characteristics were assessed using descriptive statistics. IBD disk scores were compared using Wilcoxon test for paired subjects and Mann-Whitney test for non-paired ones, followed by additional post hoc analyses.

Results. A total of 21 participants were successfully paired (65% male, median age 24.5 years (interquartile range (IQR) 22.25-40 years), 72.7% Crohn's disease). Prior to the pandemic, 66.7% of paired participants were treated with biologics compared to 71.4% during the pandemic. Median pandemic survey ranks were statistically lower for the following 3 IBD disk items: abdominal pain (Z=-2.5, p=0.01); regulating defecation (Z=-2.1, p=0.04); and joint pain (Z=-2.5, p=0.01). After analyzing non-paired participants, a total of 138 subjects were enrolled in the pre-pandemic survey and 102 in the pandemic survey (50.4% male, median age 35.5 years (IQR 26-49 years), 54% Crohn's disease). Prior to the pandemic, 46.7% of non-paired participants were treated with biologics compared to 64.7% during the pandemic. Median pandemic questionnaire rank was statistically lower for joint pain (U=5855, p=0.03), but higher for interpersonal interactions (U=5610, p=0.02).

Conclusion. Our cohort of IBD patients reported abdominal pain, regulating defecation and joint pain as less disabling in the pandemic period. However, further research with a larger sample size is required to see if adopted precautions such as use of protective aids, improved hygiene, modifications of daily practices, decreased social contacts and home officing may have contributed to lower impact of disease burden on everyday life.

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THE IMPACT OF COVID-19 PANDEMIC ON LIVER TRANSPLANTATION – WHERE ARE WE STANDING?

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Introduction and aim. The COVID-19 pandemic has brought about unique changes and imposed an enormous burden on all aspects of the healthcare system. Regardless of the fact that liver transplantation (LT) is a vital procedure and the only treatment method, preliminary global data suggest that many countries have seen a significant reduction in the procedure after the pandemic outbreak. The aim of our study was to investigate the impact of the COVID-19 pandemic on the LT program in Merkur University Hospital comparing the available data from 2019 (pre-COVID-19 era) with the data from 2020 and 2021.

Methods. In our study, we processed data from the Merkur University Hospital transplantation unit database on the period from January 1, 2019 to September 27, 2021.

Results. Compared to 2019, the number of LTs was reduced by 22.72% in 2020, and by 21.11% in 2021. The time spent on the LT waiting list was extended, with median waiting of 33 days in 2019, 32 days in 2020, and

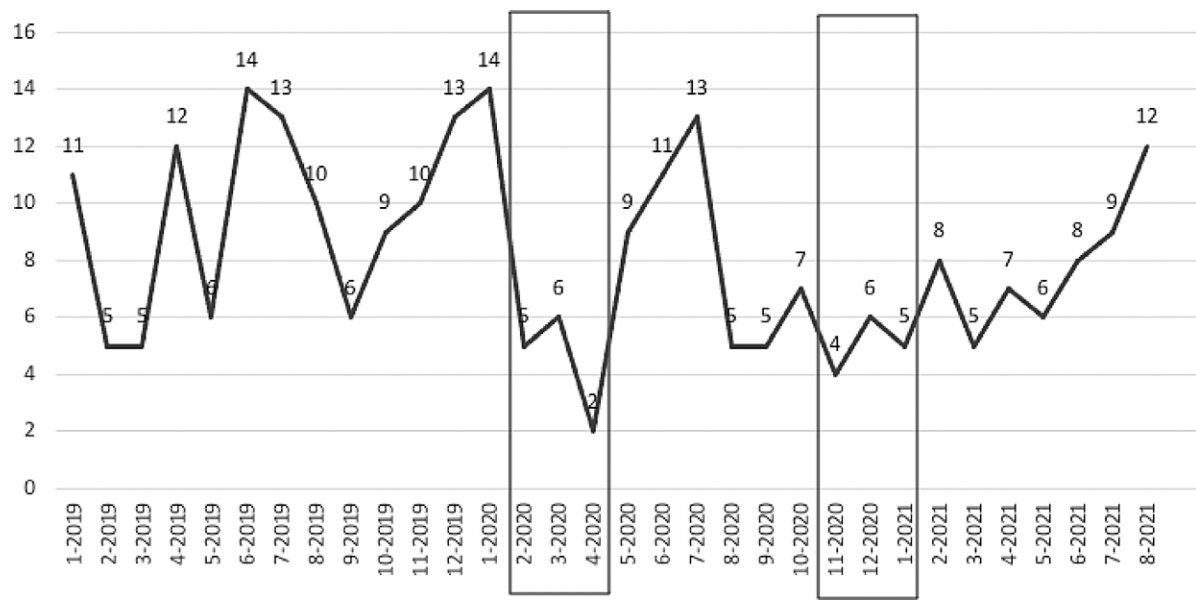


Fig. 1. Number of liver transplantations per months/years.

87.5 days in 2021 (2021 *vs*. 2019, p=1.070). The number of available donors was 29.2% in 2019 and 22.7% in 2020 *per* million inhabitants. The utilization of offered donors was increasing (2019 *vs*. 2020, 86% *vs*. 90%). An increase in the severity of liver disease (Model for End-Stage Liver Disease, MELD) was observed among candidates on the waiting list. Thus, the median (interquartile range) increased from 16 in 2019 to 22 in 2020, and to 20 in 2021. Moreover, a change occurred in the structure of basic indications for LT, with an increase in the share of patients with acute liver failure (8% *vs*. 18.4% *vs*. 11.4%) and malignant diseases (26.5% *vs*. 20.6% *vs*.

35.8%), and reduction among those with alcoholic cirrhosis (34.5% *vs*. 28.7% *vs*. 21.4%). Furthermore, the number of patients processed and newly registered for LT dropped by 5%, among patients in active status on the waiting list the number of transplanted patients decreased by 8%, and the number of those deceased and ineligible for LT increased by 7%. The number of transplanted organs by months/years was inversely proportionate to the number/care of patients with severe COVID-19 (Fig. 1).

Conclusion. The COVID-19 pandemic has had a significant impact on the LT program in Croatia. Redirection of healthcare activities towards treating patients with severe COVID-19 has resulted in a reduced number of donors and newly registered patients, longer waiting for LT, increase in the number of candidates and in the number of deaths/ineligible cases on the LT waiting list. LT candidates with increasingly difficult forms of liver disease (higher MELD, acute liver failure and need for highly urgent LT) are being transplanted, which not only impacts mortality on the list, but also outcomes following LT, eventually resulting in an increased number of re-transplantations.

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NONINVASIVE DIAGNOSIS OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION AND HIGH-RISK ESOPHAGEAL VARICES BY TWO-DIMENSIONAL SHEAR WAVE ELASTOGRAPHY

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Introduction and objective. Noninvasive criteria for diagnosing clinically significant portal hypertension (CSPH) and ruling out high-risk varices (HRV) have been recommended by Baveno VI consensus and extensively validated in clinical practice. However, less is known considering the use of other elastographic methods, such as two-dimensional shear wave elastography (2DSWE). Moreover, available results were obtained mostly in patients with decompensated cirrhosis, which limits the use of these results in real-life clinical practice. In this study, we aimed to assess diagnostic performance of 2DSWE in parallel with transient elastography (TE) for diagnosing CSPH and HRV specifically in patients with compensated advanced chronic liver disease (cACLD).

Methods. Consecutive patients suspected of cACLD [liver stiffness measurement (LSM) ≥10 kPa by TE, or morphological signs suggestive of cACLD on imaging], with no history of liver decompensation, underwent hepatic venous pressure gradient (HVPG) measurement, transjugular liver biopsy and esophagogastroduodenoscopy, which served as the reference methods for diagnosing CSPH, cACLD and HRV. All patients underwent LSM and spleen stiffness measurements (SSM) by 2DSWE and TE.

Results. Seventy-six patients were included (78% men, mean age 62 years, body mass index 28.3 kg/m^2, 36.8% alcoholic, 30.3% nonalcoholic fatty liver disease, 14.5% viral hepatitis). Of them, 80.3%, 69.7%, 52.6% and 22.4% had cACLD, cirrhosis, CSPH and HRV, respectively. LSM performed better than SSM in diagnosing CSPH and HRV. For CSPH, AUROCs (0.926 *vs*. 0.866), optimal cut-offs (20.1 *vs*. 20.2 kPa) and sensitivity/specificity (80.5%/94.3% *vs*. 77.5% /86.1%) were comparable for 2DSWE and TE. Ruling out CSPH by 2DSWE (LSM at cut-off with ≥90% sensitivity (13.5 kPa) and platelets ≥150x10^9/L) performed comparably to TE, with only 1/24 cases falsely classified as negative. For HRV, AUROCs were similar (0.875 2DSWE, 0.851 TE) with similar optimal LSM cut-offs (19.3 kPa 2DSWE and 20 kPa TE), enabling 100% sensitivity and ruling out HRV. In keeping with Baveno VI rules, the combination of 2DSWE (LSM ≤19.3 kPa) with platelet counts ≥150x109/L identified 29/74 (39.2%) patients meeting these criteria, who might avoid endoscopy, and all 29 were true negatives for the presence of HRV.

Conclusion. In respect to diagnosing CSPH and HRV in patients with cACLD, LSM measured by 2DSWE appears to perform equally well as does LSM by TE.

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PRESENCE OF LIVER CIRRHOSIS IS ASSOCIATED WITH INCREASED MORTALITY OF PATIENTS HOSPITALIZED WITH COVID-19

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Introduction and objective. Presence of comorbidity is a well-recognized risk factor for the aggravated course of coronavirus disease 2019 (COVID-19). In this study, we aimed to analyze 30-day outcomes of patients with chronic liver disease (CLD) hospitalized with COVID-19.

Methods. We reviewed medical files of 4014 patients hospitalized due to COVID-19 at a single center over a 12-month period. Patients with CLD were identified based on discharge diagnoses according to ICD-10 classification. These patients were followed for 30 days of admission, and outcomes (intensive care unit (ICU) admission, mechanical ventilation (MV) or death) were analyzed.

Results. Out of 4014 patients, 110 (2.7%) had CLD and 49 (1.2%) had cirrhosis. Median age of CLD patients was 67.5 years (IQR: 57.3-75), 79 (71.8%) were males, 224 (23.5%) were obese, 56 (50.9%) reported alcohol abuse, 24 (21.8%) had nonalcoholic fatty liver disease, 11 (10%) had viral hepatitis, and 98 (89.1%) had pneumonia. Median length of hospitalization for CLD patients was 12 days, 32 (29.1%) patients required ICU admission, 23 (20.9%) MV, and 43 (39.1%) died. On univariate analysis, the presence of cirrhosis was associated with worse 30-day survival when compared to the age-, sex- and COVID-19 duration matched cohort (45% for cirrhosis *vs*. 73% for controls, HR=2.95; p<0.001), whereas no such difference existed between the non-cirrhotic CLD and controls (74% *vs*. 73%, p>0.05). On Cox regression analysis, liver cirrhosis but not CLD predicted inferior survival independently of age, comorbidity burden, and severity of COVID-19, with a 2-fold higher adjusted risk of 30-day mortality.

Conclusion. Liver cirrhosis is an important risk factor for the aggravated course of COVID-19. It is independently associated with 2-fold higher 30-day mortality in patients hospitalized with COVID-19.

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LARGE TUBULOVILLOUS ADENOMA AND INVASIVE ADENOCARCINOMA OF THE GALLBLADDER: A CASE REPORT

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Introduction. Presentation of a case of large tubulovillous adenoma of the gallbladder which progressed to invasive adenocarcinoma.

Case report. A 70-year-old female presented to the internist department for the first time in 2020 due to abdominal pain and vomiting that had lasted for five days. During examination, the right subcostal area was painful to palpation, and a large firm process formation was palpated, but without signs of peritoneal irritation and without indications for emergency surgery. The patient was admitted to the internal ward with a diagnosis of acute calculous cholecystitis, where with appropriate antibiotic therapy the condition improved and the patient was discharged home with the recommendation of biliary diet and follow-up. Later on, the patient was admitted to the hospital for planned cholecystectomy. Laparoscopic approach was initially performed under general anesthesia to verify a markedly enlarged gallbladder to which the omentum and transverse colon were attached. Conversion of the surgical procedure into laparotomy was performed, and cholecystectomy was done together with resection of the affected part of the intestine. Department of Pathology received an enlarged gallbladder measuring 14x5 cm on cross section. The lumen was completely filled with a mostly necrotic villous tumor that was histologically composed of villous and tubular structures lined with highly dysplastic to atypical epithelium. In 3 samples, there was tumor invasion of the lamina propria and muscular layer of the gallbladder wall. Immunohistochemical labeling showed positive reaction to CK20 and CK19, focal luminal positive to MUC1 and MUC5AC, and negative reaction to CK7, p53 and CA 19.9. No invasion was found in the histologically examined samples of the resected part of the colon. After histologic findings, the patient was referred to an oncologist for further oncologic treatment.

Conclusions. We present the case of a patient in whom imaging methods showed an enlarged gallbladder that was surgically removed. The lumen of the gallbladder was filled with a villous tumor, histologically tubulovillous adenoma, with foci *in situ* and invasive adenocarcinoma. Adenomas of the gallbladder are uncommon and they are generally smaller. Villous and tubulovillous adenomas of gallbladder are rare and they are considered to be a premalignant lesion that can progress to adenocarcinoma.

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ADHERENCE TO THE MAASTRICHT V/FLORENCE CONSENSUS REPORT ON MANAGING *HELICOBACTER PYLORI* INFECTION AMONG PRIMARY CARE PHYSICIANS AND MEDICAL STUDENTS IN CROATIA

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Introduction and aim. Eradication of *Helicobacter pylori* (*H. pylori*) infection is becoming increasingly difficult[1]. The aim of our cross-sectional study was to establish and compare the knowledge and views of primary care physicians and medical students in Croatia to the current guidelines for the management of *H. pylori* infection, set in the Maastricht V/Florence Consensus Report[2].

Subjects and procedures. The study was carried out with primary care physicians and medical students in order to determine the level of adherence to the European guidelines for the management of *H. pylori* infection, i.e. the Maastricht V/Florence Consensus Report. The survey was distributed by e-mail to 2338 family practices in the Republic of Croatia and to medical students in the fourth, fifth and sixth year of the medical study program at the University of Split School of Medicine. Responses were collected by e-mail in the period from June 23 to August 26, 2020.

Results. The study included 249 primary care physicians and 169 medical students. Bismuth-based quadruple therapy or non-bismuth based quadruple therapy (concomitant), which are first-line treatments for eradication of *H. pylori* infection, were the choice in 4.8% of primary care physicians and 13% of medical students in Croatia, while 66.3% of primary care physicians and 79.9% of medical students would choose clarithromycin-based triple therapy, which is not in line with the current guidelines. Bismuth-based quadruple therapy was the most common choice for second-line treatment (which is consistent with the guidelines) in 45.4% of primary care physicians and 34.9% of medical students. However, only 2.8% of primary care physicians and 7.1% of medical students would accurately recommend first- and second-line treatment for eradication of *H. pylori* infection. A significantly higher percentage of students preferred the C13-urea breath test compared with primary care physicians (50.3% *vs*. 6.4%). Only 59.0% of primary care physicians would treat *H. pylori* in all patients, including asymptomatic ones. Medical students recognized the association between *H. pylori* infection and stomach cancer significantly more often compared with physicians (92.9% *vs*. 73.5%).

Conclusions. Primary care physicians and medical students in Croatia are insufficiently familiar with treatment guidelines for *H. pylori* infection. Continuous targeted educational interventions are needed to change the views and knowledge of diagnosing and treating *H. pylori* infection because adherence to the guidelines is of utmost importance.

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References

1. Malfertheiner P, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, *et al*. Management of *Helicobacter pylori* infection – the Maastricht V/Florence Consensus Report. Gut. 2017;66(1):6-30.
2. Boltin D, Kimchi N, Dickman R, Gingold-Belfer R, Niv Y, Birkenfeld S. Attitudes and practice related to *Helicobacter pylori* infection among primary care physicians. Eur J Gastroenterol Hepatol. 2016;28(9):1035-40.

ENDOSCOPIC MANAGEMENT OF BURIED BUMPER SYNDROME – A CASE SERIES

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Introduction and aim. Buried bumper syndrome (BBS) is an uncommon and late-onset condition with potential serious and life-threatening consequences, in which the internal bumper of percutaneous endoscopic gastrostomy (PEG) is partially or completely overgrown by the hypertrophic gastric mucosa and embedded into the gastric wall. The aim of this paper is to present different endoscopic management approaches for BBS as a reliable, fast, accessible and successful removal methods.

Methods. We present 6 cases of BBS in patients with PEG that were diagnosed and treated in our hospital over a 3-year period (2017-2020).

Results. The Ponsky 'pull' technique was used for primary PEG implantation in all patients. In two of the patients, BBS was resolved using only sphincterotome-based technique (performing radial star-like incisions of gastric mucosa over the bumper); in three of the patients, a combination of sphincterotome-based technique and additional needle knife or a hook knife technique (performing radial star-like incisions of the gastric inner wall with an ESD knife to expose the bumper) was used; while in one of the patients, we managed to pull out the partially retained bumper using a polypectomy snare. In four patients, new gastrostomy tube was implanted through a new fistula, and in two patients PEG was reimplanted through an existing one. Median period from PEG implantation to BBS diagnosis was 23 months (6-26 months) and upon endoscopic evaluation, in five of the patients, complete mucosal overgrowth over the internal fixation bumper was observed. Median duration of the endoscopic removal procedure was 35 minutes (7-60 min). No serious complications in terms of significant bleeding or infection were noted, but we observed recurrence of BBS after 27 days in one patient.

Conclusion. Despite all precautionary measures, late complications such as BBS do occur. Therefore, early detection and proper management should be offered to afflicted patients. Sphincterotome-based technique is a well suited and reliable method for endoscopic management of completely buried bumper syndrome.

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ASSOCIATION BETWEEN ELASTOGRAPHIC PARAMETERS OF LIVER STEATOSIS AND FIBROSIS WITH SARCOPENIA

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Introduction and aim. Over the last years, the association between metabolic syndrome, nonalcoholic fatty liver disease and sarcopenia has been under research. The association between elastographic parameters of hepatic steatosis and fibrosis and sarcopenia in patients with type 2 diabetes mellitus (T2DM) has not been studied yet. The aim of this study was to establish if there is an association between sarcopenia and elastographic parameters of hepatic steatosis (controlled attenuation parameter, CAP) and fibrosis (liver stiffness measurements, LSM) in a larger cohort of patients with T2DM.

Methods. A total of 703 patients with T2DM (373 male), mean age 61.66±11.17, were analyzed in the period from October 5, 2019 until September 8, 2021. Sarcopenia was assessed using bioelectric impedance analysis (BIA). A FibroScan device was used to assess hepatic steatosis (CAP) and fibrosis (LSM). Steatosis was defined as CAP ≥238 dB db/m, and fibrosis as LSM ≥7.0 kPa (for M probe) and LSM ≥6.2 kPa (for XL probe).

Results. Of the 703 study patients, 603 had hepatic steatosis, based on CAP results. On the other hand, 227 patients had fibrosis based on LSM results. Patients with hepatic steatosis had a significantly higher body mass index (BMI) (31.51±4.97 *vs*. 27.15±3.92; p=0.004), higher circumference of the waist (105.39±13.94 *vs*. 93.70±14.25; p<0.0001), hips (110.09±11.36 *vs*. 103.32±7.94; p<0.0001), and upper arms (31.85±4.12 *vs*. 29.81±3.71; p<0.0001) compared to patients without hepatic steatosis. Based on BIA results, patients with hepatic steatosis had a significantly higher percentage of fatty tissue compared to patients without steatosis (32.26±7.89 *vs*. 25.05±7.12; p<0.0001). Moreover, patients with hepatic steatosis had a significantly lower percentage of muscle mass compared to patients without steatosis (63.67±9.26 *vs*. 72.93±6.18; p<0.0001). Patients with hepatic fibrosis had a significantly higher percentage of fatty tissue compared to patients without fibrosis (36.59±7.51 *vs*. 28.67±7.21; p<0.0001). Patients with hepatic fibrosis had a significantly lower percentage of muscle mass compared to patients without hepatic fibrosis (57.50±9.53 *vs*. 68.56±7.03; p<0.0001). On multivariate analysis, independent predictors of reduced muscle mass (sarcopenia) were CAP, LSM, BMI, and female sex.

Conclusion. The study demonstrated a significant association between elastographic parameters of hepatic steatosis and fibrosis with sarcopenia. Elastographic parameters of hepatic steatosis and fibrosis are independent predictors of reduced muscle mass in patients with T2DM.

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ELASTOGRAPHIC PARAMETERS OF LIVER STEATOSIS AND FIBROSIS PREDICT INDEPENDENTLY THE RISK OF INCIDENT CHRONIC VASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction and background. The aim of this prospective study was to examine the relationship between controlled attenuation parameter (CAP) and liver stiffness measurements (LSM) with the risk of developing a composite endpoint inclusive of incident acute myocardial infarction (AMI), cerebrovascular insult (CVI), or chronic kidney disease (CKD) in people with type 2 diabetes mellitus (T2DM).

Methods. This was an observational longitudinal study with the primary outcome to assess the prognostic value of the elastographic parameters of hepatic steatosis (CAP) and fibrosis (LSM) for predicting the development of chronic vascular complications (i.e., AMI, CVI and CKD) in a cohort of 238 T2DM individuals without a prior history of AMI, CVI or CKD. Patients were defined as having hepatic steatosis if CAP measurement was ≥238 dB/m. Clinically significant fibrosis was defined by the presence of LSM value ≥7.0 or ≥6.2 kPa, using either M or XL probes, respectively.

Results. The patient population was followed for a median period of 7.6 years. Kaplan-Meier survival analyses showed that there was a higher proportion of patients who developed the aforementioned composite outcome ($p<0.001$ by the log-rank test), as well as CKD ($p<0.001$) or AMI alone ($p=0.014$) among those with elevated CAP values (≥238 dB/m) at baseline. Similarly, Kaplan-Meier survival analyses showed that there was a higher proportion of patients who developed the composite outcome ($p<0.001$), as well as CKD ($p<0.001$) or AMI alone ($p<0.001$) among those with elevated LSM values (≥7.0/6.2 kPa). In multivariable regression analyses, the presence of elevated CAP (adjusted-hazard ratio 2.34, 95% CI 1.32-4.15) and elevated LSM (adjusted-hazard ratio 2.84, 95% CI 1.92-4.21), independently of each other, were associated with a higher risk of developing the composite outcome, as well as incident AMI or CKD alone after adjusting for traditional cardiovascular risk factors and diabetes-related variables.

Conclusions. This prospective study shows for the first time that FibroScan®-detected liver fibrosis is strongly associated with an increased incidence of chronic vascular complications of diabetes over a median follow-up period of 7.6 years in an outpatient cohort of T2DM patients in primary prevention of CVD, independently of established cardiovascular risk factors, diabetes-related variables and hepatic steatosis (as assessed by CAP and ultrasonography).

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INTRADUCTAL RADIOFREQUENCY ABLATION IN THE TREATMENT OF MALIGNANT BILIARY HILAR OBSTRUCTION: PRELIMINARY RESULTS FROM A TERTIARY CENTER IN THE REPUBLIC OF CROATIA

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Introduction. Biliary radiofrequency ablation (bRFA) is a new endoscopic palliation therapy for malignant biliary obstruction[1]. The aim of this prospective, randomized study was to evaluate the safety and efficacy (in terms of stent patency and survival) of intraductal bRFA combined with biliary stent placement for nonresectable malignant hilar biliary obstruction.

Methods. Patients with proven nonresectable Klatskin tumor were included. Two groups were defined: RFA group (n=4) in whom intraductal bRFA combined with plastic biliary stent placement was performed and control group (n=5) that was treated only with the plastic biliary stent placement. RFA was performed by using Habib™ EndoHPB (Boston Scientific) catheter according to the previously reported technique[2]. In both groups of patients, two 10F plastic biliary stents were always placed in the left and right hepatic duct. Primary endpoints included safety, stent patency time, and survival rates.

Results. The technical success rate for both groups was 100%. The median time of stent patency in the RF ablation and control groups were 2.8 months (range, 1.8-3,1) and 2.1 months (range, 1.4-2,1), respectively (Kaplan-Meier analysis: p=0.03). The median survival times in the RF ablation and control groups were 5.2 months (range, 1.8-8.2) and 4.9 months (range, 2.2-6.5), with no significant difference according to Kaplan-Meier analysis.

Conclusion. Preliminary results demonstrated that intraductal RF ablation combined with biliary stent placement for nonresectable malignant hilar biliary obstruction is safe and effectively increases plastic biliary stent patency time. However, in our small cohort of patients, it did not improve patient survival.

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References

1. Dolak W, Schreiber F, Schwaighofer H, *et al*. Endoscopic radiofrequency ablation for malignant biliary obstruction: a nationwide retrospective study of 84 consecutive applications. Surg Endosc. 2014;28:854-60. doi: 10.1007/s00464-013-3232-9
2. Steel AW, Postgate AJ, Khorsandi S, *et al*. Endoscopically applied radiofrequency ablation appears to be safe in the treatment of malignant biliary obstruction. Gastrointest Endosc 2011;73:149-53. doi: 10.1016/j.gie.2010.09.031

CAP AND LIPID PANEL MEASUREMENTS CORRELATION IN PBC PATIENTS

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Introduction and aims. Primary biliary cholangitis (PBC) is an autoimmune liver disease characterized by destruction of intrahepatic bile ducts, eventually resulting in cholestasis and fibrosis. Elevated level of serum cholesterol is a common finding in patients with PBC due to the liver role in its elimination *via* bile. Considering the liver role in excretion of excess cholesterol, serum cholesterol levels are generally elevated in the group of cholestatic liver diseases. Poor lecithin cholesterol acyltransferase activity, direct release of cholesterol and lecithin in the bloodstream due to destruction of small bile ducts, and augmented cholesterol synthesis are the main culprits for the above state. In later stages of the disease, there is usually a drop in serum cholesterol levels due to poor bile flow and loss of the liver synthetic function. Even though hypercholesterolemia is one of the key factors in the pathogenesis of cardiovascular disease, currently there is not enough evidence for a higher cardiac death incidence in patients with PBC. The aim of the study was to investigate the correlation between lipid panel measurements and controlled attenuation parameter (CAP) in a group of patients with PBC, as well as to determine the incidence of steatosis.

Methods. The study employed CAP method (Fibroscan, Echosens) to determine liver steatosis. Serum levels of cholesterol, triglycerides, LDL, and HDL were determined within 24 hours of Fibroscan. Serum level of cholesterol below 5 mmol/L and serum level of LDL below 3 mmol/L were perceived as regular. Study sample consisted of 30 PBC patients, 28 (93.3%) females and 2 (6.7%) males, age range 22-83, average age 60 years.

Results. Out of 30 patients, 17 (57%) had serum cholesterol level above 5 mmol/L, 14 of (47%) of them also showing LDL level above 3 mmol/L. Out of 17 patients with hypercholesterolemia, 4 (24%) had CAP above 260 dB/m, 3 of them showing CAP above 290 dB/m. The criteria for liver steatosis were met by 24% of the patients with hypercholesterolemia.

Conclusion. Study results indicated a significant incidence of hypercholesterolemia in this sample of PBC patients. However, according to the literature, there is no proof of greater morbidity or mortality due to cardiac disease in these patients as compared to the general population. In our sample, CAP did not correlate well with lipid panel measurements, which is consistent with the existing body of research.

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HYPOVITAMINOSIS D IN AUTOIMMUNE LIVER DISEASES

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Introduction and aims. The group of autoimmune liver diseases includes autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC). In AIH, autoimmune mechanisms target hepatocytes, whereas in both PBC and PSC epithelial cells of biliary ducts are targeted. Hypovitaminosis D is a common finding in all three of the abovementioned diseases and is considered an important factor in the pathogenesis of autoimmune diseases in general, as well as a possible prognostic factor. The lack of vitamin D immunomodulatory effect in the liver considerably facilitates development of local inflammation. Vitamin D acts by suppressing the expression of MHC-II antigens and stimulates the production of cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Moreover, by stimulating the synthesis of MED 14, it intensifies the anti-inflammatory effect of glucocorticoids. The process of vitamin D hydroxylation diminishes local inflammation, resulting in Th2 polarization due to inactivation of proinflammatory cytokines and facilitation of interleukin (IL)-4, IL-5 and IL-10. In addition, vitamin D induces the expression of cathelicidin in biliary epithelium, contributing to suppression of local inflammation. Adequate levels of vitamin D in serum are essential for development of iNKT cells, and active form of vitamin D acts as a promotor of MPK-1 action, eventually resulting in MAPK disablement. The aim of the study was to assess the incidence of hypovitaminosis D among patients with autoimmune liver diseases.

Methods. Serum levels of vitamin D were measured and density of liver parenchyma was determined using transient elastography (FibroScan, FS 520, Echosens) in a random sample of patients with autoimmune liver diseases. The sample consisted of 62 patients, 54 females and 8 males, age range 22-83, median 54 years. The sample included 16 patients with AIH, 32 with PBC, 1 with PSC and 13 patients with overlap syndromes, 7 of them with PBC/AIH and 6 with PSC/AIH. Hypovitaminosis D was defined as serum level of vitamin D below 75 nmol/L. The stage of liver fibrosis was determined using FibroScan. Normal density of liver parenchyma was defined as values below 6 kPa, stage 1 fibrosis (F1) as density of 7-8 kPa, stage 2 (F2) as density of 9-11 kPa, stage 3 (F3) as density of 11-15 kPa, and stage 4 (F4) as density above 15 kPa.

Results. Hypovitaminosis D was found in 46 out of 62 (74.2%) patients, of which 75% of AIH patients, 78% of PBC patients, and 62% of patients with overlap syndromes. Suboptimal vitamin D levels were recorded in 74% of female and 75% of male patients. Vitamin D deficiency was found in 71% of patients aged 22-40, 77% of those aged 40-65, and 71% of those older than 65. Out of 46 patients with hypovitaminosis D, 20 (44%) showed liver density >6 kPa. Twelve patients manifested stage 3 and stage 4 liver fibrosis and they all were vitamin D deficient.

Conclusion. This study results indicate a high percentage of vitamin D deficiency in our cohort. Hypovitaminosis D was found in all of our patients in advanced stages of liver fibrosis (F3, F4). According to the literature, serum level of vitamin D may be a valuable prognostic factor of disease progression, which is consistent with our data. Whether vitamin D supplementation in early stages of disease could affect the onset of liver fibrosis, is yet to be investigated in a greater patient sample.

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ENDOSCOPIC THERAPY FOR ANASTOMOTIC DEHISCENCE FOLLOWING UPPER GASTROINTESTINAL TRACT SURGERY – EXPERIENCE FROM THE ZAGREB UNIVERSITY HOSPITAL CENTER

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Introduction and aim. This is a retrospective case report on dehiscence of surgical anastomosis following surgeries of upper gastrointestinal (GI) tract and endoscopic resolution of the said complication.

Methods. From September 2018 until April 2021, 15 patients with postoperative leak (dehiscence) of surgical anastomosis were referred to the Department of Gastroenterology, Zagreb University Hospital Center (UHC). Nine patients had undergone surgery at Zagreb UHC Zagreb, whereas another 6 patients were referred from other institutions. We provide retrospective analysis of patient data and techniques used to resolve the said complication.

Results. Of the 15 referred patients, 10 were male and 5 female, mean age 69 (range 52-80) years. In all 15 patients, the reason for surgery was a tumor process, i.e. gastrointestinal stromal tumor in one patient, squamous cell carcinoma of the mid/distal esophagus in 5 patients, adenocarcinoma (junction cancer) of the E-G junction in 4 patients, and stomach cancer in 5 patients. Two types of surgery were performed, i.e. resection of the distal/mid esophagus with resection of the proximal stomach region with esophagogastric anastomosis (9 patients), and total gastrectomy with esophagojejunal anastomosis (6 patients). Dehiscence was proven in all patients within 5-7 days of surgery by computed tomography (administration of oral contrast agent) to which they were referred due to inadequate postoperative recovery, pain, fever, or increase in inflammatory parameters. In 14 patients, dehiscence was resolved endoscopically by placing an esophageal stent, in 12 cases with a completely covered stent (all 11 cm in length), and in two cases with a partially covered stent of 12 cm in length. All stents were placed by classic endoscopic technique, and in two cases the stent was placed without x-ray control (one in endoscopy unit and the other in the operating room, intraoperatively). In one patient, dehiscence was closed using metal clips and over-loop. The patients were then monitored on surgical ward with follow-up contrast x-ray usually 3-4 days after the intervention; if complete remediation of dehiscence was proven, oral feeding was introduced and discharge planned usually 7-10 days following the intervention, and upon stent extraction (if a completely covered stent was used) 6-8 weeks after the intervention. One patient had additional radiological percutaneous drainage of the collection instead of dehiscence. In 2 patients (one with a partially covered stent and the other with closing performed with clips and loop), adequate recovery was not observed, leak persistence with intra-abdominal collection was proven radiologically, and they had to undergo reoperation. Three of the 15 patients died (two due to the extensive malignant disease and one patient with failed dehiscence closing with clips and loop died from postoperative complications).

Conclusion. Placement of a completely covered self-expanding esophageal stent should be the first treatment option for postoperative dehiscence following upper GI tract surgery.

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EXPERIENCE WITH FECAL MICROBIOTA TRANSPLANTATION IN HEMATOLOGY PATIENTS AT THE ZAGREB UNIVERSITY HOSPITAL CENTER

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Introduction and aim. Fecal microbiota transplantation (FMT) is becoming an increasingly utilized procedure in the treatment of gastroenterological conditions. We present our experience with FMT in hematology indications and patients.

Methods. From October 2020 until April 2021, 5 FMT procedures were carried out in hematology patients at the Division of Gastroenterology, Zagreb University Hospital Center (Zagreb UHC). The transplant was prepared by standard processing techniques from a healthy donor at the Department of Microbiology. The hematology team of the Zagreb UHC was in charge of selecting patients with appropriate indications for FMT. The FMT procedure was performed with standard endoscopes, in four patients by applying the transplant into distal duodenum by a gastroscope, and in one patient by a colonoscope from the cecum aborally.

Results. The indications and FMT results are described below.

Patient #1: status post hematopoietic stem cell transplantation (alloHSCT) (brother) due to acute T lymphoblastic leukemia, after development of acute graft-*versus*-host disease (GVHD) and then relapsing *Clostridium difficile* (CD) colitis; FMT was performed colonoscopically by applying the 200-mL transplant from the cecum to the rectum, with achievement of adequate clinical effect and CD toxin negativization.

Patient #2: status post alloHSCT from an unrelated donor due to myelodysplastic syndrome (MDS). The patient developed severe GVHD of the small intestine refractory to several lines of immunosuppression. Two FMTs were performed with a gastroscope and the transplant was applied in distal duodenum (in three-week intervals, 200 mL each). Although relatively good clinical recovery was observed in the 6-8 weeks following FMT, the patient died after 4 months from respiratory insufficiency and multiple organ failure.

Patient #3: patient with acute myelomonocytic leukemia in preparation for bone marrow transplant. Due to repeated isolation of *Pseudomonas aeruginosa* from stool culture, FMT was performed by applying 200-mL transplant in the duodenum in order to decolonize the bowels prior to bone marrow transplant. Two weeks after FMT, follow-up stool cultures showed physiological flora and the planned bone marrow transplantation was performed.

Patient #4: patient with alloHSCT due to primary myelofibrosis, who developed GVHD in the bowels and CD colitis. He had 200-mL transplant applied in distal duodenum. His condition quickly improved and on further monitoring CD toxin was negativized, but due to only partial improvement of GVHD symptoms after FMT, photopheresis was also performed, which resulted in GVHD symptoms being in remission for now.

Patient #5: patient with acute monoblastic leukemia in which multiresistant *Enterococcus faecium* was isolated in stool culture on several occasions during chemotherapy. Prior to the planned bone marrow transplant, FMT was performed in order to decontaminate the bowels using a gastroscope with the application of 200-mL transplant into distal duodenum. Stool analysis 2 weeks after FMT suggested physiological flora and the planned bone marrow transplantation was subsequently performed.

Conclusion. Our experience suggests that FMT is a useful method in the treatment of gastrointestinal pathology (GVHD, bowel decontamination prior to bone marrow transplantation, and treatment of CD colitis) in hematology patients.

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COMPARISON OF ADVERSE EVENTS BETWEEN CONCOMITANT AND HYBRID THERAPY IN THE TREATMENT OF *HELICOBACTER PYLORI* INFECTION

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Introduction and aim. The aim of the study was to compare adverse events between concomitant and hybrid eradication therapy in the first-line treatment of *Helicobacter pylori* (*H. pylori*) infection in the Split-Dalmatia County. Concomitant therapy is the preferred choice in the first-line treatment of *H. pylori* in the regions with >20% resistance to clarithromycin, such as the Split-Dalmatia County[1,2]. Long-term use of therapy and a large number of involved antibiotics raise questions of the potential side effects and patient quality of life. On the other hand, hybrid therapy, which involves fewer antibiotics, has been recognized as a possible alternative to concomitant therapy in the regions with similar resistance[1].

Methods. In an open-label, randomized, controlled trial, a total of 140 patients with confirmed *H. pylori* infection were randomized to two arms: concomitant (oral esomeprazole 40 mg, amoxicillin 1 g, metronidazole 500 mg, clarithromycin 500 mg, BID for 14 days), and hybrid (oral esomeprazole 40 mg and amoxicillin 1 g BID for 14 days, with metronidazole 500 mg and clarithromycin 500 mg BID for the last 7 days) treatment arms[3]. Upon completion of therapy, the patients were administered a questionnaire with questions on adverse events. Adverse events were divided into groups based on tolerability, as follows: no adverse events; mild (no impact on daily activities); moderate (partially limited daily activities); and severe (completely limited daily activities).

Results. Adverse events were statistically significantly more pronounced in the concomitant treatment arm compared to the hybrid one (26/69 (37.6%) *vs*. 11/71 (15.5%), p=0.002). Nausea was the most common adverse event in both arms (16/69 (23.1%) *vs*. 10/71 (14.1%), p=0.166). Second in terms of frequency in the concomitant arm was abdominal pain (3/69 (4.3%)) and vomiting (3/69 (4.3%)), while in the hybrid arm metallic taste disorders ranked second (1/71 (1.4%)). According to severity, most adverse events were mild in both arms (22/69 in the concomitant group and 11/71 in the hybrid group). Four patients in the concomitant arm had moderate adverse events, but with no need for hospitalization.

Conclusion. Hybrid therapy demonstrated lower prevalence of adverse events compared to concomitant therapy in the first-line treatment of *H. pylori* infection.

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References

1. Malfertheiner P, Megraud F, O'Morain CA, *et al*. Management of *Helicobacter pylori* infection – the Maastricht V/Florence Consensus Report. Gut. 2017;66:6-30.
2. Tonkic A, Tonkic M, Brnic D, Novak A, Puljiz Z, *et al*. Time trends of primary antibiotic resistance of *Helicobacter pylori* isolates in southern Croatia. J Chemother. 2012;24:182-4.
3. Mestrovic A, Perkovic N, Bozic J, *et al*. Randomised clinical trial comparing concomitant and hybrid therapy for eradication of *Helicobacter pylori* infection. PLoS ONE. 2020;15:e0244500.

SCREENING FOR PATIENTS WITH INCREASED RISK OF LIVER AND PANCREAS INJURY DUE TO EXCESSIVE ALCOHOL CONSUMPTION

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Introduction and aim. Alcohol consumption is a common habit, and according to research Croats are at the top of the world, with the average Croat drinking 12.2 liters of pure alcohol *per* year[1,2]. The aim of this study was to find a screening mechanism for gastroenterological patients who are at risk of liver and pancreatic injury due to excessive alcohol consumption.

Methods. In this cross-sectional descriptive study, patients completed the AUDIT-C questionnaire while waiting for examination in the gastroenterological clinic to detect those consuming alcohol excessively and being at an increased risk of developing complications of such consumption.

Results. The questionnaire was filled out by 217 subjects (n(M)= 92), mean age 52.59±14.83 years. There were 26.7% of positive questionnaires (n=58), where 63.8% of positive responses were given by male subjects (n=37). According to gender distribution, 40.2% of male and 16.8% of female patients were drinking excessively. The mean age of male patients with positive questionnaire was 49.38±16.05 and female 45.95±17.00 years. The mean corpuscular volume (MCV) value in the positive questionnaire group was 92.75±5.44 fL (83.0-97.2). Considering the referral diagnosis, the highest proportion of positive questionnaires was found among patients with altered hepatogram, liver disease (cirrhosis not included), iron deficiency anemia, and small bowel and colon diseases (40%, 35.29%, 31.25% and 26.85%, respectively). The lowest proportion of positive questionnaires was among patients referred for biliary disease (12.5%) and inflammatory bowel disease (14.9%).

Conclusion. It is justified to perform screening using the AUDIT-C questionnaire among male, middle-aged patients referred due to the aforementioned diagnoses with an increased proportion of positive questionnaires, and even more so because the mean MCV as one of the most sensitive indicators was within the reference values. Those who would meet the criteria for excessive alcohol consumption could be referred for additional laboratory workup aimed at detecting liver and pancreatic injury.

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References

1. who.int [Internet]. Geneva: world Health Organization, [cited 2021 Oct 10]. Available from: https://www.who.int/substance_abuse/publications/global_alcohol_report/msb_gsr_2014_3.pdf
2. Pavanello S, Snenghi R, Nalesso A, *et al*. Alcohol drinking, mean corpuscular volume of erythrocytes, and alcohol metabolic genotypes in drunk drivers. Alcohol. 2012 Feb;46(1):61-8.

UNUSUAL CAUSE OF ACUTE ABDOMINAL PAIN: A CASE REPORT

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Introduction. Portal vein thrombosis is a rare cause of acute abdominal pain, and when diagnosed it is mainly caused by the presence of a malignant disease, liver cirrhosis or infection[1]. The aim of the paper is to present a rare case of portal vein thrombosis caused by a thrombophilic condition due to a mutation of the clotting factor II gene manifested as acute abdominal pain.

Case report. A 48-year-old patient was admitted to the emergency department with acute abdominal pain, predominantly described as a sense of discomfort, which was localized in the epigastrium, and had lasted for several days before admission. The symptoms were constant and were not accompanied by nausea and vomiting. Also, they were not preceded by a fatty meal and were independent of feeding. The patient did not have elevated body temperature. Physical examination revealed only mild pain on deep palpation in the epigastrium. Laboratory findings showed mild leukocytosis with elevated concentration of C-reactive protein. In further course of diagnostic workup, abdominal ultrasound and color doppler were performed, which showed absence of flow in the portal vein, and the diagnosis was further confirmed by the finding of computerized tomography (CT) of the abdomen. The patient was hospitalized at the Department of Gastroenterology for treatment of the disease and further diagnostic evaluation to find the cause since CT scan excluded two of the most common ones, i.e. liver cirrhosis and malignant disease. Infection was subsequently excluded. Laboratory findings showed no protein C and S and antithrombin III deficit, or presence of antiphospholipid antibodies. Molecular analysis found a gene mutation for clotting factor II for which the patient was a heterozygote. The finding of mutation for the *MTHFR* and *PAI-1* genes was not considered a possible cause of the disease, but it contributes to the formation of thrombosis along with factor II mutation. Gene mutation for JAK2 V617F and clotting factor V was not found. Conservative treatment measures with application of an adequate dose of low-molecular heparin led to clinical improvement, and the patient was discharged home without symptoms and scheduled for follow-up visits.

Conclusion. A rare case of portal vein thrombosis is presented as the cause of acute abdominal pain and first manifestation of thrombophilic condition caused by gene mutation for clotting factor II.

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Reference

1. Intagliata NM, Caldwell SH, Tripodi A. Diagnosis, development, and treatment of portal vein thrombosis in patients with and without cirrhosis. Gastroenterology 2019;156(6):1582-99.

LIVER TRANSPLANTATION IN ACUTE-ON-CHRONIC LIVER FAILURE – A SINGLE CENTER EXPERIENCE

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Introduction and aim. Acute-on-chronic liver failure (ACLF) is an entity characterized by acute decompensation of chronic liver disease triggered by a precipitating event, preceded by one or more extrahepatic organ failures (OFs) with a high mortality rate[1,2]. The primary outcome of this study was to determine recipient and graft survival rates based on the pre-transplant ACLF status, and secondary outcomes were to explore the association between various complications after liver transplantation (LT) with respect to the ACLF status.

Methods. We analyzed patients having undergone LT at Merkur University Hospital (UH) during the period from January 2012 to February 2019. ACLF is defined according to the European Association for the Study of Chronic Liver Failure (EASL-CLIF) criteria[3]. The research was approved by the Ethics Committee of Merkur UH. Statistical analysis was done in the Medcalc program.

Results. Out of 576 patients with liver cirrhosis, 87 (15.9%) met the criteria for ACLF, and various ACLF grades (1-3) were almost equally distributed (36.8%, 39% and 24.1%, respectively). By comparing recipients with ACLF (86.2%, 74.7% and 71.1%), those without ACLF had a statistically significantly higher (97.4%, 90.4% and 83.8%) 1-month, 1- and 5-year survival, respectively. Respective survival rates decreased with the increase of ACLF grade. Independent predictors of recipient survival were ACLF grade, acute rejection crises, ASA score, cardiovascular (CV) event in first hospitalization after LT, number of LT procedure and other vascular complications, CLIF-C-ACLF grade >64, and recipient age. Interestingly, there were no statistically significant differences in graft survival according to ACLF status (p=0.606). Compared to recipients without ACLF, ACLF recipients had longer intensive care unit stay and hospital stay, as well as four times higher rates of early sepsis (16.1% *vs*. 4.5%) and CV events in first hospitalization after LT (11.3% *vs*. 3.5%). All results were positively correlated with ACLF grade.

Conclusion. Our results support the use of salvage LT in ACLF patients. Additional prospective multicenter studies are needed for better stratification of LT eligible candidates, to assess the best time for LT depending on the degree of ACLF, and to assess the need for prioritization of candidates on the list for LT with developed ACLF.

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References

1. Hernandez R, Solà E, Moreau R, Ginès P. Acute-on-chronic liver failure: an update. Gut. 2017;66:541-53.
2. Arroyo V. Acute-on-chronic liver failure in cirrhosis requires expedited decision for liver transplantation. Gastroenterology. 2019;156:1248-9.
3. Moreau R, Jalan R, Ginès P, *et al*. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013;144:1426-37.

BOCAVIRUS VIREMIA IN SOLID ORGAN AND HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS – RESULTS OF A PILOT STUDY FROM THE HEPVIROTRANSPLANT PROJECT

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Background. Patients undergoing solid organ transplantation (SOT) or hematopoietic stem cell transplantation (HSCT) are at an increased risk of infectious complications. Human bocavirus (HBoV) is a respiratory pathogen that also may be associated with several extrapulmonary manifestations. The burden of HBoV viremia in the adult Croatian population is unknown. This study aimed to evaluate the occurrence of HBoV viremia before and after SOT and HSCT.

Methods. Blood samples were collected before and within one month after liver, kidney, or kidney/pancreas transplantation or autologous HSCT in a single institution from January to August 2021. Nested polymerase chain reaction (PCR) targeting the VP1/2 region of both HBoV1 and HBoV2 was used to detect viral DNA.

Results. HBoV DNA was detected in 3.5% (2 of 57) of total transplant candidates (HSCT 16; kidney 12; kidney/pancreas 2, liver 27). Only one kidney and one liver transplant candidate tested HBoV DNA positive, resulting in organ-specific kidney and liver prevalence of 8.3% and 3.7%, respectively. Both patients were without respiratory symptoms with normal chest x-rays and received no prior immunosuppression at the time of transplant. The indication for kidney transplantation was IgA nephropathy, and for liver transplantation it was cholangiocelullar carcinoma. The kidney recipient received no blood products before or during the procedure, while the liver recipient received red blood cells (1300 mL). The procedures and posttransplant courses were uneventful, and both patients tested HBoV DNA negative within a month after the transplant. Within one month after the transplant, HBoV DNA was detected in 2.9% (1 of 34) transplant recipients (HSCT 7; kidney 10; kidney/pancreas 2; liver 15). Only one (previously negative) liver recipient tested HBoV DNA positive (6.7%). The patient was transplanted due to alcoholic cirrhosis and received fresh frozen plasma (1400 mL) and red blood cells (800 mL). At the time of sampling, he was asymptomatic.

Conclusion. Although the prevalence of HBoV viremia was low, further studies on a large sample of SOT and HSCT are needed to confirm this observation and clinical significance of HBoV infection in the transplant population.

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THE COVID-19 BURDEN IN LIVER TRANSPLANT RECIPIENTS IN CROATIA – THE SECOND PANDEMIC WAVE

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Introduction. The coronavirus disease (COVID-19) has a major impact on the whole health system and especially on transplantation medicine. However, data on COVID-19 in liver transplant recipients (LTRs) in Croatia are unknown. This study aimed to analyze the seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Croatian LTRs.

Methods. A cross-sectional screening for COVID-19 was performed in adult LTRs from September until November 2020, at the beginning of the second COVID-19 pandemic wave. Serum samples were tested for SARS-CoV-2 IgG antibodies using a commercial enzyme-linked immunosorbent assay (ELISA; Vircell Microbiologists, Granada, Spain). All positive samples were confirmed using a virus neutralization test (VNT). Data on the risk exposure and COVID-19 related symptoms were collected using a questionnaire.

Results. The study included 280 LTRs (median age 63, range 22-83 years; male 72.5%). The overall seroprevalence detected by ELISA and VNT was 21.1% and 3.6%, respectively. SARS-CoV-2 IgG antibodies were found in both symptomatic and asymptomatic patients. There were no significant differences in the VNT positivity rates regarding blood products received (3.0%; 95%CI=0.1-15.8 *vs*. 1.1%; 95%CI=0.2-3.1, p=0.496) or attendance to large community events (5.6%; 95%CI=0.1-27.3 *vs*. 1.0%; 95%CI=0.1-3.7, p=0.242). However, a significant difference was found regarding traveling habits (20.0%; 95%CI=2.5-55.6 *vs*. 1.0%; 95%CI=0.13.5, p=0.015). Neutralizing (NT) antibodies were more frequently detected in patients who reported cough (10.5%; 95%CI=1.3-33.1 *vs*. 1.0%; 95%CI=0.1-3.7, p=0.047 and breathing difficulties (23.0%; 95%CI=0.5-53.8 *vs*. 0.5%; 95%CI=0-2.7, p=0.001). Symptomatic VNT positive patients showed significantly higher (p=0.031) NT antibody titers (median 128, interquartile range (IQR)=32-128) compared to asymptomatic patients (median 16, IQR=16-48).

Conclusions. The first COVID-19 seroprevalence study in Croatian LTRs showed that 17% of SARS-CoV-2 ELISA IgG positive patients developed SARS-CoV-2 NT antibodies indicating protective immunity. In immunocompromised populations, it is necessary to understand the SARS-CoV-2 immune response and identify factors associated with inadequate antibody response among those who failed to seroconvert. Therefore, further studies are needed to assess the dynamics of NT antibodies and COVID-19 immunity duration in this endangered group.

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ASSOCIATION BETWEEN CXCL9 AND CXCL10 CHEMOKINE GENE POLYMORPHISMS AND ACUTE GRAFT REJECTION AFTER LIVER TRANSPLANTATION

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Introduction and aim. Despite improvement and optimization of immunosuppression protocols, acute cellular rejection (ACR) is still a common complication after liver transplantation. While elevated CXCL9/10 serum concentrations are associated with the occurrence of ACR, the association of *single nucleotide polymorphism (SNP) for* CXCL9/10 and ACR following liver transplantation has not yet been investigated. The aim of this study was to examine the association of SNP for CXCL9 and CXCL10 with ACR following liver transplantation.

Methods. In the present case-control study, SNP for CXCL9 (rs10336) and CXCL10 (rs3921) was determined using polymerase chain reaction in 215 liver transplant recipients in the period from January 2009 to March 2017. An ACR episode was diagnosed by biopsy (Banff ≥3) within 6 months of liver transplantation. All patients received the same immunosuppression protocol consisting of calcineurin inhibitor, steroids (discontinued after 3 months) and mycophenolate mofetil.

Results. The study included 59 patients with ACR and 156 patients without ACR. There were no statistically significant differences according to age, sex or MELD score at the time of transplantation between the rejection and non-rejection groups. Genotypes were in Hardy-Weinberg equilibrium (p>0.05), with strong linkage disequilibrium (D'=0.99, r=0986) between CXCL9 and CXCL10. In the rejection group, 22 (37.3%) patients had GG, 25 (42.4%) had AG, and 12 (20.3%) had AA genotype of CXCL9 polymorphism, with a similar distribution of genotypes in the non-rejection group, in which 54 (34.6%) patients had GG, 75 (48.1%) had AG, and 27 (17.3%) had AA genotype. The lack of association between CXCL9 genotypes and ACR incidence was found in the co-dominant, dominant, recessive, predominant or log-additive model (p>0.05). Similar results were also obtained for CXCL10 genotypes. On the other hand, a significant association was observed between CXCL9 and CXCL10 genotypes at the time of ACR occurrence. Patients with CXCL9 genotype AA developed ACR earlier (median 5 days; interquartile range (IQR) 4.0-7.5) than patients with genotype GG (median 8 days; IQR 6.0-18.3; p=0.003), with similar results for the CXCL10 gene (CC *vs*. GG; p=0.005).

Conclusion. Single nucleotide polymorphisms for CXCL9 (rs10336) and CXCL10 (rs3921) are not associated with the incidence of ACR following liver transplantation. However, patients with CXCL9 genotype AA developed ACR significantly earlier, which suggests the involvement of CXCL9 in ACR development.

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ASSOCIATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISM FOR CXCL9 (RS10336) AND CXCL10 (RS3921) AND HEPATOCELLULAR CARCINOMA IN PATIENTS WITH ALCOHOLIC LIVER DISEASE

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Introduction and aim. Hepatocarcinogenesis is a complex process in which external and genetic factors interfere and contribute to malignant transformation in patients with chronic liver disease. C-X-C chemokines take part in hepatocarcinogenesis, and recent data have shown an association between single nucleotide polymorphism (SNP) for CXCL9 and CXCL10 and development of liver fibrosis. The aim of this study was to examine the association between CXCL9 and CXCL10 SNPs and hepatocellular carcinoma (HCC).

Methods. The study included 158 patients transplanted due to alcoholic liver disease (52 with HCC and 106 patients without HCC matched by age and sex) during the 2009-2017 period. All patients had DNA isolated from peripheral blood, and polymorphisms for CXCL9 (rs10336) and CXCL10 (rs3921) were determined using the commercially available TaqMan SNP tests with polymerase chain reaction. HCC diagnosis and definition according to the Milan criteria were established on the explanted liver.

Results. Genotypes were in Hardy-Weinberg equilibrium ($p>0.05$), with strong disequilibrium of linkages ($D'=0.999$, $r=0.986$) between CXCL9 and CXCL10. In the HCC group, 22 (42.3%) patients had GG, 21 (40.4%) had AG, and 9 (17.3%) had AA genotype of CXCL9 polymorphism, with a similar genotype distribution in the group without HCC, where 37 (34.9%) patients had GG, 52 (49.1%) had AG, and 17 (16%) had AA genotype. No association was found between CXCL9 genotypes and HCC in the co-dominant, dominant, recessive, predominant or log-additive model ($p>0.05$). Similar results were also obtained for CXCL10 genotypes. It is interesting that a small increase was observed in the share of HCC patients outside the Milan criteria in CXCL9 (AA/AG/GG; 22.2%/28.6%/36.4%) and CXCL 10 genotypes, but without reaching statistical significance.

Conclusion. In this study, we found no association between SNPs for CXCL9 (rs10336) and CXCL10 (rs3921) and HCC in patients with alcoholic liver disease. However, further research is needed to establish their association with morphological criteria and their possible role in hepatocarcinogenesis.

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IDENTIFICATION OF NEW CANDIDATE BIOMARKERS FOR CLINICALLY SIGNIFICANT PORTAL HYPERTENSION BY SERUM PROTEOMIC PROFILING OF PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE

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Introduction and objective. Complications of portal hypertension begin to develop at hepatic vein pressure gradient (HVPG) ≥10 mm Hg (considered as clinically significant portal hypertension, CSPH), hence early identification of patients with CSPH is of high importance. HVPG is an invasive procedure, with limited availability, thus noninvasive tests represent an attractive diagnostic alternative. In this study, we aimed to identify the potential new serum biomarkers for CSPH in patients with compensated advanced chronic liver disease (cACLD) by serum proteomic profiling.

Methods. The presence of CSPH in patients with cACLD and no history of liver decompensation was assessed by HVPG measurement. Serum samples were pooled based on HVPG result into groups without (HVPG <10 mm Hg, n=18) and with CSPH (HVPG ≥10 mm Hg, n=30). Serum pools were purified using HiTrap heparin sepharose columns and analyzed by liquid chromatography-mass spectrometry. Samples were analyzed in triplicates and proteins identified with at least one peptide were considered relevant for analysis. Functional enrichment analysis was conducted using FunRich 3.1.3 analysis tool.

Results. A total of 48 patients were included (75% males; median age: 59.9±9.8 years; the majority with alcoholic (48%) and non-alcoholic (23%) fatty liver disease. A total of 357 proteins were identified in CSPH and 359 in no-CSPH group, and were classified into several functional subsets. Serum level of proteins involved in platelet degranulation, lipid transport and vasodilatation were more represented, those involved in immune response were less represented in the CSPH group, whereas proteins involved in extracellular matrix (ECM) regulation were equally represented in both groups. The proteins with the most striking difference between the groups were metalloproteinase inhibitor 2 (involved in the ECM regulation) and protein S100-A8 (involved in the inflammatory and immune response), both with 11-fold higher concentration in the CSPH group. Other proteins with >2x higher concentrations in the CSPH group were fibulin-1, mannose-binding protein C, macrophage colony-stimulating factor 1 receptor, plexin domain-containing protein 2, and phosphatidylcholine-sterol acyltransferase.

Conclusion. We identified candidate serum biomarkers for early recognition of CSPH in patients with cACLD. These proteins are likely involved in the pathophysiology of portal hypertension development and might represent potential therapeutic targets, which warrants further investigation.

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References

1. Iwakiri Y, Trebicka J. Portal hypertension in cirrhosis: pathophysiological mechanisms and therapy. JHEP Rep. 2021 Jun 4;3(4):100316. doi: 10.1016/j.jhepr.2021.100316. PMID: 34337369; PMCID: PMC8318926.
2. Greuter T, Shah VH. Hepatic sinusoids in liver injury, inflammation, and fibrosis: new pathophysiological insights. J Gastroenterol. 2016 Jun;51(6):511-9. doi: 10.1007/s00535-016-1190-4. Epub 2016 Mar 3. PMID: 26939970.
3. Bosch J, Abraldes JG, Berzigotti A, García-Pagan JC. The clinical use of HVPG measurements in chronic liver disease. Nat Rev Gastroenterol Hepatol. 2009 Oct;6(10):573-82. doi: 10.1038/nrgastro.2009.149. Epub 2009 Sep 1. PMID: 19724251.

VALIDATION OF NONINVASIVE ALGORITHMS FOR DIAGNOSING HIGH-RISK ESOPHAGEAL VARICES IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE: A SINGLE-CENTER RETROSPECTIVE DATA REVIEW OVER A 5-YEAR PERIOD

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Introduction and objective. Baveno VI criteria (B6C) have been in place for 6 years, but they have been challenged by some other noninvasive tests that rely mainly upon the biochemical parameters. In this study, we aimed to validate diagnostic performance of several noninvasive algorithms for high-risk esophageal varices (HRV) among patients with compensated advanced chronic liver disease (cACLD).

Methods. Retrospective analysis of patients who underwent liver stiffness measurement (LSM) by transient elastography (TE) in a single center over a 5-year period, with available results of esophagogastroduodenoscopy (EGD). Only patients with suspicion of cACLD as defined by LSM ≥10 kPa, with no previous decompensation were included in final analysis. Original and expanded B6C, controlled attenuation parameter (CAP), platelet count (Plt), aspartate aminotransferase-to-platelet ratio index (APRI), Fibrosis-4 (FIB-4) index and model for end-stage liver disease (MELD) score were evaluated against the results of EGD that served as the reference method.

Results. Of 861 patients with LSM and EGD results available, 73 had LSM ≥10 kPa and EGD performed within 3 months (median age 62 years, 80.8% (59/73) of males, 74% (54/73) with alcoholic/nonalcoholic fatty liver disease, 21/73 (28.8%) with HRV). On multivariate logistic regression analysis, only LSM and platelets were independently associated with HRV. The best performing tests for ruling out HRV (% of spared EGD; % of missed HRV) were as follows: LSM <20 kPa (53.4%; 0%), B6C (38%; 0%), expanded B6C (47.9%; 4.8%); Plt >214 (21.9%; 0%); FIB-4 ≤1.8 (21.4%; 0%), APRI ≤0.34 (12.3%; 0%). CAP, MELD=6 alone or combined with Plt >150 did not show acceptable performance in our cohort.

Conclusion. The best performing noninvasive algorithms for ruling out HRV in our cohort of patients with cACLD were based on LSM, whereas biochemical tests might also be used, but with a lower number of potentially spared endoscopies.

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ENDOSCOPIC ULTRASOUND GUIDED FINE NEEDLE BIOPSY (EUS-FNB) AS A RELIABLE NONINVASIVE DIAGNOSTIC TOOL IN THE DIAGNOSIS OF AUTOIMMUNE PANCREATITIS

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Introduction. Autoimmune pancreatitis (AIP) is a rare chronic pancreatic inflammation. The diagnosis is most often made by surgically obtained samples since collecting adequate tissue specimen using less invasive methods can be very challenging. We report a case of AIP diagnosis based on endoscopically acquired sample.

Case report. A 49-year-old Caucasian male presented with painless obstructive jaundice 7 days prior to initial hospitalization at our clinical center for further evaluation of suspected autoimmune pancreatitis observed on *magnetic resonance cholangiopancreatography* (*MRCP*) ('sausage-like' appearance). Upon arrival, laboratory findings showed elevated CA 19-9 (194 U/mL) and bilirubin levels (410 mmol/L). We performed endoscopic ultrasound that revealed enlarged, hypoechoic pancreas and dilated common bile duct. Endoscopic ultrasound guided fine needle biopsy (EUS-FNB) using Boston Acquire 22 G needle was performed for specimen acquisition,

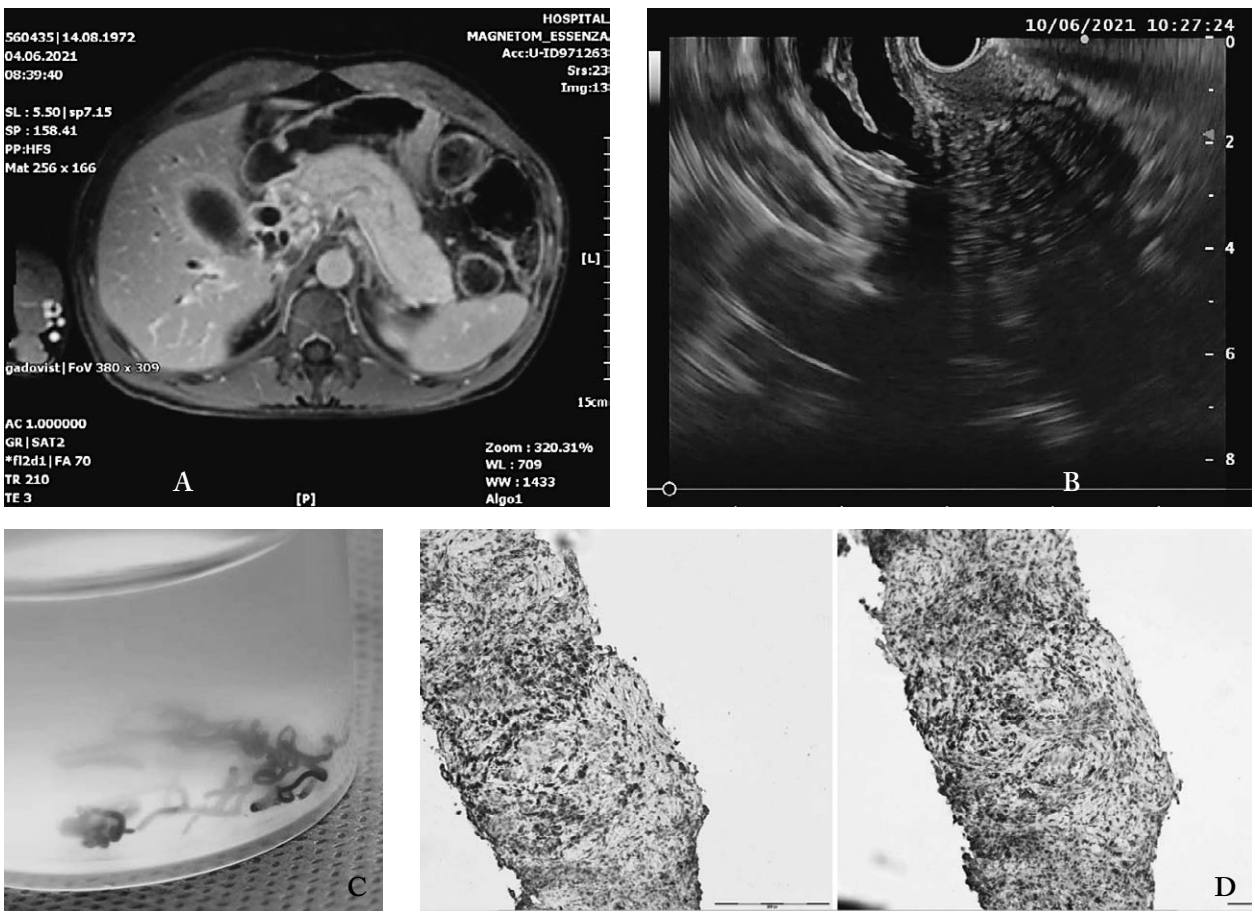


Fig. 1. (A) MRCP: 'sausage-like' appearance of the pancreas; (B) EUS: enlarged, hypoechoic head of the pancreas; (C) tissue specimen acquired via EUS-FNB; (D) immunohistochemical IgG and IgG4 staining: 60 IgG positive plasma cells/high power field (left panel); 40 IgG positive plasma cells/high power field; IgG:IgG4 ratio = more than 40% (magnification x100; scale bar 200 mm) (right).

followed by decompression of the biliary system using endoscopic retrograde cholangiopancreatography. Histopathology of the acquired tissue showed microscopic features of both type 1 and type 2 AIP which is, according to the literature, not very common finding. Immunoglobulin G4 antibodies that came positive around the time of histopathology investigation additionally confirmed the diagnosis. Prednisolone therapy at a starting dosage of 40 mg was initiated and the patient was discharged from the hospital. At regular outpatient follow up, significant reduction in the size of the pancreas was confirmed on computed tomography, as well as complete normalization of laboratory findings. Since the patient was at a high risk of relapse, azathioprine 50 mg was also initiated.

Conclusion. To our knowledge, this is the first case described in Croatia where the diagnosis of AIP was made by EUS-FNB. It highlights the reliability of EUS-FNB as a noninvasive tool in obtaining adequate specimen for tissue diagnosis, not only for focal but also for other, diffuse diseases of the pancreaticobiliary system.

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ULTRASOUND ASSESSMENT OF LIVER STEATOSIS USING ARTIFICIAL NEURAL NETWORK

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Introduction and objective. Nonalcoholic fatty liver disease is the most prevalent type of liver disease affecting approximately 25% of the population[1]. Using B mode ultrasound to subjectively assess liver steatosis has been done for decades. In this pilot study, our objective was to investigate the applicability of artificial neural networks for qualitative assessment of liver steatosis using a single ultrasound B mode image.

Methods. In this prospective study, we included 63 patients who underwent abdominal ultrasound in Sestre milosrdnice University Hospital Center in May 2020. The procedure was performed by an experienced gastroenterologist using Hitachi Arietta V 70 with a convex probe (1-6 MHz). Steatosis was determined by Hamaguchi score >3[2]. With an ultrasound probe in the subcostal position, an image containing both liver and right kidney was saved for every patient. After labeling the images, 33 patients with fatty liver and 30 normal controls were included in the final dataset. Images were first cropped and downsized to 150 by 150 pixel format. Data augmentation was used to increase dataset by randomly changing rotation and brightness of the processed images. This yielded the final dataset of 396 images, which was split in 80% training and 20% testing set. The dataset was then used to train and evaluate a convolutional neural network.

Results. Final neural network consisted of 3 convolutional and 1 dense layer. The specificity was 0.81 and sensitivity 0.80 with AUC of 0.914. The mean time for a single image calculation was 0.047 s.

Conclusion. The results further confirmed that neural networks could be successfully used to classify ultrasound images even on small datasets and without the need for expensive equipment.

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References

1. Mundi MS, Velapati S, Patel J, Kellogg TA, Abu Dayyeh BK, Hurt RT. Evolution of NAFLD and its management. Nutr Clin Pract. 2020;35(1):72-84. doi: 10.1002/ncp.10449
2. Ferraioli G, Soares Monteiro LB. Ultrasound-based techniques for the diagnosis of liver steatosis. World J Gastroenterol. 2019;25(40):6053-62. doi: 10.3748/wjg.v25.i40.6053

VALIDATION OF THE NEW DIAGNOSTIC CRITERIA FOR CLINICALLY SIGNIFICANT PORTAL HYPERTENSION IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE BY USING PLATELET COUNT AND TRANSIENT ELASTOGRAPHY

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Introduction and objective. Baveno VI consensus established criteria for noninvasive ruling in clinically significant portal hypertension (CSPH) by using liver stiffness measurements (LSM) by transient elastography (TE). However, only recently the new criteria have been proposed for ruling out CSPH by using a combination of LSM by TE and platelet count (Plt). In this study, we aimed to validate these newly proposed noninvasive criteria for diagnosing CSPH specifically in patients with compensated advanced chronic liver disease (cACLD).

Methods. Diagnostic performance of noninvasive criteria for CSPH (LSM ≥25 kPa to rule in and Plt ≥150x10^9/L + LSM ≤15 kPa to rule out CSPH) was retrospectively tested in an independent cohort of consecutive patients who underwent hepatic venous pressure gradient (HVPG) measurements and liver biopsy due to suspicion of cACLD. Suspicion of cACLD was based on LSM ≥10 kPa by TE or results of liver imaging, without overt signs of CSPH. Patients with conditions known to affect LSM results (alanine aminotransferase >5x upper limit of normal, liver congestion, extrahepatic biliary obstruction, infiltrative liver neoplasms) were excluded.

Results: Seventy-six patients were included, 78.9% of males, mean age 62 years, 36.8% suffered from alcoholic and 30.3% from nonalcoholic fatty liver disease, 14.5% from chronic viral hepatitis, 30.3% were obese, 52.6% had HVPG ≥10 mm Hg, 56.6% had Plt ≥150x10^9/L. LSM ≥25 kPa showed 67.5% sensitivity (95% CI 50.9-81.4), 88.9% specificity (73.9-96.9), 87.1% positive predictive value (PPV) (70.2-96.4) and 71.1% negative predictive value (NPV) (55.7-83.6), to rule in CSPH. Plt ≥150 + LSM ≤15 kPa had 100% sensitivity (91.1-100), 66.6% specificity (49.0-84.1), 76.9% PPV (63.2-87.5) and 100% NPV (85.8-100) to rule out CSPH. Altogether, 53/76 (69.7%) patients would fit into the suggested criteria, thus obviating the need for HVPG measurement, with the cost of falsely ruling in CSPH in 4/76 (5.3%) patients, without false negative classification.

Conclusion: By using these simple noninvasive criteria 49/76 (64.5%) patients could be classified correctly for the presence/absence of CSPH, thus obviating the need for HVPG measurements.

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IGG4-RELATED SCLEROSING CHOLANGITIS – A CASE REPORT: IS SURGERY ALWAYS THE ANSWER?

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Introduction. IgG4-associated sclerosing cholangitis (IgG4-SC) is a separate type of cholangitis of unknown etiology. It is most commonly diagnosed in men (3:1) between the ages of 60 and 70[1], while the exact prevalence of the disease is unknown. A case is presented of a female patient who eventually underwent liver transplantation (LT) due to complications of unrecognized IgG4-SC.

Case report. A 50-year-old female patient was hospitalized at our Department in January 2019 for treatment of a persistent cholestatic liver lesion. In January 2018, while she was hospitalized at another institution, the patient was diagnosed and confirmed by multi-slice computed tomography (MSCT) with acute interstitial pancreatitis with dilatation of the intrahepatic bile ducts. After that, she was hospitalized on two occasions due to acute cholangitis (July and August 2018). Initial abdominal ultrasound showed that the liver was free of focal lesions, the hepatic artery was permeable, and only mild dilatation of the intrahepatic bile ducts was found. No biliary tree pathology was found by *endoscopic retrograde cholangiopancreatography* and abdominal MSCT was performed, which then raised suspicion of cholangiocellular carcinoma (CCC) based on the findings of dilatation of the intrahepatic bile ducts. Tumor marker values (*carcinoembryonic antigen*, Ca19-9, alpha-fetoprotein) were normal and biopsy of the remaining liver tissue supported secondary biliary cirrhosis. Subsequently, exploratory laparotomy was performed, during which sclerosed pancreas, as well as sclerosis of the entire course of ductus choledochus were found. No malignant cells were found in the resected part of the choledochus. Serum IgG4 level was 5.57 g/L (normal, up to 2.01 g/L). In the context of recurrent cholangitis and difficult provision of biliary drainage, the patient underwent a LT in April 2019. Storiform connective tissue amplification around the hilar bile ducts with infiltration >50 IgG4 positive plasma cells *per* high-power field was found in the explanted liver and the diagnosis of IgG4-SC was confirmed.

Discussion. IgG4-SC is a biliary manifestation of IgG4-related disease which manifests as tumor-like swelling of target organs. Most cases are associated with type 1 autoimmune pancreatitis (AIP 1)[2]. Hilar CCC is the most important differential diagnosis of IgG4-SC and both diseases are characterized by a complex diagnostic procedure and wide differential diagnosis, but differ significantly in treatment. The diagnosis of IgG4-SC is made according to HISORt criteria (as for AIP1) and it is treated with glucocorticoids or immunomodulators in early stages[3]. CCC treatment requires an aggressive surgical approach due to poor prognosis and high chances of disease recurrence. LT is indicated in selected patients with hilar CCC, as well as in patients with late-stage IgG4-SC due to decompensated cirrhosis or other complications.

Conclusion. IgG4-SC is a rare disease which needs to be included in the differential diagnosis of all stenotic bile duct lesions, and early detection of the disease can reduce the need for surgery, as well as the possibility of complications. When it comes to LT, it is important that IgG4-SC is diagnosed before development of secondary biliary cirrhosis and the very need for LT, which in addition to surgical complications entails long-term immunosuppression.

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References

1. Okazaki K, Uchida K, Koyabu M, Miyoshi H, Ikeura T. IgG4 cholangiopathy – current concept, diagnosis, and pathogenesis. J Hepatol. 2014;61:690-5.
2. Zen Y, Nakanuma Y. IgG4 cholangiopathy. Int J Hepatol. 2012;2012:472376. doi: 10.1155/2012/472376
3. Retrieved from: https://www.researchgate.net/figure/HISORt-criteria-for-the-diagnosis-of-autoimmune-pancreatitis_fig1_281295492. Accessed Oct 9, 2021.

EDA – ENDOSCOPY DIGITAL ASSISTANT HELPING PHYSICIANS TO INDICATE COLONOSCOPY

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Introduction and aims. Digital health assistants have different functions, i.e. they can give instructions, answer specific questions, or monitor health status and symptoms. These computer programs are designed to simulate communication *via* a voice or text interface. Endoscopy Digital Assistant (EDA) was developed to provide assistance to family physicians in decision making on referring patients for colonoscopy[1,2]. It is based on the recommendations of the European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE II) and the criteria for the suitability of indications for colonoscopy.

Methods. EDA was developed using an algorithm based on recommendations and with an interface in Croatian language. In accordance with the EPAGE II criteria, EDA offers 11 possible clinical scenarios, based on patient history, symptoms, and results of the previous work-up. By entering the required data, one of three possible outcomes is recommended: colonoscopy is required; colonoscopy is not required; and referral to a gastroenterologist. Pilot validation of the EPAGE II criteria was performed on the initial cohort of patients referred for colonoscopy at the Zagreb University Hospital Centre.

Results. From January to March 2021, we made comparison of indications for colonoscopy and the recommendations using EPAGE II criteria in 181 patients (58% of men, mean age 62 years) referred for colonoscopy. In 116 patients, the results of colonoscopy revealed that the procedure was necessary, while using the EPAGE II criteria, colonoscopy was assessed as necessary in 107 (92%) patients. In 37 referred patients, the procedure was found to be unnecessary, and according to the EPAGE II criteria, colonoscopy was unnecessary in 35 (94%) patients. In total, about 30% (55/181) of the indicated endoscopies were rated as unnecessary.

Conclusion. EDA provides assistance to family physicians in making decision on patient referral for colonoscopy. In this pilot validation of EPAGE II criteria, used in the development of EDA, we found high accuracy (>90%) of the criteria in assessing the need for referring patients for invasive diagnostic examination, i.e. colonoscopy. In further development of the project, the goals are EDA validation on a larger cohort of patients and development of a mobile application.

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References

1. Jover R, Herráiz M, Alarcón O, Brullet E, Bujanda L, Bustamante M, *et al*. Clinical practice guidelines: quality of colonoscopy in colorectal cancer screening. Endoscopy. 2012 Apr;44(4):444-51.
2. EPAGE (European Panel on the Appropriateness of Gastrointestinal Endoscopy) [Internet]. [cited 2020 Oct 25]. Available from: https://www.epage.ch/EPAGE_ADM/start2.html

COVID-19 AND ACUTE PANCREATITIS – A CASE REPORT

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Introduction. For almost two years, we have been witnessing the struggle with the COVID-19 infection, which has become a major public health issue around the world. Although SARS-CoV-2 is primarily a respiratory virus, in addition to the lungs, it damages numerous other organs, and the question also frequently arises whether it can cause acute pancreatitis. As a possible pathogenesis, literature describes a direct cytopathic effect of the virus on pancreatic tissue, then within the framework of localized vasculitis and thrombotic microangiopathy, systemic inflammatory response and multi-organ dysfunction, and drug-induced acute pancreatitis.

Case report. A 36-year-old male with COVID-19 presented on day 8 of the disease with aggravated dyspnea, chest pain, and high fever. He had a history of arterial hypertension, treated with perindopril. He was hospitalized at the COVID-19 ward, and started on oxygen supplementation through a simple face mask. Baseline laboratory findings showed neutrophilia with mildly elevated C-reactive protein, alpha-amylase 164 U/L, and partial respiratory insufficiency in the acid-base status. Despite oxygen therapy, the patient still had respiratory insufficiency and tachypnea, and was fitted with a Venturi mask. On day 4 of his hospital stay, he experienced further aggravation of respiratory insufficiency and was transferred to the COVID Respiratory Center, received orotracheal intubation, and was connected to mechanical ventilation. On day 3 of intensive treatment, laboratory findings showed an increase in inflammatory parameters and conjugated hyperbilirubinemia, alpha-amylase 176 U/L, lipase 203 U/L, while abdominal ultrasound revealed an inhomogeneous pancreatic head. On day 8 of intensive treatment, sudden aggravation of respiratory insufficiency occurred, multi-slice computed tomography pulmonary angiography was performed and demonstrated massive pulmonary embolism. The patient underwent thrombectomy and targeted thrombolysis *via* a transfemoral catheter, but with no success. Despite high doses of vasoactive medications, the patient was extremely hemodynamically unstable with respiratory insufficiency. Peripheral VVA ECMO was placed and soon converted into central VVA ECMO. Despite all the intensive treatment measures undertaken, the patient died on day 16 of intensive treatment.

Conclusion. The report describes a patient whose pancreatic impairment in terms of laboratory and imaging findings could be associated with the COVID-19 infection. So far, there has been no scientifically based evidence for the link between the two diseases, and further animal model studies are required, as well as larger epidemiological studies to establish whether SARS-CoV-2 virus causes acute pancreatitis.

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USE OF BALANCED CRYSTALLOID SOLUTIONS IN EARLY TREATMENT OF ACUTE PANCREATITIS – PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Aim. To assess the potential beneficial and harmful effects of a balanced crystalloid solution (Plasmalyte) compared to normal saline in the early treatment of patients with acute pancreatitis (AP).

Methods. Consecutive patients diagnosed with AP admitted to our hospital were randomly assigned to receive a balanced crystalloid solution (group 1) as an initial bolus of 10 mL/kg body weight within 60 min after randomization and then continued at a rate of 3.0 mL/kg body weight/h during the next 72 hours, or normal saline (group 2) administered in an identical manner. In cases of severe hypovolemia, bolus doses were repeated and the administration of fluid was continued at a rate of 3.5 mL/kg/h, and increased to a maximum of 5.0 mL/kg/h if needed. Clinical assessment with systemic inflammatory response syndrome (SIRS) and laboratory parameters was performed at 8 to 12, 24, 48, and 72 hours after randomization. We assessed the incidence of SIRS as the primary outcome. Secondary outcomes were mortality, organ failure (OF; persistent and transient), local complications, infected pancreatic necrosis, need for endoscopic, percutaneous and surgical interventions, and length of hospital stay.

Results. We present preliminary results on 50 randomized patients. Thirty-one patients were randomized to receive a balanced crystalloid solution, while 19 received saline. There was no significant difference according to age (64.42±12.33 *vs*. 55.84±20.87 years; p=0.07) and severity of disease at admission defined by BISAP index (median in both groups = 1; p=0.236). The occurrence of SIRS was similar in both groups, with 2 patients having experienced SIRS in group 1 and none in group 2 (p=0.699). No deaths were reported in either group. OF occurred in 6 compared to 4 patients, with transient OF being confirmed in 5 *versus* 3 patients (p=0.698), and persistent in 1 patient from each group (p=0.715). Specific types of OF occurred in 2/31 *vs*. 0/19 patients for cardiovascular failure (p=0.699), 2/31 *vs*. 0/19 patients for renal failure (p=0.699), and 5/31 *vs*. 4/19 patients for respiratory failure (p=0.952). Necrotizing pancreatitis was confirmed by abdominal computed tomography in 11/31 group 1patients and 6/19 group 2 patients (p=0.980). There was no significant difference in the development of local complications including acute peripancreatic fluid collections (6/31 *vs*. 5/19; p=0.822), acute necrotic collections (9/31 *vs*. 5/19; p=0.907), and walled-off necrosis (1/31 *vs*. 0/19; p=0.804). No cases of pseudocysts and infected pancreatic necrosis were recorded.

Discussion. Intensive fluid resuscitation is the cornerstone of treatment of AP. Current guidelines recommend use of Ringer's lactate as a balanced crystalloid solution instead of normal saline, while data on other types of balanced crystalloids are extremely scarce. Our meta-analysis of randomized controlled trials assessing balanced crystalloids in AP included only three studies with a total of 127 patients, which assessed the use of Ringer's lactate, but no studies evaluated other types of solutions. A recently published randomized controlled trial with 11052 patients comparing balanced crystalloids to normal saline in critically-ill patients did not show significantly reduced 90-day mortality.

Conclusion. Use of balanced crystalloid solutions in patients with AP is still insufficiently researched. According to current knowledge, there are theoretical potential benefits in using balanced crystalloids, especially in reducing renal failure and metabolic acidosis, however, further studies are needed to gain solid evidence.

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References

1. Radovan A, Vranic L, Stimac D, Poropat G. Specific crystalloid solutions *versus* normal saline for acute pancreatitis (AP) – meta-analysis with trial sequential analysis. Pancreatology. 2019;19(Suppl 1):S42.
2. Zampieri G, Machado FR, Biondi RS, *et al*. Effect of intravenous fluid treatment with a balanced solution *vs* 0.9% saline solution on mortality in critically ill patients. JAMA 2021;326(9):818-29. doi: 10.1001/jama.2021.11684

A RARE CAUSE OF ACUTE ABDOMINAL PAIN IN A YOUNG MALE: EPIPLOIC APPENDAGITIS

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Introduction and objective. Epiploic appendages are peritoneal structures on the outer surface of the bowel wall composed of adipose tissue and surrounding blood vessels. These structures can get inflamed, most commonly from torsion, resulting in a condition called epiploic appendagitis[1].

Methods. Here we discuss a case report of a 29-year-old previously healthy male who presented to emergency department with sharp pain in the left lower quadrant of the abdomen, which had started two days before admission.

Results. Laboratory tests showed elevated inflammatory markers while multi-slice computed tomography scan revealed epiploic appendagitis around the lower parts of ascending colon. The patient was treated with antibiotic and analgetic therapy for 7 days without recurrence of the symptoms during 3-month follow-up period.

Conclusion. Although this is a rare cause of acute abdominal pain, it should not be misdiagnosed with more common conditions such as diverticulitis or appendicitis. In this case, computed tomography scan was crucial to make an accurate diagnosis.

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Reference

1. Suresh Kumar VC, Mani KK, Alwakkaa H, Shina J. Epiploic Appendagitis: an often misdiagnosed cause of acute abdomen. Case Rep Gastroenterol. 2019;13:364-8. DOI: 10.1159/000502683

LEMMEL SYNDROME AS A RARE CAUSE OF OBSTRUCTIVE JAUNDICE: A CASE REPORT

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Introduction and objective. Lemmel syndrome is defined as an obstructive jaundice caused by periampullary duodenal diverticulum compressing the common bile duct in the absence of choledocholithiasis or neoplasm.

Methods. We discuss a case of a 62-year-old previously healthy woman presented to emergency department for evaluation of epigastric pain and jaundice that had been present for a week.

Results. Physical examination on admission revealed mild epigastric pain, scleral icterus, and yellowish pigmentation of the skin. Laboratory values of liver function tests and inflammatory markers were elevated. *Magnetic resonance cholangiopancreatography* was performed to show normal gallbladder, intra- and extrahepatic biliary dilatation with common bile duct dilatation measuring 1.5 cm, and periampullary inflamed duodenal diverticulum measuring up to 4 cm in the long axis. Surgery was consulted and advised conservative medical treatment with elective surgery after resolution of inflammation. She was treated with 10-day course of broad spectrum antibiotics with no recurrence of symptoms within 6 months and complete normalization of the previously mentioned laboratory tests.

Conclusion. Although this is a rare cause of biliary obstruction, it should be considered in cases of obstructive jaundice with no evidence for choledocholithiasis or malignancy. To conclude, imaging analysis is crucial for identification of this uncommon condition.

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RELATIONSHIP BETWEEN C-REACTIVE PROTEIN TO ALBUMIN RATIO AND DISEASE ACTIVITY IN PATIENTS WITH CROHN'S DISEASE

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Introduction and objective. Numerous biochemical markers have been used to assess Crohn's disease activity in clinical practice, but none of them are specific[1]. Furthermore, an increasing number of studies are investigating the role of the C-reactive protein (CRP) to albumin ratio as a potential biomarker for assessing disease activity[2,3].

Methods. In this retrospective study, serum CRP, albumin (Alb), erythrocyte sedimentation rate (ESR), and white blood cell count (WBC) were measured. Additionally, the CRP/Alb ratio was determined. Crohn's disease activity index (CDAI) was used to assess the disease activity.

Results. A total of 28 patients participated in the study, 14 men and 14 women, mean age 72.36 (range 49-85) years. The mean CDAI was 133.89 (range 11-469). There was a significant correlation between CRP/Alb and ESR (ρ=0.409, p=0.031). Correlation coefficient between CRP/Alb and CDAI (ρ=0.293, p=0.131) and between CRP/Alb and WBC (ρ=0.160, p=0.415) was not statistically significant. Observing CRP and albumin values separately, a positive correlation was found between CRP and ESR (ρ=0.454, p=0.015) and between CRP and Alb (ρ=0.473, p=0.011).

Conclusion. There was no significant association of CRP/Alb ratio with disease activity measured by CDAI in the study sample. This could be attributed to the small sample size and using only CDAI. Additional studies are needed to examine the possible association of CRP/Alb ratio with other disease activity scales and endoscopic findings.

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References

1. Xu M, Cen M, Chen X, Chen H, *et al*. Correlation between serological biomarkers and disease activity in patients with inflammatory bowel disease. Biomed Res Int. 2019 Dec 25;2019:6517549. DOI: 10.1155/2019/6517549
2. Chen YH, Wang L, Feng SY, Cai WM, *et al*. The relationship between C-reactive protein/albumin ratio and disease activity in patients with inflammatory bowel disease. Gastroenterol Res Pract 2020;2020:3467419. DOI: 10.1155/2020/3467419
3. Zhou FS, Gao N, Sun X, Jiang XY, *et al*. C-reactive protein/abumin ratio is a useful biomarker for predicting the mucosal healing in the Crohn disease: a retrospective study. Medicine (Baltimore). 2021;100:e24925. DOI: 10.1097/MD.0000000000024925

SPECIFICITY OF ABDOMINAL FORM OF HEREDITARY ANGIOEDEMA IN A PREGNANT WOMAN

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Introduction. Hereditary angioedema (HAE) is a rare but life-threatening illness due to the attacks of painless, limited, recurrent swelling of submucosal, subcutaneous and interstitial tissues. The attack lasts for several hours to several days. The incidence is 1:50 000, and in our country, there are about 100 patients in the register. Abdominal form is a particular entity of this disease due to the ability of mimicry and presentation as any other form of acute abdominal events.

Methods. The abdominal type of HAE is manifested with abrupt abdominal pain, followed by abdominal distension and nausea. These symptoms occurring in approximately 70%-90% of the patients (depending on the authors). As the disease is presented as acute abdomen, physicians often reach for an urgent surgical procedure, expecting acute appendicitis, small bowel obstruction, diverticulitis, biliary attack, etc. Diagnostic procedure is complicated by the unusual nature of the disease, i.e. the ability to self-relieve, so the time to set up the correct diagnosis will often be prolonged to up to 10 years. Diagnostic procedure includes assessment of basic C3 and C4 components, and abdominal ultrasound to prove or exclude free fluid in the abdominal cavity. Abdominal multi-slice computed tomography will show relaxed and thickened bowels with free liquid release, without signs of obstruction. By excluding obstruction of any vascular structure or other etiology, acute surgery will be avoided because HAE is a partially or completely 'self-relieving' disease.

Case report. A 35-year-old pregnant woman was treated for HAE from childhood, now by Firazyr (icatibant), as needed. During pregnancy, she had HAE attacks almost twice a week, which were in part controlled by the injection of Cinryze (INN-C1 inhibitor) and Berinert (INN-C1 inhibitor). She had frequent HAE attacks in the form of swelling of the extremities, severe abdominal pain accompanied by diarrhea, and occasional swelling of one side of the face and half of the lips. In early March, 2021, cesarean delivery was done. The Commission for Medicines of the Zadar General Hospital approved the injection of Firazyr for home use.

Conclusion. If there is a lump with recurrent pain in the abdomen and unclear etiology, it is important to think about HAE and to direct diagnostic workup towards this rare but life-threatening illness.

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Reference

1. Marković AS, Rozmanić V, Anić B, Aberle N, Racić G, Novak S, Sunara D, Grdinić B, Karadza-Lapić L, Radas MR, Karanović B, Kvenić B. Smjernice za dijagnostiku i liječenje hereditarnog angioedema. Lijec Vjesn. 2014;136(5-6):117-29. (in Croatian)

THE ROLE OF WNT-SIGNALING PATHWAY COMPONENTS IN THE DEVELOPMENT OF DIFFUSE GASTRIC CARCINOMA

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Introduction and objective. Diffuse gastric carcinoma (DGC) is characterized by highly invasive growth patterns, poor prognosis, and resistance to the systemic therapeutic agents available. Wnt signaling pathway is one of the basic mechanisms in cell signalization, cell proliferation, regulation, differentiation, morphology, and mobility. A large number of studies confirmed the role of proteins, molecular participants of Wnt signaling pathway in the tumorigenesis of gastric carcinoma but the mechanism underlying dysregulation of this pathway in DGC has not been elucidated. The study aimed to investigate the expression profiles of Dishevelled family, secreted frizzled-related protein (SFRP) and transcription factor TCF-1, the molecular components of the Wnt signaling pathway, in DGC and healthy gastric tissue samples and to compare the results with pathological and clinical parameters.

Methods. Samples of 62 archived DGC and healthy gastric mucosa tissues were collected retrospectively from the Department of Pathology, Zagreb University Hospital Center. All tumors were studied by pathologists and classified as DGC according to the WHO criteria. Immunohistochemistry was performed to establish the levels of expression and cellular localization of SFRP1, SFRP3, DVL-2, DVL-3 and TCF-1. Patient demographic and clinical data (location of DGC and tumor staging parameters) were retrieved from their corresponding medical records.

Results. Immunohistochemical and stereological quantitative analysis revealed a statistically significant difference in the expression of SFRP1, SFRP3, TCF-1, DVL2 and DVL3 proteins. The expression of SFRP1 and SFRP3 in tumor tissue was significantly lower compared to healthy tissue, while the expression of DVL2, DVL3 and TCF-1 was significantly higher in tumor tissue compared to healthy tissue. No statistically significant difference in expression was found for any of the proteins in relation to the patient clinical and pathological characteristics, however, taking into consideration that the tumor was diagnosed in an advanced stage in over 80% of the patients analyzed.

Conclusion. The results obtained indicated a significant role of the Wnt signaling pathway components in gastric carcinogenesis, i.e. the loss of Wnt inhibitors and overexpression of Wnt cell fate regulators in tumor tissues play an important role in the development of DGC.

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References

1. Ansari S, Gantuya B, Tuan VP, Yamaoka Y. Diffuse gastric cancer: a summary of analogous contributing factors for its molecular pathogenicity. Int J Mol Sci. 2018;19:2424. doi: 10.3390/ijms19082424
2. MacDonald BT, Tamai K, He X. Wnt/β-catenin signaling: components, mechanisms and diseases. Dev Cell. 2009;17(1):9-26. doi: 10.1016/j.devcel.2009.06.016
3. Zhan T, Rindtorff N, Boutros M. Wnt signaling in cancer. Oncogene. 2017;36(11):1461-73. doi: 10.1038/onc.2016.304

MULTIPLE GIST IN THE SETTING OF NEUROFIBROMATOSIS TYPE 1

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Introduction. Gastrointestinal stromal tumors (GISTs) make up 1% of all digestive tract tumors. A great majority stains immunohistochemically for KIT (CD117), with 90% typically bearing mutations in c-KIT or PDGFRA genes, whereas the remaining 10% are classified as *wild type* (*wt*). *Wt*-GISTs constitute a heterogeneous group, with a rare variant in the setting of neurofibromatosis type 1 (NF1) being presented here.

Case report. A 61-year-old male with a history of prostate and renal carcinoma, as well as hypertension was referred to our hospital for further evaluation of small bowel tumors observed on abdominal computed tomography scan. The patient presented with dyspeptic symptoms accompanied by weight loss and dark colored stools in the last few months. During physical examination, numerous diffuse neurofibromas, café au lait spots and axillary freckling were appreciated without other notable pathology. Laboratory findings showed moderate microcytic anemia. Magnetic resonance enterography verified multifocal, lobulated, exophytic neoplasms of duodenum and jejunum up to 5 cm in size consistent with lymphoma or GIST. Furthermore, endoscopic ultrasound delineated these subepithelial lesions as arising from the 4th layer of the gastrointestinal wall (*muscularis propria)* and allowed for FNA/B sampling. Histopathology revealed streaks of spindle cells, staining for CD117, negative for SMA, CD34 corresponding to the diagnosis of GIST. Additionally, a dermatologist was consulted to validate the diagnosis of NF1. The oncologic multidisciplinary team indicated supportive treatment with tyrosine kinase inhibitors (TKI) due to locally advanced inoperable disease with recommendation of 3-month follow up.

Conclusion. Based on current data, NF1 is in significant correlation with the incidence of GIST and is a causative agent in 1%-2% of all, and 5%-7% of small bowel GISTs. We aimed to highlight the importance of recognizing NF1-GIST as a separate clinical entity due to its unique phenotype and difference in therapeutic approach since 10%-15% of these tumors are malignant. According to current guidelines (European Society for Medical Oncology 2021), it is advisable to run a mutation analysis on all GISTs before implementation of treatment. This applies especially to *wt*-NF1-GIST which lacks the characteristic c-KIT/ PDGFRA mutations that act as target molecules for TKI therapy, making its application of limited value.

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References

1. Andersson J, Sihto H, Meis-Kindblom JM, *et al*. NF1-associated gastrointestinal stromal tumors have unique clinical, phenotypic, and genotypic characteristics. Am J Surg Pathol. 2005;29(9):1170-6. doi: 10.1097/01.pas.0000159775.77912.15
2. Cheng SP, Huang MJ, Yang TL, *et al*. Neurofibromatosis with gastrointestinal stromal tumors: insights into the association. Dig Dis Sci. 2004;49:1165-9. doi: 10.1023/b:ddas.0000037806.14471.a2
3. Ylä-Outinen H, Loponen N, Kallionpää RA, Peltonen S, Peltonen J. Intestinal tumors in neurofibromatosis 1 with special reference to fatal gastrointestinal stromal tumors (GIST). Mol Genet Genomic Med [Internet]. 2019;7(9):e927. [cited 2021 Sep 18]. Available from: https://onlinelibrary.wiley.com/doi/10.1002/mgg3.927

NEOADJUVANT THERAPY IN LIVER TRANSPLANTATION FOR CHOLANGIOCARCINOMA

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Introduction and aim. The use of neoadjuvant chemoradiotherapy in the treatment of cholangiocellular carcinoma (CCC) by liver transplantation as part of the treatment protocol established in 1993 by the Mayo Clinic, resulted in considerable improvement in 5-year survival of patients with the above diagnosis. The method of using neoadjuvant radiotherapy (NRT) modeled after the said Mayo protocol has been applied in the treatment of CCC at the Division of Gastroenterology, Merkur University Hospital, since 2019. The aim of this study was to evaluate the outcomes of using this protocol.

Methods. The study included 41 patients transplanted due to CCC in the period from 2011 to 2021. We analyzed demographic, clinical and histopathological data, with emphasis on the incidence of relapses and treatment outcomes.

Results. During the study period, 3.2% of liver transplantations were performed due to CCC, with median waiting on the list of 11 days (interquartile range (IQR) 4.7-27.8). Median age of transplanted patients was 62, of which 39% were women and 61% were men. NRT was received by 19.5% of patients. Median follow-up was 662 days (IQR 234-1191), while for patients with NRT it was 461.5 days (IQR 39.5-712.5). A total of 41.5% of study patients had disease relapse, while none of the patients with NRT experienced relapse during follow-up. The 5-year survival of the overall patient cohort was 35.9% (*vs*. 76% according to Mayo protocol). However, in patients with no NRT, 2-year survival was 45.8%, whereas in those with NRT it was 72.9%. Bearing in mind the small cohort of patients with NRT and shorter follow-up with the level of significance, so far, no correlation was established between NRT and the incidence of relapse and fatal outcome (p=0.4392) (Fig. 1). Furthermore, 5-year survival of patients without relapse was 57.4% (comparable to 60% according to the Mayo protocol); 73.9% of patients whose disease resulted in death also experienced a relapse. It was also the most significant factor associated with the risk of fatal outcome (p<0.0071). The risk of relapse was associated with the presence of macrovascular invasion (p=0.0474) and microsatellites (p=0.00612) in the explantation report.

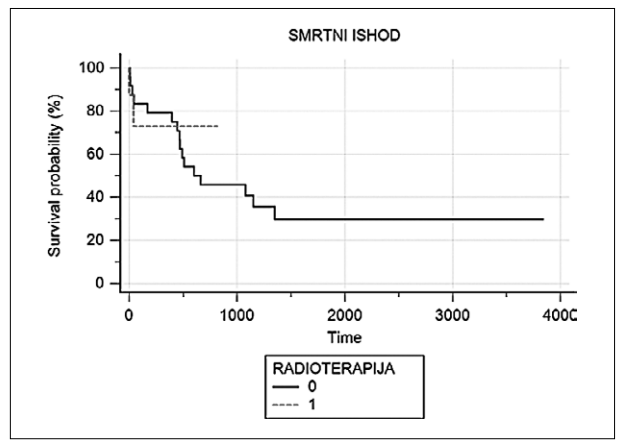


Fig. 1. Patient survival by use of neoadjuvant radiotherapy prior to liver transplantation.

Conclusion. CCC is a malignant neoplasm of the hepatobiliary system the treatment of which depends on surgical methods. Despite the small number of patients in the radiotherapy cohort, their result of 2-year patient survival of 72.9% *vs.* 45.8% of 2-year survival without radiotherapy was significant. These encouraging results highlight the importance and need to search for the optimal protocol for neoadjuvant therapy in the treatment of CCC by surgical methods, including liver transplantation.

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PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG): A FOUR-YEAR CLINICAL EXPERIENCE AT SPLIT UNIVERSITY HOSPITAL CENTER

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Introduction and aim. Enteral tube feeding (enteral nutrition) is nutrition therapy administered *via* a tube or stoma into the gastrointestinal tract distal to the oral cavity[1]. If enteral nutrition is needed for a limited time (usually up to six weeks), nasogastric tube feeding can be used. However, when long-term enteral nutrition is required, percutaneous endoscopic gastrostomy (PEG) is the preferred access device[2,3]. The objective of this study was to determine the exact number of patients with PEG, their characteristics, indications for PEG insertion, methods used for PEG placement, existence of periprocedural complications, and actual feeding time after PEG placement, in order to establish an archive of patients with PEG and to serve as a pilot project for the future, prospective investigation.

Methods. Medical records of all patients having undergone PEG tube placement at the Split University Hospital Center from January 2018 until September 2021 were reviewed in order to conduct a retrospective analysis.

Results. From January 2018 until the end of September 2021, PEG was introduced to 175 patients, 56% of them male, mean age 65.18 years. Malignancy was the indication for PEG placement in 38.56% of patients, with head and neck malignant tumors in 88.13% of them. Neurological diseases were the indication for PEG in 57.51% of patients, 39.77% of these with cerebrovascular incident. PEG was inserted using pull through technique in 69.56% and by direct puncture with gastropexy in 15.21% of patients. Immediate complications were recorded in 9.3% of patients. Late feeding, 24 h after PEG placement, was recommended to all patients.

Conclusion. At the Split University Hospital Center, the number of patients with PEG has been rising over the past four years. However, the year 2020 was an exception to this trend due to the COVID-19 pandemic, establishment and operation of the Respiratory Intensive Center. PEG is a safe and minimally invasive procedure associated with low percentage of immediate complications. It is the method of choice for long-term administration of enteral nutrition.

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References

1. Cederholm T, Barazzoni R, Austin P, *et al*. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017 Feb;36(1):49-64. https://doi.org/10.1016/j.clnu.2016.09.004
2. Krznarić Ž, Vranešić Bender D, Ljubas Kelečić D, *et al*. Hrvatske smjernice za prehranu osoba starije dobi. Dio II. Klinička prehrana. Lijec Vjesn. 2011;133:299-307. (in Croatian)
3. Bischoff SC, Austin P, Boeykens K, *et al*. ESPEN guideline on home enteral nutrition. Clin Nutr. 2020 Jan;39(1):5-22. https://doi.org/10.1016/j.clnu.2019.04.022

THE INCIDENCE OF HYPERTENSION IN AUTOIMMUNE LIVER DISEASES

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Introduction. Autoimmune hepatitis (AIH), primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) make a group of autoimmune liver diseases. Autoimmune diseases have traditionally been perceived as a cardiovascular risk factor due to a number of reasons. Firstly, suboptimal levels of vitamin D, which are a common finding in autoimmune diseases, are related to non-dipper hypertension. In addition, many studies address the issue of augmented arterial stiffness in autoimmune liver diseases measured by carotid-*to*-femoral pulse-wave velocity (cfPWV). Such a phenomenon is thought to be due to the fact that autoantibodies and inflammatory cells promote the expression of adhesive molecules (VCAM-1 and ICAM-1) while oxidative stress potentiates endothelial injury, all together leading to hypertension.

Methods. In this study, continuous measurement of blood pressure and measurement of arterial stiffness was performed using cfPWV. Study sample consisted of 68 patients, 19 (27.9%) with AIH, 31 (45.5%) with PBC, 4 (5%) with PSC, and 14 patients with overlap syndromes, including 7 (10%) with PBC/AIH, 6 (8.8%) with PSC/AIH and 1 (1.4%) with PSC/non-alcoholic steatohepatitis. There were 55 (80%) female and 13 (20%) male patients, age range 22-80 years. Hypertension was defined as the average 24-h measurement of systolic blood pressure >130 mm Hg and/or diastolic blood pressure >80 mm Hg, or a previous diagnosis of hypertension. In addition, serum level of vitamin D was determined in all study patients and hypovitaminosis D was defined as a serum level of vitamin D below 75 nmol/L.

Results. Out of 68 patients, 24 (35%) were previously diagnosed with hypertension, 21 female and 3 male patients. Nine (13.5%) patients, all females, were found to suffer from hypertension. Out of 68 patients, 33 (48.5%) suffered from hypertension, and 24 (73%) patients with hypertension were also found to have hypovitaminosis D.

Conclusion. The results of this study indicated a significant incidence of hypertension within the population of autoimmune liver disease patients. In addition, a significant incidence of hypovitaminosis D was found among patients with hypertension, suggesting that further research in terms of vitamin D supplementation should be encouraged. Considering that hypertension is one of the leading factors in the pathogenesis of cardiovascular disease, it is essential that both detection and treatment be conducted in a timely manner. Autoimmune liver diseases are likely to be the culprits of accelerated development of arterial stiffness and, by extension, of hypertension itself, therefore screening for hypertension is of utmost importance in this group of patients.

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INTERSTITIAL NEPHRITIS SECONDARY TO VEDOLIZUMAB MAINTENANCE TREATMENT FOR ULCERATIVE COLITIS

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Introduction and aim. Vedolizumab (VDZ) is a humanized, 'gut-selective' monoclonal antibody used to treat ulcerative colitis (UC) and Crohn's disease. It achieves its anti-inflammatory effect by binding selectively to α4β7 integrin, thus preventing the migration of lymphocytes into the intestinal mucosa. We present a case of VDZ-induced nephrotoxicity as a rare, unexpected, serious side effect of its administration.

Case report. We present a 51-year-old male patient who was diagnosed with moderate to severe, extensive UC (E3S2-3) nineteen years before. Four and a half years before, therapy with tumor necrosis factor inhibitors (first adalimumab and then infliximab) was started, which was then switched to VDZ two years before due to secondary loss of response. Owing to regular follow-up of the patient, sustained 'steroid-free' remission was achieved with VDZ maintenance therapy. Accidentally, as part of a routine check-up indicated by a general practitioner, pathologic urine test (hematuria and leukocyturia) was detected with normal serum creatinine value. A wide range of renal function test studies were performed by the nephrologist, which finally included kidney biopsy. Electron immunofluorescence microscopic findings provided evidence for moderate nephroangiosclerosis with superimposed lymphocytic interstitial nephritis, supporting a conclusion of drug-induced nephrotoxicity. As the patient was receiving only VDZ, and a couple of similar cases of VDZ-induced nephrotoxicity were found in the literature, its use was discontinued. Systemic steroid therapy was administered over 12 weeks, which led to complete normalization of renal function. During regular patient follow-up, early moderate to severe clinical, biochemical and endoscopic relapse of UC occurred; therefore, treatment switch with administration of a novel biologic from different class was commenced.

Discussion and conclusion. Interstitial nephritis as an immune allergic-mediated delayed hypersensitivity reaction is a very rare side effect of VDZ, described so far in less than a dozen of cases according to the available literature. Discontinuation of the monoclonal antibody and administration of systemic steroid therapy appear to lead to improved renal function in most of the cases described. Despite the rare occurrence of renal impairment due to conventional and biologic therapy for the treatment of inflammatory bowel disease, we want to emphasize the importance of regular periodic monitoring of renal function in this group of patients.

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ESOPHAGUS VISUALIZATION BY GASTROINTESTINAL ENDOSCOPY WITH PERCUTANEOUS RETROGRADE APPROACH *VIA* JEJUNOSTOMY

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Introduction. Head and neck squamous cell carcinoma can often be accompanied or followed by second esophageal squamous cell neoplasia. In patients with a history of surgical treatment of head and neck tumors, standard anterograde upper gastrointestinal endoscopy can pose a diagnostic challenge.

Case report. A 64-year-old male with a history of surgical treatment of hypopharyngeal carcinoma with closed esophageal stump, gastric resection and surgical percutaneous jejunostomy formation presented with imaging signs of second esophageal neoplasm. Retrograde endoscopy *via* jejunostomy was performed with esophageal tumor visualization and biopsy specimen collection. Histopathologic analysis confirmed esophageal squamous cell carcinoma.

Conclusion. Upper gastrointestinal endoscopy with a percutaneous retrograde approach is a feasible method for easy and effective imaging, biopsy specimen collection and potential therapeutic interventions in obstructed/closed esophagus.

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EXPRESSION OF BORIS IN COLORECTAL CARCINOMA: LACK OF ASSOCIATION WITH MAGE-A10 EXPRESSION

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Introduction. Brother of the Regulator of Imprinted Sites (BORIS) is a mammalian paralog of CTCF and member of the cancer-testis antigen (CTA) gene family. BORIS and CTCF activity is mutually exclusive in somatic cells, while they are both active in germ and tumor cells. CTCF/BORIS switching with ectopically expressed BORIS protein and RNA interplays with epigenetic upregulation of promoter activation of silenced CTA, which correlates with growth, aggressive behavior and survival of a variety of cancer cell lines. Melanoma-associated antigen-A10 (MAGE-A10) is the most immunogenic member of MAGE family, which has also been observed to be overexpressed in a variety of subtypes of cancer cell lines. Some authors suggest that ectopically expressed BORIS may replace CTCF function and have an effect on regulation of most other CTA genes such as MAGE-A10. There is a lack of data on the expression pattern and potential association of cytoplasm-localized BORIS and MAGE-A10 protein in non-metastatic and metastatic colorectal cancer (CRC) patients.

Aims and methods. The aim of this study was to determine and evaluate the potential association between immunohistochemical BORIS and MAGE-A10 expression in metastatic and non-metastatic CRC. Formalin-fixed and paraffin-embedded tumor sections were collected retrospectively from 95 patients (50 non-metastatic and 45 metastatic with liver metastases) surgically resected for CRC. Immunohistochemical staining for BORIS and MAGE-A10 was performed. The expression of BORIS and MAGE-A10 was correlated using a nonparametric correlation assay.

Results. No significant correlation between epithelial expression of cytoplasm-localized BORIS and MAGE-A10 protein in primary metastatic/non-metastatic CRC was detected (p=0.113). There was a positive and statistically significant association between stromal BORIS and epithelial MAGE-A10 protein expression in primary tumors (p=0.001). There also was a statistically significant association between epithelial MAGE-A10 and BORIS protein expression in the samples of liver metastasis (p=0.009), as well as stromal MAGE-A10 and BORIS expression in liver metastasis (p=0.011).

Conclusion. Our data indicated that there was no obvious or implicit association between ectopic expression of BORIS and MAGE-A10 activation in metastatic or non-metastatic CRC.

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References

1. Kim S, Yu NK, Kaang BK. CTCF as a multifunctional protein in genome regulation and gene expression. Exp Mol Med. 2015;47(6):e166. DOI: 10.1038/emm.2015.33
2. Pugacheva EM, Suzuki T, Pack SD, Natsuki Kosaka-Suzuki N, Yoon J, Vostrov AA *et al*. The structural complexity of the human BORIS gene in gametogenesis and cancer. PLoS One. 2010;5(11):e13872. DOI: 10.1371/journal.pone.0013872

GIANT RECTAL VILLOUS ADENOMA CAUSING MCKITTRICK-WHEELOCK SYNDROME SUCCESSFULLY TREATED BY A COMBINATION OF ENDOSCOPIC RESECTION PROCEDURES

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Introduction. We present a case of extremely large rectal villous adenoma causing severe McKittrick-Wheelock syndrome, completely resected by a combination of endoscopic procedures.

Case report. A 50-year-old female presented with symptoms of oliguria, general weakness, muscle cramps, nausea and dizziness caused by chronic diarrhea and consequent potentially lethal dehydration. After renal function and electrolyte status had been normalized, endoscopic procedures were performed. Colonoscopy revealed a huge laterally spreading nodular rectal lesion taking up to 75% of rectal circumference and extending approximately 12 cm in total diameter. The lesion was successfully removed *in toto* with a combination of endoscopic submucosal dissection and repeated endoscopic mucosal resections.

Conclusion. Electrolyte depletion accompanied by diarrhea should always incite clinicians to include McKittrick-Wheelock syndrome in their differential diagnosis. If there are no signs of invasion, endoscopic procedures should be the preferred treatment method.

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IS THERE AN ASSOCIATION BETWEEN DEPRESSION AND OBESITY IN CROATIAN IBD PATIENTS – A CROSS SECTIONAL SINGLE CENTER STUDY

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Introduction. Correlation between obesity and psychiatric disorders, particularly depression and anxiety, is well established. The burden of depression among inflammatory bowel disease (IBD) patients is also significant. Analyzing morphological characteristics in our IBD population, an increase in BMI and a higher proportion of overweight and obese patients have been observed. Therefore, we aimed to investigate the association between obesity and depression in our IBD cohort.

Methods. Consecutive IBD patients from the outpatient clinic were invited to anonymously fill-out multiple mixed-methods (quantitative/qualitative) Quality of Life questionnaires (SF-36, IMPACT, SIBDQ, IBD disk). In addition, morphological, demographic and treatment specific questions were asked. The survey was conducted from October 2019 to January 2020. Participant characteristics were assessed using descriptive statistics. Normal probability plots and Kolmogorov-Smirnov test were used to assess normal distribution. Independent continuous variables were compared using t-test.

Results. The study population included 159 patients (51% male, median age 37.5 years, interquartile range 25-54 years, 50.7% Crohn's disease), of which 49.4% were treated with biologics. The mean body mass index (BMI) in the study population was 24.9±4.7 kg/m^2, slightly lower in the cohort treated with biologics, but without a statistically significant difference; 46% of the patients were overweight/obese (BMI >25 kg/m^2). Depressive episodes were reported by 32.1% of subjects and 27.6% revealed high interference of their emotions with daily activities. Up to 21.5% of patients said that emotions negatively influenced their productivity at work. Interestingly, the patients affected by depressive symptoms had a statistically significantly lower BMI compared to those without emotional burden (23.5 kg/m^2 *vs*. 25.4 kg/m^2, $t(154)=2.39$, p=0.02).

Conclusion. The trend of obesity was quite pronounced in our cohort of Croatian IBD patients. Moreover, according to patient self-assessment, depressive disorder was a common finding in this population. Despite the fact that obesity is a risk factor for mood disorders in the general population, co-occurrence of both was not detected in our subgroup of overweight/obese IBD patients.

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ULCERATED JEJUNAL LIPOMA – AN UNCOMMON CAUSE OF GASTROINTESTINAL BLEEDING

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Introduction. In patients with gastrointestinal (GI) bleeding, when the culprit lesion is not detected by standard endoscopic and radiographic methods, in approximately 3/4 cases the source of bleeding is located in the small bowel. Small bowel neoplasms are rare lesions of variable nature and diverse presenting signs and symptoms. Lipomas are the second most common benign tumors arising in the small bowel. Their most common presenting symptoms include abdominal pain, nausea/vomiting, and GI bleeding[1].

Case report. A 65-year-old female with a history of unresolved iron deficiency anemia presented to our emergency department with signs and symptoms of acute upper GI bleeding including melena and severe normocytic anemia requiring blood transfusion. Repeated upper and lower endoscopic procedures were performed without identifying the source of bleeding. Meckel's diverticulum scan did not identify areas of ectopic gastric mucosa, but detected signs of 99m technetium pertechnetate in the proximal small bowel. Video capsule endoscopy revealed traces of fresh blood in the proximal jejunum, but the culprit lesion was not detected. Therefore, enteroscopy was performed, which revealed a large, polypoid shaped, protruding subepithelial lesion with ulcerated surface mucosa in the proximal jejunum. The whole lesion was successfully removed by endoscopic snare resection. Histopathologic analysis confirmed an ulcerated small bowel lipoma 30 mm in maximum diameter. Following endoscopic resection and iron supplementation, the patient was discharged from the hospital. At the follow-up examination after 2 months, she was without signs or symptoms of recurrent GI bleeding, and her hemoglobin level returned to normal.

Conclusion. Small bowel lipomas are rarely located in the jejunum where they can lead to complications such as small bowel bleeding. Although open and laparoscopic surgery represent the most common treatment strategies of small bowel lipomas, endoscopic resection can be the method of choice for the treatment of protruding symptomatic lesions.

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Reference

1. Farkas N, Wong J, Bethel J, Monib S, Frampton A, Thomson S. A systematic review of symptomatic small bowel lipomas of the jejunum and ileum. Ann Med Surg (Lond). 2020;58:52-67. doi: 10.1016/j.amsu.2020.08.028. PMID: 32953101

SYNCHRONOUS PERIAMPULLARY BRUNNER'S GLAND HAMARTOMA AND AMPULLARY ADENOCARCINOMA

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Introduction. Ampullary tumors account for 0.2%, and periampullary tumors for 7% of all digestive tract tumors. In early stage, they present with biliary obstruction and are most frequently surgically resectable. Brunner gland hamartoma (BGH) is a benign proliferation of duodenal Brunner's glands. It is often accidental finding during endoscopy, but can also present with bleeding or obstruction and require endoscopic or surgical resection.

Case report. A 68-year-old female patient was hospitalized due to painless obstructive icterus accompanied by weakened appetite and significant weight loss. Abdominal ultrasound and multi-slice computed tomography suggested suspicion of ampullary tumor process with dilation of intra- and extrahepatic bile ducts, which abruptly ended in the papilla of Vater area, where a soft-tissue neoplasm with contrast accumulation was observed, 16x17x23 mm in size, with pancreatic duct dilation. Guided by endoscopic ultrasound, aspiration cytology of the described formation was performed, with cytology results suspect of adenocarcinoma cells. In view of the localized disease, Whipple's procedure

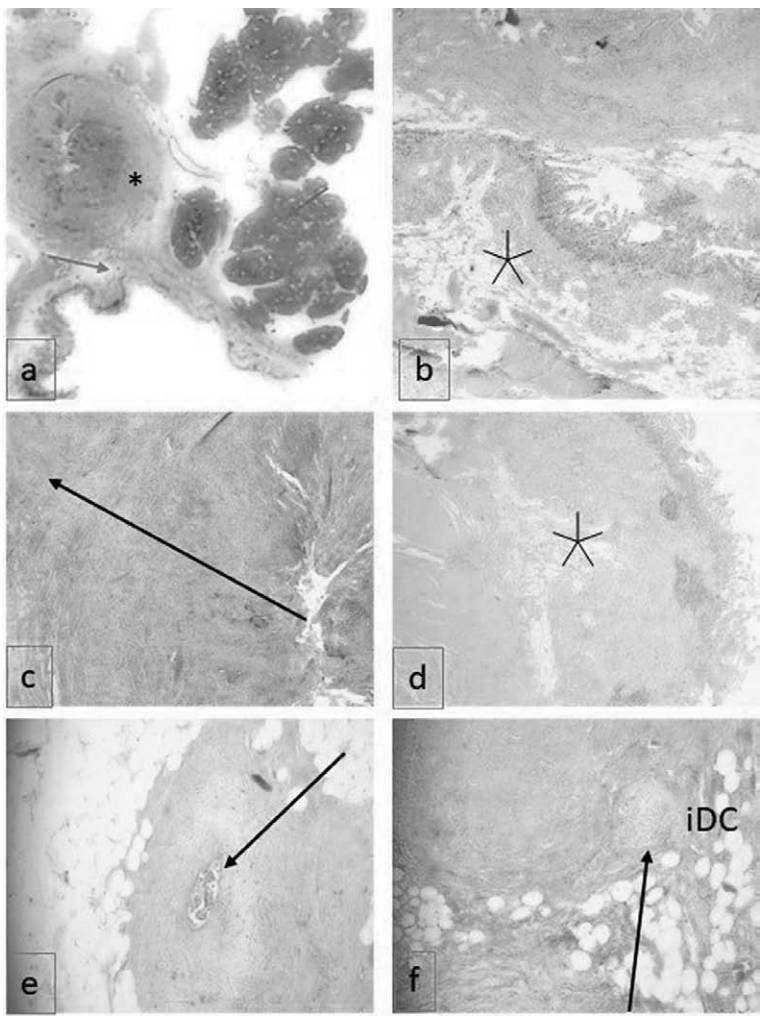


*Fig. 1. Synchronous periampullary Brunner's gland hamartoma and ampullary adenocarcinoma (of the ductal segment): (a) presentation of the relationship between ampullary tumor and other structures (ductal segment) (*ampulla–ductal segment; blue arrow – pancreas; green arrow – duodenum); (b, d) periampullary segment (duodenum) with hamartoma (black star; hematoxylin-eosin (HE), x100); (c, e, f) ampullary adenocarcinoma (ductal section) (black arrow); expansion by more than 0.5 cm into the surrounding pancreatic parenchyma; (f) infiltration from the external side of intrapancreatic section of the choledochus (iDC) (HE, x100).*

(pancreaticoduodenectomy) was performed. Histopathologic report macroscopically described circular periampullary thickening of the duodenum around the papilla of Vater, of 2 cm in diameter, which microscopically corresponded to BGH without contact with the terminal (ductal) part of the ampulla, in which a well-differentiated adenocarcinoma was infiltrating throughout the wall thickness with expansion into the surrounding pancreatic parenchyma by more than 0.5 cm, without lymph node metastases, and classified as pT3N0, G2. Postoperatively, the patient received adjuvant capecitabine therapy, and after 3-month follow-up she showed no signs of disease relapse.

Conclusion. This is a rare case of concomitant benign and malignant tumor of the ampullary region, where the accurate diagnosis resulted in successful curative treatment.

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Reference

1. Ahn DH, Bekaii-Saab T. Ampullary cancer: an overview. Am Soc Clin Oncol Educ Book. 2014:112-5.

A HIGH-IMPACT EXERCISE PROGRAM SIGNIFICANTLY IMPROVED BONE MINERAL DENSITY AND BODY COMPOSITION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE IN REMISSION

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Introduction and aim. Chronic inflammatory bowel disease (IBD) in children is associated with adverse changes in body composition, such as reduced bone mineral density (BMD) and reduced share of lean body mass (LBM), even when stable remission has been achieved. Regular exercise is associated with increase in muscle mass and BMD. The aim of our research was to investigate the effect of an exercise program on body composition of children with IBD in remission.

Methods. A total of 42 children with IBD in remission (25 boys; mean age 15.3±2.08 years; type of disease: Crohn's disease (CD) n=22, ulcerative colitis (UC) n=18, IBD unclassified (IBD-U) n=2) were enrolled in the study and participated in a 6-month high-impact exercise program. Dual-energy x-ray absorptiometry (DXA) was used to measure BMD, expressed in g/cm^2, and as Z-score dependent on age and sex, and to assess fat mass (FM) and LBM, expressed in grams and as Z-score based on age, sex and height at baseline and upon completion of the exercise program.

Results. On the basis of baseline and final measurements, an increase was reported in total body mass in study subjects from 53.32±11.02 kg to 56.24±12.27 kg ($p<0.001$), with an increase in absolute BMD (from 0.947±0.135 g/cm^2 to 0.983±0.144 g/cm^2, $p<0.001$), FM (from 16.59±7.28 kg to 17.41±7.23, $p<0.001$), and LBM (from 36.90±8.53 kg to 38.41±10.16 kg, $p=0.012$). BMD Z-score increased significantly (from -0.336±1.075 to -0.261±0.979, $p=0.020$), whereas LBM Z-score did not change significantly (from -1.69±1.25 to -1.71±1.44, $p=0.908$). In separate statistical analysis, a significant increase was observed in BMD ($p<0.001$), BMD Z-score ($p=0.017$), and LBM ($p<0.001$) among children with CD, while in other groups only an increase in absolute BMD ($p=0.001$) was reported. Furthermore, boys had a significant improvement in BMD ($p<0.001$), BMD Z-score ($p=0.043$), and LBM ($p<0.001$), with no significant change in LBM Z-score ($p=0.126$), whereas girls had a significant increase in BMD ($p=0.046$). It was established that there was no association between improvement in BMD and LBM and variables such as age at diagnosis, disease duration, and use of biologic therapy. No adverse events were reported, and only one participant withdrew from the study.

Conclusion. A significant increase in absolute BMD and Z-score was observed among study subjects. Children with CD and boys also experienced an increase in LBM.

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CHRONIC HEPATITIS C INFECTION PATIENT CHARACTERISTICS AND TREATMENT RESULTS USING DIRECT-ACTING ANTIVIRAL DRUGS: OUR EXPERIENCE

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Introduction and aims. Since their introduction in Croatia in 2016, combinations of direct-acting antiviral agents (DAAs) have become the standard treatment of chronic hepatitis C virus (HCV) infection. The aim of this study was to evaluate results of HCV treatment by DAAs in our cohort of patients treated for chronic HCV in our Hepatology Unit.

Methods. A retrospective analysis of patient records treated for chronic HCV infection by DAAs in the period from December 2016 to September 2021 was performed.

Results. A total of 34 patients (27 male, 7 female) were treated by DAAs. Their mean age was 54.4 (range, 39-77) years. Ten patients had been previously treated with interferon and ribavirin, and 24 were treatment-naïve. The majority of patients had high HCV viral load (mean, 2.39E+6 IU/mL). Patient characteristics and treatment combinations used are shown in Figure 1. Ribavirin was added to DAAs in 11 patients. Sixteen (47%) patients had cirrhosis, and 11 of them had decompensated cirrhosis. Seventeen (50%) patients had at least one extrahepatic manifestation present; two patients were on dialysis. Seven patients were treated for psychiatric conditions other than drug addiction. All patients who completed the therapy achieved end of treatment response

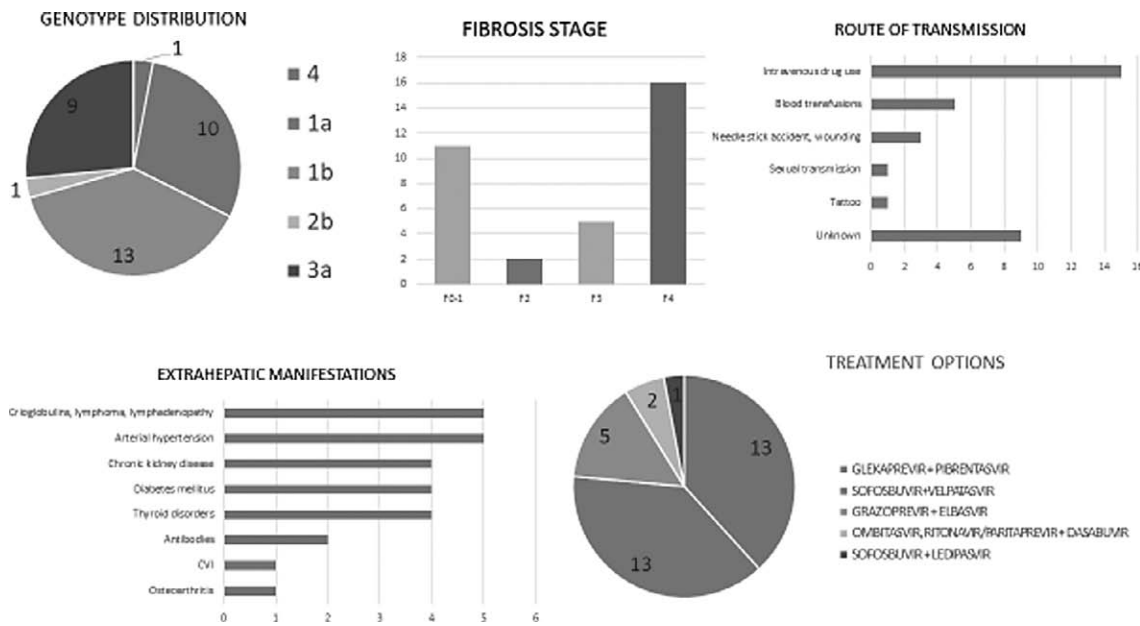


Fig. 1. Patient characteristics and treatment combinations.

and sustained viral response (SVR), with SVR results still pending for 5 patients. One patient with cirrhosis and severe comorbidities died after 6 weeks of treatment due to unrelated cause (with negative HCV RNA), resulting in an SVR of 97% of intention-to-treat patients. Following treatment, the mean values of AST decreased from 56.7 to 26.9 U/L and ALT from 78.3 to 21.0 U/L. Adverse events were rare and mild. One patient was diagnosed with hepatocellular carcinoma after successful treatment.

Conclusion. The majority of patients in our cohort had advanced liver disease, significant comorbidities, and extrahepatic manifestations of HCV infection. Treatment was effective in resolving HCV infection and improving patient liver enzymes, function, and quality of life.

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APPENDIX CARCINOMA PRESENTING AS CROHN'S DISEASE IN A YOUNG MALE

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Primary signet ring cell carcinoma is a rare event in surgery. It looks like acute appendicitis and it is difficult to diagnose it on clinical grounds alone. The diagnosis is always confirmed by histopathology of a surgically removed appendix. A young man aged 22 years presented with vomiting, diarrhea and cramps in his abdomen, without abdominal tenderness (mild abdominal discomfort in the right lower abdominal quadrant without signs of peritoneal irritation) during the previous month. The first endoscopic results showed only changes of mucosa that could be attributed to endoscopic and clinical presentation of Crohn's disease. A few days after the initiation of therapy with amino salicylates and corticosteroids, the patient went into ileus and was transferred to the Department of Surgery, where he underwent emergency right-sided hemicolectomy with resection of the transverse colon and forming of an ileostomy. The first histopathological diagnosis was pseudomembranous colitis. As the patient's condition was deteriorating, revision of the histopathological diagnosis was done. After careful revision and extensive sampling, a signet ring cell carcinoma arising in the appendix with infiltration of the ileocecal region was found. Immunohistochemically, tumor cells were positive for CDX-2 CK7, CK20, CK19 and carcinoembryonic antigen and negative for chromogranin A. Sixteen isolated lymph nodes were negative. Although the patient had a disease that was localized to the appendix and ileocecal region with no apparent distal metastasis, his clinical condition was worsening rapidly and he died after 2 months. This case shows the aggressive biological behavior of the appendix signet ring cell carcinoma. Scrupulous histopathological examination of the appendix is an obligatory procedure. Elimination of the signet ring cell carcinoma from other carcinoma subtypes is of special importance as it has an exceptionally poor prognosis when diagnosed in advanced stages.

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HEPATIC CYST INFECTION IN AN ELDERLY MAN – A CASE REPORT

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Introduction. Hepatic cysts are most commonly asymptomatic and of no major clinical significance. However, complications in terms of abscess, obstructive icterus, rupture or bleeding are possible[1].

Case report. An 81-year-old male patient presented to the Emergency Department due to fever and pain under the right costal margin. Laboratory findings showed extremely high levels of inflammatory parameters, while imaging methods (ultrasound (US) and abdominal computed tomography (CT)) revealed multiple cysts in the liver parenchyma, of which the largest two (14 and 8.2 cm in longer diameter, respectively) were localized in the right liver lobe and filled with more hyperechogenic, denser content (Fig.1). The patient was hospitalized and empirical dual antibiotic therapy was initiated. Conservative treatment resulted in partial response, and in the further course we opted for drainage. An US-guided drain was inserted, and a total of 800 mL of pus was evacuated. Follow-up abdominal US showed multiple cysts of the liver parenchyma, but now in the right liver lobe without fluid collection. Cytologic analysis of the cyst content suggested necrotic-purulent content, and in view of the *Escherichia coli* (*E. coli*) isolated from blood culture, antibiotic therapy was now continued in a targeted manner. The patient experienced significant clinical and laboratory improvement and was discharged from the hospital.



Fig. 1. Abdominal computed tomography revealed multiple cysts in the right liver lobe filled with more hyperechogenic, dense content.

Conclusion. Hepatic cyst infections most commonly develop *via* bile ducts or by hematogenous route[1]. Since repeated US proved dilation of the biliary tree, and *E. coli* was isolated from blood culture, this was probably biliary sepsis due to bile duct cholestasis. In patients with verified multiple hepatic cysts who develop fever and abdominal pain (most commonly under the right costal margin), hepatic cysts are considered to be the infection site. Such patients require regular monitoring by imaging techniques (US and/or CT), even if initially they do not present with typical symptoms and signs.

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Reference

1. Mori E, Akai Y, Matsumoto T, et al. Hepatic cyst infection in a healthy older male. BMJ Case Rep 2012. DOI: 10.1136/bcr.04.2011.4136

CHRONIC PSEUDO-OBSTRUCTION OF SIGMOID COLON – A CASE REPORT

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Introduction. Chronic intestinal pseudo-obstruction is a syndrome in which clinical picture and symptoms resemble those of mechanical obstruction, but without a clear cause[1]. The two most important pathophysiological types are myopathies and neuropathies[2].

Case report. A 49-year-old female patient reported to our Emergency Department due to constipation accompanied by pain under the left costal margin. Abdominal computed tomography demonstrated focal thickening of a segment of the splenic flexure, and along the dolichosigma intermittent areas of wider and narrower

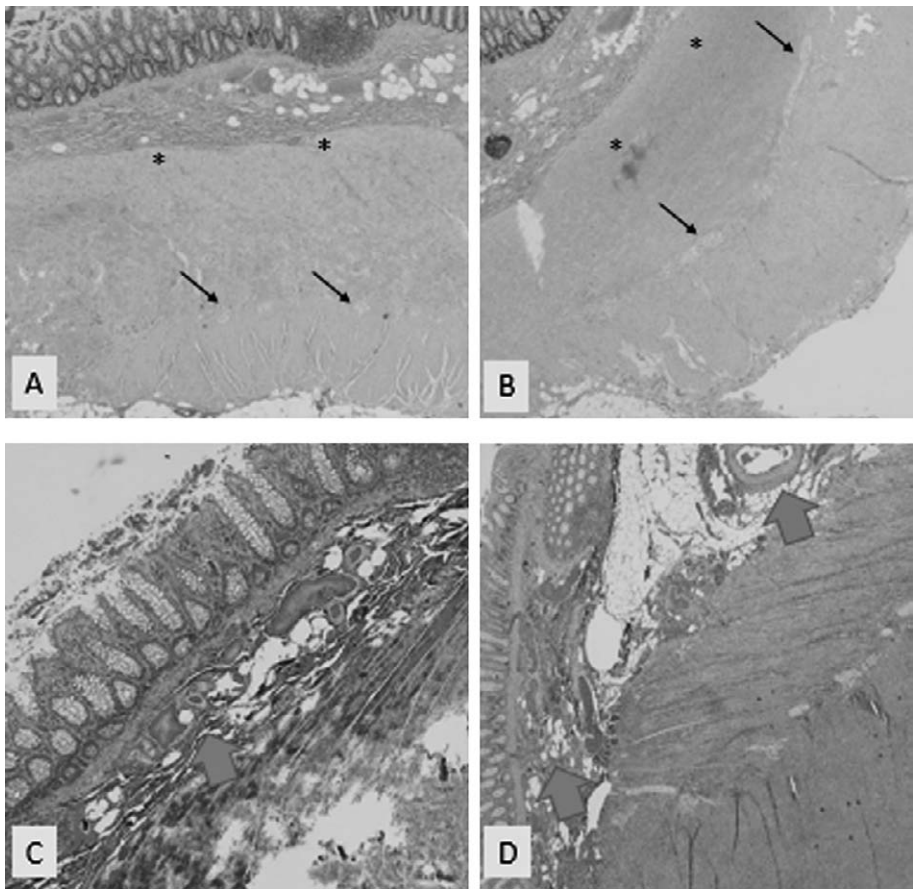


Fig. 1. Alterations in chronic pseudo-chronic obstruction of the colon: A and B show disappearance of Meissner's plexus, which is usually found in submucosa, between the circular muscle and mucosa. Auberbach's myenteric plexus is preserved, located between the longitudinal and circular muscle layers (black arrows); C and D show proliferation of the submucosal layer and perivascular fibrosis (blue arrows), secondary to chronic intestinal pseudo-obstruction.

caliber, with maximum diameter of up to 4.7 cm, with no certain sign of obstruction. Colonoscopy visualized dolichosigma with normal mucosa, and histopathology in lamina propria showed more prominent lymphatic tissue of follicular distribution, with reactively altered germination centers. Magnetic resonance imaging enterography also showed distension of sigmoid colon loops. Given persistent complaints, the patient agreed to elective sigmoid colon resection. Following surgery, the complaints regressed and the patient continued outpatient gastroenterology follows-ups with significant improvement in her quality of life.

Conclusion. This is a case reports on a patient with the anatomical variant of dolichosigma that resulted in the clinical picture of subileus. The patient had more pronounced and long-term symptoms. We conclude that in case of intestinal pseudo-obstructions, symptom progression should be recognized on time and elective surgical treatment considered.

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References

1. Ji Soo Choi, Joon Seok Lim, Hoguen Kim, Jin-Young Choi, Myeong-Jin Kim, Nam Kyu Kim, Ki Whang Kim. Colonic pseudoobstruction: CT findings. AJR Am J Roentgenol. 2008 Jun;190(6):1521-6. doi: 10.2214/AJR.07.3159
2. Napat Angkathunyakul, Suporn Treepongkaruna, Sani Molagool, Nichanan Ruangwattanapaisarn. Abnormal layering of muscularis propria as a cause of chronic intestinal pseudo-obstruction: a case report and literature review. World J Gastroenterol. 2015 Jun 14;21(22):7059-64. doi: 10.3748/wjg.v21.i22.7059

FIBROSCAN-AST SCORE IS INDEPENDENT PREDICTOR OF SHORT-TERM CLINICAL OUTCOMES IN PATIENTS INITIALLY HOSPITALIZED WITH NON-CRITICAL FORM OF COVID-19

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Introduction and objective. Patients hospitalized due to coronavirus disease 2019 (COVID-19) are frequently burdened by metabolic comorbidities, including overweight/obesity, diabetes mellitus, and arterial hypertension. Consequently, many of them are expected to have nonalcoholic fatty liver disease. In this study, we aimed to investigate the potential association of noninvasive surrogates of liver steatosis, fibrosis and inflammation by using transient elastography (TE) and liver biochemistry with clinical severity and 30-day outcomes in patients hospitalized due to COVID-19.

Methods. Patients with non-critical COVID-19 at admission, capable of giving informed consent, were included. Liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) were assessed by TE, provided the absence of conditions known by their influence on LSM (alanine aminotransferase (ALT) >5x upper limit of normal (ULN), congestive liver disease, extrahepatic biliary obstruction, liver neoplasms). FibroScan- aspartate aminotransferase (FAST) score was calculated from the LSM, CAP and aspartate aminotransferase (AST) values according to the original formula[1]. Clinical severity of COVID-19 was assessed by the 4C Mortality Score (4CMS) and need for high-flow nasal cannula (HFNC) oxygen supplementation. Composite 30-day outcome of the need for mechanical ventilation (MV) or death was analyzed.

Results. The study included 218 patients (66.5% of males, median age 65 years, 4.6% with a history of chronic liver disease). Twenty-four (11.1%) patients met 30-day composite outcome. Median LSM, CAP and FAST score were 5.2 kPa, 274 dB/m and 0.31, respectively, and none was associated with clinical severity of COVID-19. However, FAST >0.36 and LSM interquartile range (IQR) ≤5% were associated with adverse outcomes. On multivariate analysis, FAST >0.36 (odds ratio (OR) 3.19, p=0.036), 4CMS (OR 1.68, p=0.002) and HFNC (OR 7.03, p=0.001) were independent predictors of composite adverse outcome of 30-day mortality or need for MV.

Conclusion. Whereas LSM and CAP failed to show correlation with COVID-19 severity and outcomes, FAST score was an independent risk factor for 30-day mortality or need for MV.

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Reference

1. Newsome PN, Sasso M, Deeks JJ, *et al*. FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study. Lancet Gastroenterol Hepatol. 2020;5(4):362-73. doi: 10.1016/S2468-1253(19)30383-8

WHICH BIOCHEMICAL FACTORS INFLUENCE LIVER STIFFNESS IN ELDERLY PATIENTS ON CHRONIC HEMODIALYSIS?

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Introduction and objective. In the past decade, an increasing number of adults aged ≥65 started renal replacement therapy each year[1,2]. Factors influencing liver stiffness (LS) in elderly hemodialysis populations (age >65) are still unclear[3]. The aim of the study was to identify biochemical parameters associated with elevated LS in elderly population on chronic hemodialysis.

Methods. This single-center prospective pilot study was conducted at the Split University Hospital Center and included a group of elderly (older than 65) patients on chronic hemodialysis. LS measurements were done using real-time two-dimensional shear wave elastography after one hemodialysis session.

Results. The mean age of the study population was 77.32±6.59 years; 70.2% were males. LS >7 kPa suggesting clinically relevant fibrosis was found in 59.5% of study patients. C-reactive protein (p=0.024), parathyroid hormone (p=0.026) and total bilirubin (p=0.045) were biochemical parameters associated with elevated LS.

Conclusion. C-reactive protein, parathyroid hormone and total bilirubin were in positive correlation with LS values. Laboratory parameters should always be taken in consideration when interpreting LS findings. Further prospective studies with larger series are needed.

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References

1. Collins AJ, Foley RN, Chavers B, *et al*. US Renal Data System 2013 Annual Data Report. Am J Kidney Dis. 2014;63(1 Suppl):A7. doi: 10.1053/j.ajkd.2013.11.001
2. Schoolwerth AC, Engelgau MM, Rufo KH, *et al*. Chronic kidney disease: a public health problem that needs a public health action plan. Prev Chronic Dis; 2006;3(2):A57. PMCID: PMC1563984
3. Shan R, Yin H, Yang W, *et al*. Influencing factors of transient elastography in detecting liver stiffness. Exp Ther Med. 2016;12(4): 2302-6. doi: 10.3892/etm.2016.3617

COLORECTAL CARCINOMA AND VITAMIN D LEVELS – A PROSPECTIVE CASE-CONTROL STUDY

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Background. The reported health benefits of vitamin D have recently extended from musculoskeletal health to focus on the potential relationships in colorectal carcinoma (CC), irritable bowel syndrome (IBS), and inflammatory bowel disease. A recently reviewed meta-analysis of the potential relationship between vitamin D and CC identified a significant inverse association between dietary vitamin D intake and CC risk. Moreover, high levels of plasma 25-hydroxyvitamin D are associated with lower CC mortality. Our study evaluated vitamin D levels, changes in metabolic hormones, and *Helicobacter (H.) pylori* infection in patients with CC and IBS.

Methods. To the best of our knowledge, this is the first prospective non-randomized case-control study that compared vitamin D status and changes in metabolic hormones in patients with CC and IBS. Our study enrolled 32 Caucasians (16 females, 16 males) examined at the Zagreb University Hospital Center. Twelve of them (mean age, 68.6 yrs) had endoscopically and histopathologically confirmed CC. Stage of the disease was evaluated by computed tomography; only one patient had metastatic disease. Other 20 patients (mean age, 47.3 yrs) fulfilled the ROME IV criteria for the diagnosis of IBS. Standard laboratory parameters, vitamin D, parathyroid hormone, thyroid hormones, cortisol, growth hormone, insulin-like growth factor-1 (IGF-1), oral glucose tolerance test, fasting and postprandial insulin levels were recorded in both groups of patients, as well as *H. pylori* stool antigen.

Results. The CC group had a statistically significantly higher value of platelets and triiodothyronine, as well as lower levels of thyroxine and IGF-1. Glucose levels after 2-h oral glucose tolerance test were higher in patients with CC. Difference in vitamin D levels and its regulatory hormone between the two patient groups did not reach statistical significance even after comparison of age-adjusted subgroups. Despite the fact that *H. pylori* stool antigen was more often positive in the CC group, it was not statistically significant either.

Conclusion. It can be assumed that difference in vitamin D levels and parathyroid hormones between CC patients and control group was not verified due to the very small patient sample, so further investigation is planned. Patients with CC more often have diabetes and hypertension, which both are well-known risk factors. Lower values of IGF-1 in CC patients may have been due to their older age.

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References

1. Kulie T, Groff A, Redmer J, Hounshell J, Schrager S. Vitamin D: an evidence-based review. J Am Board Fam Med. 2009;22:698. doi: 10.3122/jabfm.2009.06.090037
2. Zhang X, Giovannucci E. Calcium, vitamin D and colorectal cancer chemoprevention. Best Pract. 2011;25:485-94. doi: 10.1016/j.bpg.2011.10.001
3. Touvier M, Chan DS, Lau R, Aune D, Vieira R, Greenwood DC, *et al*. Meta-analyses of vitamin D intake, 25-hydroxyvitamin D status, vitamin D receptor polymorphisms, and colorectal cancer risk. Cancer Epidemiol Biomark Prev. 2011;20:1003-16. doi: 10.1158/1055-9965.EPI-10-1141