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# **10<sup>th</sup> Update** on Hepatology Course

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## **10**<sup>th</sup> **Update** on Hepatology Course



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#### 0P-01

#### IMPROVED BODY COMPOSITION DECREASES THE FAT CONTENT IN NON-ALCOHOLIC FATTY LIVER DISEASE, A META-ANALYSIS AND SYSTEMATIC REVIEW OF LONGITUDINAL STUDIES

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**BACKGROUND:** Based on cross-sectional studies, there is a link between body composition parameters and steatosis in non-alcoholic fatty liver disease (NAFLD). However, whether long-term changes in different body composition parameters will result in NAFLD resolution is unclear.

**AIM:** We aimed to summarize the literature on longitudinal studies evaluating the association between NAFLD resolution and body composition change.

**METHODS:** Based on the recommendations of the Cochrane Handbook, we performed a systematic search on September 26th, 2021, in four databases. Eligible studies reported on patients with NAFLD (liver fat >5%) and examined the correlation between body composition improvement and decrease in steatosis. We did not have pre-defined body composition or steatosis measurement criteria. Next, we calculated pooled correlation coefficient (r) with a 95% confidence interval (CI). Furthermore, we narratively summarized the articles.

**RESULTS:** We included 15 studies in our narrative review and five in our quantitative synthesis. Based on two studies with 85 patients, we found a pooled correlation coefficient of r=0.49 (CI: 0.22-0.69, Spearman's correlation) between the change of visceral adipose tissue and liver steatosis. Similarly, based on three studies with 175 patients, the correlation was r=0.33 (CI: 0.19-0.46, Pearson's correlation). On the other hand, based on two studies with 163 patients, the correlation between subcutaneous adipose tissue change and liver steatosis change was r=0.42 (CI: 0.29-0.54, Pearson's correlation). Furthermore, based on the narrative synthesis, body composition improvement was associated with steatosis resolution.

**CONCLUSIONS:** Body composition improvement is associated with a decrease in liver fat content in NAFLD.

#### A NOVEL MODEL FOR PREDICTION OF FATTY LIVER DISEASE IN PRIMARY CARE SETTINGS

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**BACKGROUND:** More than a quarter of the global population suffers from fatty liver disease (FLD). Noninvasive tests are extremely beneficial in predicting this disease.

AIM: Creating a predictive model for fatty liver disease detection in primary care settings.

**METHODS:** In the study, a total of 680 patients with FLD, diagnosed by ultrasound, were included, and 96 patients represented a control group. Potential predictors were entered into a stepwise logistic regression analysis to obtain the model.

**RESULTS:** The Index for Fatty Liver Disease (IFLD) was developed based on laboratory data available in primary care settings: the serum alanine aminotransferase (ALAT), the serum aspartate transaminase, triglycerides (TG), and fasting plasma glucose (FPG); body mass index was another parameter included in this model. The area under the receiver operating characteristic curve (AUROC) for IFLD to detect FLD was 0.787 (IC95%: 0.727–0.859). At a value < 48, the IFLD could rule out FLD with a sensitivity of 91.2% (IC 95%: 90.1%–92.2%), and at a value of > 58, the IFLD could detect FLD with a specificity of 91.7% (IC 95%: 90.7%–92.7%).

**CONCLUSIONS:** This study revealed that the novel model for prediction of fatty liver disease is helpful to detect FLD in primary care settings.

**Acknowledgements:** This study was carried out under the project "Nonalcoholic Fatty Liver Disease: Diagnostic and Therapeutic Management Options," No 9/5, November 29, 2016, funded by the State University of Medicine and Pharmacy "Nicolae Testemitanu," Chisinev, Republic of Moldova.

#### LIVER STEATOSIS ASSESSMENT BY NEW ULTRASOUND-BASED QUANTITATIVE METHODS

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**BACKGROUND:** The aim of this study was to evaluate and to establish cut-off values for two new quantitative ultrasound (QUS) parameters, TSI (tissue scatter-distribution imaging) and TAI (tissue attenuation imaging) in the diagnosis of liver steatosis (LS), as compared to controlled attenuation parameter (CAP).

**MATERIAL AND METHODS:** A prospective study was conducted in which LS was assessed in the same session by QUS (Samsung Medison RS85,CA1-7A probe) and CAP (FibroScan Compact M530, M/XL probes). The CAP cut-off value used for the whole cohort for at least mild steatosis (S1) were 248dB/m; for ALD (alcoholic liver disease) cohort, 268dB/mm; for NAFLD (non-alcoholic liver disease) cohort 294dB/m. Demographic and health related datas were recorded.

**RESULTS:** A total of 285 patients, with a mean age of 56.1±12.4, 171 male, were included in the study. According to aetiology, 164(57.5%) patients had NAFLD, 61(21.4%) ALD, and 60(21.1%) other etiologies(viral, cardiac, autoimmune). The obtained TSI and TAI cut-off values for the diagnosis of at least mild steatosis (S1) are presented in *Table 1*.

Variat	ole	Overall	NAFLD	ALD
TSI	S1	>96.2	>96.5	>94.9
		AUC=0.74,p<0.0001,	AUC=0.73, p<0.0001,	AUC=0.70, p=0.003
		Se=87.9%,Sp=53.0%;	Se=90.9%, Sp=47.9%;	Se=72.9%,Sp=75.0%;
TAI	S1	>0.73	>0.75	>0.66
		AUC=0.82,p<0.0001,	AUC=0.81, p<0.0001,	AUC=0.74, p<0.0001,
		Se=78.3%,Sp=71.6%;	Se=57.5%, Sp=90.8%;	Se=84.8%,Sp=57.1%;

Table 1. Cut-off values of TAI and TSI for S1

0P-03

There were no differences between the performance of TAI and TSI, p=0.18 and p=0.24. A strong direct correlation was observed between TAI and CAP r=0.701, moderate between TSI and CAP r=0.56 for the all cohort, but for NAFLD and ALD subgroups moderate correlations were found between TAI and CAP r=0.66, and r=0.66 respectively and TSI and CAP r=0.56 and 0.66, respectively.

In univariate regression analysis, the factors associated with TSI were hypertension, Diabettes Mellitus (DM), and obesity, and all p-values were <0.0001, but in multivariate analysis, only hypertension(p=0.001) and obesity(p=0.0005) were associated. For TAI, in univariate analysis, the same factors: hypertension(p=0.004), obesity(p=0.0006) and DM(p=0.002) were associated, but in multivariate analysis, DM was the only factor associated, p=0.02. Age and gender were not correlated with any method, TSI or TAI.

**Conclusion:** TAI and TSI are non-invasive methods for screening and diagnostic of Liver Steatosis, with good accuracy. Patients with NAFLD presented highest cut-off values, probably by the presence of DM and obesity, conditions independently associated with TAI and TSI values.

#### <u>0P-04</u>

#### ROLE OF SPLEEN STIFFNESS MEASUREMENTS WITH 2D-SHEAR-WAVE ELASTOGRAPHY BY FOR ESOPHAGEAL VARICES IN PATIENTS WITH COMPENSATED ADVANCED CHRONIC LIVER DISEASE

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**BACKGROUND:** Spleen stiffness measures (SSM) as a non-invasive diagnostic technique for esophageal varices (EV) have been studied, with the majority of the data collected by transient elastography (TE). Using 2D Shear-Wave Elastography(2D-SWE.PLUS) integrated into the Supersonic Imagine Aixplorer system.

**AIM:** We aimed to determine the diagnostic performance of SSM for the presence of EV in patients with compensated advanced chronic liver disease (cACLD).

**METHODS:** We prospectively enrolled patients with cACLD (≥12.5 kPa by Transient Elastography) from January 2022 to March 2022 without history of liver decompensation. All patients included performed an esophago-gastruo-duodenoscopy (EGD) for varices assessment and a complete abdominal multiparametric assessment of liver and spleen assessment using Aixplorer MACH 30 (Supersonic Imagine, Aix-en-Provence, France).

**RESULTS:** There were 73 patients analyzed (78% were men, the mean age  $60.3 \pm 12.1$ , BMI 23.1 $\pm$  5.12 kg/m<sup>2</sup>). Eighteen (24.7%) had alcoholic liver disease, 29 (39.7%) had non-alcoholic fatty liver disease, 11 (15.1%) had chronic viral hepatitis, and 15 (20.5%) had various etiologies. The mean SSM was 38.6  $\pm$  12.8 kPa whereas the mean liver 2D-SWE.PLUS was 17.4  $\pm$  8.61 kPa. EV was detected in 37 (50.7%) patients [garde I – 11 (29.7%); grade II – 10 (27%); grade III 16 (43.2%)]. High risk EV (grades II/III) were associated with higher spleen (p <0.001) and liver (p = 0.017) 2D-SWE. PLUS, increased spleen volume (p< 0.001), portal vein (p <0.001) and splenic vein diameter (p = 0.008). A cut-off of 31.3 kPa of SSM could predict any grades of EV (Ss 92%, Sp 54%, PPV 73.7%, NPV 90%. AUROC 0.807, p < 0.001), while a value of 44.3 kPa can predict EV grade 3 whit red signs and white nipples of Sp of 92.1%, Sv of 73.1%, PPV of 37.3%, and NPV of 92.9%, AUC = 0.881, P < 0.001.

**CONCLUSION:** 2D-SWE SSM is a valid approach for ruling in or out EV in cACLD individuals. If bigger studies validate this results, up to 50% of endoscopies might be prevented in this patients.

#### 0P-05

#### DIAGNOSIS OF LIVER TUMORS BY CONTRAST-ENHANCED ULTRASOUND: ARTIFICIAL INTELLIGENCE VERSUS CLINICIANS

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BACKGROUND: Artificial intelligence applications have recently increased in the field of hepatology.

**AIM:** We aimed to evaluate the accuracy of an artificial intelligence (AI) method in characterising liver tumors using contrast-enhanced ultrasonography (CEUS) and clinical data.

**MATERIALS AND METHODS:** We used CEUS videos from 49 patients with 59 focal liver lesions, evaluated in the Department of Gastroenterology and Hepatology from the Emergency Clinical County Hospital of Craiova. The connected neural network was trained using parameters extracted from the time-intensity curve and the patient's clinical information- age, gender, and the underlying liver disease. Two readers also reviewed CEUS videos, one blinded to the clinical data and final diagnosis. The first step was categorising the liver lesions as benign or malignant and then predicting a diagnosis.

**RESULTS:** The specificity for distinguishing malignant from benign tumors was 100% for both readers and 93% for the AI method. Sensitivity for the non–blinded, blinded reader and AI method were 93.12%, 90.91% and 82%, respectively. When considering the main types of liver tumors from our study: hepatocellular carcinoma (HCC), liver metastases and liver hemangioma, the AI method obtained a categorical accuracy of 85.20%. All liver hemangiomas were correctly classified by both readers. The accuracy for liver metastases and HCC diagnosis were 94.92% and 89.33% for the clinician aware of the clinical data and 96.61%, 84.75% for the blinded evaluator.

**CONCLUSIONS:** The AI method had a good performance and may reduce the need for further investigations.

**Acknowledgements:** This work was supported by a grant of the Romanian Ministry of Education and Research, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2019-1474, within PNCDI III.

#### <u>OP-06</u>

#### PROGNOSIS SCORES AND SHORTER LIVER TRANSPLANTATION-FREE SURVIVAL IN PATIENTS WITH LARGE-DUCT PRIMARY SCLEROSING CHOLANGITIS

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**BACKGROUND:** Primary sclerosing cholangitis (PSC) is a chronic progressive cholestatic disease with poor prognosis and high need for liver transplantation (LT). The aim of our study was to assess the need for LT in patients with large-duct PSC.

**METHODS:** The revised Mayo Risk Score (rMRS), Amsterdam Oxford Model (AOM), UKPSC, PREsTo, MELD-Na score, FIB-4 and APRI scores, Majoie endoscopic retrograde cholangiopancreatography classification applied to MRCP studies were analysed in 64 patients with large-duct PSC. Univariate and multivariate Cox proportional hazards model was used to identify the need for LT.

**RESULTS:** There were included 54.7% females with a median age at diagnosis of 39.5 years. The median period of follow-up was 9.5 years since diagnosis. LT was performed in 23.5% of cases, 9.4% developed cholangiocarcinoma and 15.6% of patients died during follow-up. The following factors were associated with a lower transplant-free survival: a higher AOM score at diagnosis (p=0.004), higher negative both short- and long-term UKPSC scores (p=0.02 and p=0.03), higher score of intrahepatic ductal changes at MRCP classification (p=0.02), higher Meld-Na score (p=0.01), higher FIB-4 score (p=0.004), higher rMRS score during follow-up (p=0.004), recurrent cholangitis episodes (p=0.03). Multivariate Cox regression analysis identified the following independent prognostic factors related to the need of performing LT: a higher FIB-4 at diagnosis and rMRS score during follow-up (p=0.04). Patients with recurrent cholangitis episodes had a significantly higher mean Majoie score for the sum of intrahepatic and extrahepatic ductal changes) (p=0.06).

**CONCLUSION:** Both intra and extrahepatic ductal strictures at MRCP classification are associated with recurrent cholangitis episodes, while lower transplant free survival is predicted by FIB-4 and MRS scores.

#### 0P-07

#### CELL-BLOCK CYTOLOGY: A PROMISING DIAGNOSTIC TOOL IN CHOLANGIOCARCINOMA? A PILOT STUDY

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**BACKGROUND:** We have started to encounter more and more CCA patients in the last years. Also in the last years, the systemic treatment of CCA (including immunotherapy) has evolved. It is well known that the currently available diagnostic techniques offers an diagnostic accuracy around 50%. We first have to improve the diagnosis of these patients and thereafter systemic treatment, immunotherapy or targeted therapy.

**AIM:** The aim of this pilot study was to assess the diagnostic performance of cell-block cytology from the bile in patients with hilar type CCAs.

**METHODS:** Between October 2019 and February 2023, 52 patients diagnosed with hepatobiliary pancreatic cancer in whom the endoscopic retrograde cholangiopancreatography drainage failed, were hospitalized for percutaneous biliary drainage. At drainage, 20-50 ml of bile were collected for cell-block analysis. In the same period cell block cytology was also performed in 15 patients with choledocholithiasis (the control group).

**RESULTS:** The median age of the patients was 62 years, and 27 were women (55.6%). 40 patients were with hilar type CCA, 5 patients with gallbladder carcinoma and 7 patients with pancreatic adenocarcinoma .Overall, the accuracy of cell-block cytology was 55%. On subgroup analysis the accuracy was 65% for hilar type CCA while it reached 85% for the intraductal growing type CCA. Cell-block cytology was negative for malignancy in all patients with choledocholithiasis

**CONCLUSIONS:** We showed here that cell-block cytology is a new method for a definite histological diagnosis of hilar type CCA. Larger studies are needed to validate the results.

#### <u>0P-08</u>

#### OVEREXPRESSION OF SURVIVIN-1, TAG-72 AND HERC5 IN PATIENTS DIAGNOSED WITH HEPATOCELLULAR CARCINOMA IN THE BLACK SEA COAST GEOGRAPHICAL AREA

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**BACKGROUND:** The standard biomarker used for HCC assessment is alfa-fetoprotein. Literature suggests that it doesn't improve HCC evolution, prognosis or survival rates. Current guidelines lack diagnostic biomarkers to better characterize patients with HCC.

**AIM:** To asses the overexpression of Survivin-1, tumor-associated glyocoprotein 72 (Tag-72), and HECT/RLD domain containing E3 ubiquitin protein ligase 5 (HERC5) as tissue biomarkers for HCC characterization.

**METHODS:** 30 liver HCC specimens and a similar number of benign liver tumors of selected biomarkers were studied. IHC assessment of 4-mm sections of formalin-fixed, paraffin-embedded tissue blocks were assesed. Student t, Mann-Whitney U and Chi-square tests were used to validate results. The discriminative power of Survivin -1, Tag-72, and HERC5 overexpression was assessed using ROC curves.

**RESULTS:** The multivariate linear regression analysis revealed that Survivin-1, Tag-72, and HERC5 were significantly overexpressed in HCC samples in patients older than 50 years (P¼0.003, P¼0.006, P¼0.004), male gender (P¼0.031, P¼0.004, P¼0.020), AFP over 180 ng/dl (P¼0.012, P¼0.004, P¼0.029), serum albumin < 3 mg/dl (P¼0.031, P¼0.021, P¼0.003, respectively), portal thrombosis (P¼0.004, P¼0.020, P¼0.004, respectively), ascites (P¼0.002, P¼0.004, P¼0.019, respectively) and in BCLC B/C patients (P¼0.045, P¼0.036, P¼0.045, and P¼0.033, P¼0.001, P¼0.027, respectively). The diagnostic performance of Survivin-1, Tag-72 and HER-C5 tissue biomarkers for HCC assesment was superior to that of AFP (Survivin-1: Z statistic¼2.911, P¼0.0039; Tag-72: Z statistic¼2.789, P¼0.0049, respectively; HERC5: Z statistic¼2.844, P¼0.0043) (Z statistic¼5.022, P < 0.0001).

**CONCLUSIONS:** Our study results validate the overexpression of tissue biomarkers studied for HCC assessment and could be standardized in the current HCC management guideline.

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#### <u>PP-01</u>

#### QUALITY OF LIFE IN PATIENTS WITH HEPATITIS C VIRUS INFECTION TREATED WITH DIRECT ACTING ANTIVIRALS

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**BACKGROUND:** HCV infection is a condition with multiple implications, both on physical, emotional and social health that has a significant impact on the quality of life (QoL) for persons with this diagnosis. The burden of disease for the patients with HCV affects not only the individuals, but also their families and community.

AIM: To assess the level of QoL of the subjects with HCV infection under DAAs' treatment.

**METHODS:** Longitudinal study on a sample consisted of 90 patients diagnosed with HCV infection, included in the National Interferon-free treatment program for hepatitis C, and being monitored in the Gastroenterology Clinic of Craiova County Emergency Clinical Hospital, between August 1, 2017 – December 31, 2018. Their QoL was measured using the WHO-QOL Bref scale at three moments: onset and end of DAAs treatment, respectively 12 weeks sustained viral response (SVR).

**RESULTS:** The DAAs treatment has led to a zero level of viremia at SVR for all the subjects. The quality of life, measured by using the WHO-QQL-Bref scale was improved during the study period. The domains of QoL as measured by the working tool were significantly improved as following: physical health (women p<0.00001; men p< 0.01), mental health (women p<0.00001; men p<0.0001; men p<0.001), and for the environment (women p<0.00001; men p<0.0001).

**CONCLUSIONS:** The DAAs treatment does not only significantly improve the clinical status of the patients with HCV infection, but also their quality of life.

#### EPIDEMIOLOGY OF CHRONIC VIRAL HEPATITIS B/D AND C IN THE VULNERABLE POPULATION IN THE NORTH-EAST AND SOUTH-EAST REGIONS OF ROMANIA – INTERMEDIATE STAGE RESULTS IN THE LIVE(RO)2 · EAST SCREENING

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**BACKGROUND:** In order to meet the requirements of the WHO, namely - the eradication of viral hepatitis by 2030, UMF "Grigore T. Popa" from lasi together with ARAS and the Hospital "St. Spiridon" from lasi, carries out since 2020 the project "LIVE(RO) 2 - Integrated regional program for prevention, early detection (screening), diagnosis and targeting treatment of patients with chronic liver disease secondary to viral infections with liver viruses B/D and C in the North-East and South-East regions".

**AIM:** This study aimed to assess the epidemiological characteristics of the vulnerable population in the eastern part of the country diagnosed with chronic B/D and C viral infection.

**METHODS:** Between July 2021 and December 2022, we performed a prospective screening of chronic viral hepatitis B/D and C in vulnerable people in the counties of North-East and South-East of Romania, within the national program LIVE(RO) 2 - EST. Rapid diagnostic tests were used to detect HBs antigen (HBsAg) and anti-HCV antibodies (HCVA): HBV (Wama Immuno-Rapid HBV<sup>®</sup>) and HCV (Wama Immuno-Rapid HCV<sup>®</sup>). Rapid test-positive patients were tested for HBV DNA and HCV RNA and those eligible under the national protocol were treated with antivirals.

**RESULTS:** The study included 55593 individuals tested rapidly, of which 2160 (3.8%) patients were tested positive (1120 women, 1040 men, mean age 55.86  $\pm$  6.023 years, predominantly rural background - 76.19%). Of these, 1077 (49.8%) were HBsAg positive, 918 (42.5%) with HCV positive needle, 37 (1.7%) HBV/HCV coinfection and 128 (5.9%) HBV/VHD coinfection. HBV-DNA was performed in 724 (67.3%) individuals, of which 452 (62.5%) subjects > 2,000 children/ml. Also, 518 (54.3%) patients with HCV-positive Ac had detectable HCV RNA, of which 375 (72.3%) received antiviral treatment. Depending on the ethnicity, the prevalence of viral infection was 4.29% in Roma people and 3.23% in Romanian people. Among the vulnerable groups determined by work, inactive people (27.7%), uninsured people (11.2%), unskilled people (1.87%), unemployed people (0.6%) and people working in agriculture (0.59%) were predominantly tested. Among the special vulnerable groups, people with disabilities (3.99%), people addicted to alcohol (2.43%) and people with a minimum income (1.21%) were predominantly tested.

**CONCLUSIONS:** The high prevalence of B/D and C viral infection in the vulnerable population tested in the North-East and South-East Region of Romania compared to the rest of the population, indicates the significant viral spread of the infection in these people, a condition that requires further testing and the need for policies public health in vulnerable groups to promote access to existing health services and early initiation of optimal antiviral treatment.

#### PP-03

#### PATHOLOGIES DISCOVERED INCIDENTALLY IN PATIENTS WITH CHRONIC VIRAL INFECTION B / D AND C DIAGNOSED IN THE SCREENING PROGRAM LIVE (RO)2 – EAST

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**BACKGROUND:** The overall burden of B / D and C viral hepatitis remains substantial, despite the major advances in the prevention and treatment of patients in recent years, due to comorbidities and complications associated with liver disease. In this context, the national screening program LIVE (RO) 2 aims to further assess all patients identified as positive for one of the hepatitis B / D / C viruses.

**AIM:** The study aimed to identify fortuitous pathologies discovered in patients with chronic viral B / D / C infection diagnosed in the LIVE (RO) screening program 2.

**METHODS:** We conducted a prospective study that included people from vulnerable groups (poor, uninsured, rural people, people in foster care, homeless, Roma population, people with disabilities, and suffering from alcohol or drug addiction) in different areas of North-Eastern Romania, between July 2021 - December 2022, during the national screening program LIVE (RO) 2-EAST. We also investigated the presence of newly discovered conditions in patients who tested positive and directed to the Institute of Gastroenterology and Hepatology in Iasi for the staging of liver disease and the establishment of antiviral treatment.

**RESULTS:** The study group included 1176 patients, of which 422 men (35.8%) and 754 women (64.1%), aged between 35 and 83 years, with a mean age of 56.32 years. The predominant source of origin was rural (73.1%). Of the patients with positive RDTs, 635 (53.9%) patients were detected with HBsAg, 521 (44.3%) patients with anti-HCV antibodies, and 20 (1.7%) patients with anti-HVD antibodies. Of these, 215 patients (18.2%) were diagnosed with a new pathology associated with B / D / C viral infection. The most common pathologies discovered incidentally were liver cirrhosis

(94, 43.7%), liver cysts (35, 16.2%), liver hemangiomas (29, 13.4%), gallstones (24, 11.1%), type II diabetes mellitus (T2DM) (15, 6.9%), uterine fibroids (9, 4.1%), hepatocellular carcinoma (7, 3.2%), choledochal lithiasis (2, 0.9%). In addition, the presence of fortuitous pathologies was higher among patients with HBV infection than in those with HCV infection (65.3% vs. 42.1%, p = 0.012). Among the risk factors associated with hepatocellular carcinoma (HCC) are chronic alcohol consumption (43%, compared to 19% in the group of patients with HCC), and the association of T2DM in 3 patients (31%, compared to 10% in the group of patients with HCC).

**CONCLUSIONS:** Patients with chronic B / D / C viral infection had a high prevalence of incidentally detected comorbidities, which necessitates the need for public health policies in vulnerable groups to promote access to existing health services to reduce the future burden of chronic diseases but also secondary complications of chronic liver disease.

#### <u>PP-04</u>

#### COMORBIDITY ASSESSMENT IN THE VULNERABLE POPULATION DIAGNOSED WITH CHRONIC B/D AND C VIRAL INFECTION FROM THE NORTHEAST REGION OF ROMANIA – STAGE SCREENING RESULTS LIVE(RO) 2 – EAST

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**BACKGROUND:** Chronic viral hepatitis B/D and C can be complicated by comorbid conditions that may influence treatment eligibility and outcomes.

**AIM:** The aim of this study was to evaluate the presence of the most common comorbidities in patients diagnosed with chronic viral B/D and C infection using rapid diagnostic tests (TDR).

**METHODS:** Between July 2021 and December 2022, we performed prospective screening for chronic viral B/D and C infection in people in vulnerable groups (poor, uninsured, rural people, people in foster care, people without shelter, Roma people, people with disabilities, people suffering from alcohol and drug addiction) from different areas of North-Eastern Romania, during the national program for the elimination of viral hepatitis LIVE(RO) 2-EST using TDRs for hepatitis B virus (Wama Immuno-Rapid HBV<sup>®</sup>) and hepatitis C virus (Wama Immuno-Rapid HCV<sup>®</sup>). We also investigated the presence of comorbid conditions in patients tested positive and presented at the Institute of Gastroenterology and Hepatology in lasi for the staging of liver disease and the establishment of antiviral treatment.

**RESULTS:** Our study included 1176 patients who came to a tertiary center for the staging of liver disease, of which 422 men (35.8%) and 754 women (64.1%), aged 35 to 83 years, with an average age of 56.32 years. The predominant source of origin was rural (73.1%). Of the patients with positive TDR, 635 (53.9%) of patients were detected with HBsAg, 521 (44.3%) of patients with anti-HCV antibodies, and 20 (1.7%) of patients with anti-HVD antibodies. Of these, 646 patients (54.9%) had at least one comorbid condition. The most common comorbidities were cardiovascular disease (21.5%), psychiatric disorders (11.5%), type 2 diabetes (8.9%), metabolic disorders (6%), thyroid disorders (5%) and cancer (2%). In addition, the presence of comorbidities was higher among patients with HCV infection than in those with HBV infection (64.9% vs. 48.5%, p = 0.014), while psychiatric disorders were most common in patients with HBV/HVD coinfection (42.3%), most likely due to the Interferon regimen that has been administered in the past to 19 individuals.

**CONCLUSIONS:** Patients with chronic viral hepatitis B/D and C had a high prevalence of multiple comorbidities. Effective strategies are needed to manage these comorbid conditions as well as interdisciplinary collaboration to allow greater access to antiviral treatment and to reduce the future burden of advanced liver disease and its manifestations.

#### PP-05

#### NONTUMORAL PORTAL VEIN THROMBOSIS IN PATIENTS WITH HEPATITIS C VIRUS AND SUSTAINED VIROLOGICAL RESPONSE • A FURTHER CHALLENGING CONSEQUENCE OF LIVER CIRRHOSIS

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**BACKGROUND:** The advent of direct-acting antivirals (DAAs) is a major breakthrough in hepatology representing the therapeutical standard of care in patients with chronic hepatitis C virus infection over the past few years. Despite high rates of sustained virological response (SVR), DAAs therapy doesn't eliminate the risk of thrombotic events.

**AIM:** In our study we aimed to assess the prevalence of nontumoral portal vein thrombosis (PVT) after SVR and identification of risk factors associated with this complication in patients treated with direct antivirals.

**METHODS:** We prospectively analyzed a cohort of patients with HCV-related liver cirrhosis treated with paritaprevir/ritonavir, ombitasvir and dasabuvir (PrOD)  $\pm$  ribavirin and ledipasvir/sofosbuvir (LED/SOF)  $\pm$  ribavirin for 12/24 weeks, in a tertiary gastroenterology referral center from North-Eastern Romania,

between January 1st 2016 and July 1st 2019. All patients with presumption of thrombosis were evaluated by vascular Doppler, abdominal ultrasound and confirmed by CT scan.

**RESULTS:** The study included 730 patients treated with DAAs, of which 35 were diagnosed with nonmalignant PVT after-SVR (15 men and 20 women, mean age 57.86  $\pm$  7,068 years), corresponding to a prevalence of 4.8%. The mean time from SVR to complication was 290.00  $\pm$  116.639 days. Most patients with nontumoral PVT after-SVR received LED/SOF (71.4%), while the rest received PrOD (28.6%). Twenty-four patients (68.6%) diagnosed with acute PVT and 11 patients (31.4%) with chronic PVT; most patients diagnosed with acute PVT associated partial occlusion of the portal vein (19 patients - 79.2%) with occlusion in the trunk (15 patients - 62.5%). Most of the patients were diagnosed with partial PVT (23 patients, 65.7%). During the study, an improvement in liver function was observed during antiviral treatment, with an improvement in the Child-Pugh and MELD score at the time of SVR. The evolution changes slightly at the 48-week assessment, with a slight increase in the proportion of patients in the Child B class and with MELD  $\geq$  15. The pro- and anticoagulant factors evaluated in this study reflect the classic hemostatic profile of patients with liver cirrhosis and PVT, characterized by increased FII, FVIII and FvW and decreased anticoagulant factors (PC, PS, ATIII) that define the status of hypercoagulability.

**CONCLUSIONS:** We conclude that thrombotic events in patients with HCV-related liver cirrhosis treated with DAAs are not influenced by the variations of coagulation parameters, rather correspond to the hypercoagulability status and the natural evolution of the cirrhotic patient.

#### A PROSPECTIVE COMPARATIVE RANDOMIZED TRIAL OF EFFICIENCY OF SYLIMARIN VERSUS ESSENTIAL PHOSPHOLIPIDS IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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**METHODS:** Between January 2020 and May 2022, 68 patients with NAFLD were randomized to receive either Silymarin 150 mg x 2/day (27 subjects) or Phospholipids (Fortifikat forte) 825 mg x 2/day (41 subjects) for 6 months. All subjects received an individualized low-calorie and hypolipidemic diet and a supervised progressive aerobic workout. Assessment of the severity of steatosis and liver fibrosis was performed using Fibroscan with CAP at the beginning and at the end of treatment.

**RESULTS:** At inclusion in the study, the 2 groups were statistically comparable in terms of age, sex, BMI, AST, ALT, ALKP, GGT, total bilirubin, cholesterol, triglycerides, fibrosis and steatosis. After 6 months of treatment, a more significant improvement in transaminases was obtained in the Phospholipid arm compared to the Silymarin arm: AST decreased from a median of 40.5 IU/l to 25.5 (compared to  $35.5 \rightarrow 37.5$ )-p=0.03, ALT decreased from 59.5 to 41.5 (compared to  $38.5 \rightarrow 33.5$ )-p=0.05. Triglycerides decreased significantly in the Phospholipid arm (from a median of 141 mg/dl to 120) compared to the Silymarin arm (increased  $129 \rightarrow 147 \text{ mg/dl}$ )-p=0.01. In the Phospholipid arm a 1.1 kPa decrease in liver stiffness was obtained (from a median of 8KPa to 6.9 KPa), while in the Silymarin arm the stiffness increased with 0.7 KPa (from 7.2 to 7.9 KPa)-p=0.1. The reduction in hepatic steatosis was comparable between the 2 groups: it decreased with 10% of the initial value.

**CONCLUSIONS:** Essential phospholipids are superior to Silymarin in NAFLD in terms of improving laboratory parameters, and have a tendency to improve liver fibrosis estimated by Fibroscan.

#### DYNAMICS OF LILLE SCORE FOR PREDICTING OUTCOMES IN SEVERE ALCOHOLIC HEPATITIS

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**BACKGROUND:** Baseline data and the change in bilirubin level at day 7 is needed for calculating the Lille score. However, it is not clear when baseline data should be collected.

**AIM:** Our aim is to assess the changes in the Lille score according to two baseline data: admission and day one of corticosteroid treatment.

**METHODS:** All consecutive patients with a history of alcoholism, biopsy proven AH, Maddrey score > 32, were included between January 2016 - December 2022. Biological data was recorded at admission (T0) and prospectively at day 1 (T1), day 7 (T7) of corticosteroid therapy.

**RESULTS:** Two hundred thirty-nine patients were included, mean age was  $51 \pm 10$ , 77.5 % were males. 88.2 % were decompensated. Out of all patients, 82.2 % responded to the corticotherapy treatment, assessed by Lille score at day 7. One hundred patients had the blood analysis required to assess both the Lille T0 and Lille T1. AUROC curve for survival at 3 months for Lille7 T0 was 0.76  $\pm$  0.05 (95 %Cl: 0.65 - 0.86), Lille7 T1 0.78  $\pm$  0.05 (95 %Cl: 0.68 - 0.88). The median follow-up duration was 13 months (0-78 months), 55% of the patients died at the end of the follow up. Corticosteroids response assessed by Lille7 T1 predicts better one month survival than Lille7 T0, HR: 5.8 (95 %Cl: 2.4 – 14.2), p = 0.0001, respectively HR: 4.05 (95 %Cl: 2.67- 9.84), p = 0.002.

**CONCLUSIONS:** Lille score does not significantly change between admission and corticosteroid initiation.

#### THE PROGNOSTIC VALUE OF HVPG IN SEVERE ALCOHOLIC HEPATITIS

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**BACKGROUND:** Severe alcoholic hepatitis (sAH) bears a high mortality rate. HVPG was validated as the best surrogate marker for portal hypertension and also a predictor of in-hospital mortality in sAH. Only one study from 2007 set a cut-off value of 22 mmHg, higher values being considered a marker of bad prognosis.

**AIM:** We aimed to investigate the role of HVPG in predicting short and medium term mortality in sAH patients.

**METHODS:** Patients with a clinical suspicion of sAH, submitted for TJLB for diagnostic purposes and HVPG measurement were enrolled. Day 28 and 90 mortality were recorded during follow-up.

**RESULTS:** 103 biopsy proven sAH patients (74% males, median age 53 years) were included. Mortality was 10.7% (n=11) at 28 days and 18.4% (n=19) at 3 months. 74(71.8%) patients received prednisone and 54(52.4%) finalized the therapy. HVPG showed a moderate ability to predict 28 days mortality (AUROC=0.721[95%CI:0.461-0.982]), not different from Maddrey DF (AUROC=0.765[0.606-0.925]) and MELD (AUROC=0.700[0.533-0.866]). The 23.5 mmHg cut-off showed a good correlation with mortality (F= 0.003), a sensitivity (Se) of 0.97, specificity (Sp) of 0.25, positive and negative predictive values (PPV, NPV) of 79% and 75%, respectively; it correctly classified 73/93(78.5%) of patients. The previously validated cut-off value for HVPG (22 mmHg) correlated mildly with 28-days mortality (F=0.06), showing 0.75 Se and 96% NPV and correctly classifying 57/93 (61.3%) patients. HVPG  $\geq$ 23.5 mmHg also predicted 90-days mortality (F=0.01), while the 22 mmHg cut-off did not.

**CONCLUSIONS:** HVPG is an adequate predictor of short-term survival. Our cut-off value (23.5 mmHg) also predicts 90-days mortality.

#### <u>PP-09</u>

#### THE FREQUENCY AND IMPACT OF INFECTIONS IN PATIENTS WITH ALCOHOLIC HEPATITIS

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**BACKGROUND:** Severe alcoholic hepatitis (sAH) is associated with one-month mortality of 30%. Infections complicate alcoholic hepatitis (AH) and are the leading cause of death in this group of patients.

AIM: to evaluate the frequency of infections in patients with AH and the outcome of these patients.

**MATERIAL AND METHODS:** A retrospective study including 182 patients with AH over a period of 5 years was performed in which we evaluated the outcome of two groups, AH with infections and non-infectious. Prognostic factors were assessed to determine the risk of mortality in these patients.

**RESULTS:** Out of 182 patients, 82.4%(150/182 patients) were men, mean age 54.3 $\pm$ 9.4 years old, 41.3%(75) presented infections. Urinary infection was the most frequent 40%(30/75), followed by pulmonary 30.7%(23/75). Clostridium difficile was present in 9.9%(18 cases) and associated with in-hospital infection, p< 0.0001. According to Child-Pugh Score 80.2% (146/182) had C class. MDF>32 had 73.6%(134/182) and ABIC class – high – 42.9% (78/182). Corticosteroid treatment was given in 116 cases (63.7%), but it was interrupted in 37.4% patients due to infections or lack of responses. Mortality was present in 29.6%, 44%(33/75) in the infections group and 19.6%(21/107) no infection group, p=0.0004. Factors associated with a poor prognostic were: ascites p<0.0001, age>60 years p=0.01, Maddrey score p=0.002, non-responsiv LM4 p=0.04, non-responsiv LM7 p=0.01, presence of infections p=0.002. In multivariate analysis, only the MDF score was associated with poor prognostic, p=0.001.

**CONCLUSIONS:** AH is associated with a high risk of infection, so systematic screening for infections is mandatory in these patients. The presence of infections at admission was found to be an independent predictor for mortality, beside high MDF and non-response to corticotherapy.

#### AGE AND GENDER AS RISK FACTORS FOR THE PROGNOSIS OF HOSPITALIZED PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS

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**BACKGROUND:** Although known as a disease that predominantly affects the elderly, recently, the mortality rate of alcoholic liver cirrhosis (ALC) among young people, especially females, has seen a substantial increase.

**AIM:** The aim was to investigate the influence of non-modifiable risk factors on the mortality of patients with ALC.

**METHODS:** We analyzed patients hospitalized in our Institute between January 2020 and December 2022, diagnosed with alcohol-related liver cirrhosis. We identified predictors of mortality according to gender and age using univariate analyses and non-parametric coefficients of correlation.

**RESULTS:** There were 1158 patients with an average age of  $55.89\pm11.55$  years. Similar distributions were observed in survivors (903) and deceased (255), with a ratio of 2:1 in favor of men (p=0.001) and 3:1 for patients aged  $\geq$ 50 years (p=0.05). Using Cox survival regression, the death rate for men under 50 years was 12.5% at 24 months, the most important predictors being variceal bleeding and sepsis ( $\beta$ =0,5; p=0,001). Encephalopathy was associated with a death rate of 17.25% for patients over 50 years ( $\beta$ =0.42; for men and 0.69 for women, p=0,001). Regarding women under 50 years, the mortality rate at 24 months was 63.71%, determined by the association between spontaneous bacterial peritonitis (SBP) ( $\beta$ =0.69, p=0,001) and hepatorenal syndrome(HRS) ( $\beta$ =0.45, p=0,001).

**CONCLUSIONS:** The prognosis of ALC was negatively influenced by the occurrence of complications. In this study, SBP was the main predictor of mortality associated with encephalopathy for patients over 50 and HRS for women under 50.

#### <u>PP-11</u>

#### MORTALITY-RELATED PREDICTIVE FACTORS IN INFECTED CIRRHOTIC PATIENTS INCLUDED ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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**BACKGROUND:** Bacterial infections in cirrhotic patient occur in decompensated stages and are associated with poor prognosis and higher mortality rates.

**AIM:** The aim was to evaluate the prognostic factors for infections in patients with liver cirrhosis included on the waiting list (WL) for liver transplant (LT).

**METHODS:** We analyzed using Cox proportional hazard-model the following factors: Model of End-stage Liver Disease (MELD), MELD Na, MELD 3.0, albumin-bilirubin score (ALBI), occurrence of acute-on-chronic liver failure (ACLF) from grade 1 to 3, various infections, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio in 108 patients included on the waiting list (WL) for LT in the last 5 years.

**RESULTS:** From the 108 patients, 64.81% were males, with a median age of 55 ± 11.35 years. The most frequent etiology of liver cirrhosis was hepatitis B + delta (36.11%). The median waiting time was 270 ± 659.5 days. During the follow-up, 26.85% of patients developed infections. 25% of patients developed ACLF. LT was performed in 71.29% of cases, and 22.22% patients died during follow-up. Univariate analysis identified the following factors associated with mortality on the WL in infected cirrhotic patients: occurrence of ACLF episodes during follow-up (p=0.023), bacteremia (p=0.021), acute kidney injury (p=0.013), urinary tract infections (p=0.021), a higher lymphocyte-to-monocyte ratio (p=0.04), hypoalbuminemia (p=0.0145), a higher MELD score (p=0.039), MELD Na (p=0.028) and MELD 3.0 score (p=0.037). Multivariate analysis identified bacteremia (p=0.0107) as an independent prognostic factor.

**CONCLUSIONS:** For infected patients with end-stage liver disease, included on the WL for LT, bacteremia is an independent prognostic factor for high mortality.

#### RISK FACTORS FOR THE DEVELOPING INFECTIOUS COMPLICATION IN HOSPITALIZED DECOMPENSATED CIRRHOTIC PATIENTS

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**BACKGROUND:** Infections represent one of the most severe complication of decompensated liver cirrhosis (LC) influencing indication of liver transplantation. The aim of this study was to evaluate the incidence of infection in decompensated hospitalized cirrhotic patients and to identify risk factors for this complication.

**METHODS:** We performed a prospective study including 376 decompensated cirrhotic patients admitted in our tertiary center between January 1st –June 30, 2019. The patients had no clinical evidence of infection at the time of initial presentation, and all were followed-up prospectively for manifestations of infection during admission.

**RESULTS:** Sixty-nine patients developed infectious complications during hospitalization: 27 urinary tract infections, 12 spontaneous bacterial peritonitis, 13 Clostridium difficile infections, 9 lobar pneumonia, 6 skin infections and 2 angiocholithis. Univariate analysis showed that patients who developed an infection were more likely to have a high MELD score, to be admitted for hepatic encephalopathy, to stay in the intensive care unit, and to undergo invasive procedure. Logistic regression identified admission for hepatic encephalopathy [odds ratio (OR) = 2.301, 95% confidence interval (CI) = 1.7-9.8], high MELD score (OR = 2.337, 95% CI = 1.03-1.22) and corticosteroid treatment as the only three variables (OR = 4.127, 95% CI = 2.33-8.27) independently associated with the development of an infection in decompensated LC.

**CONCLUSIONS:** The present study indicates that patients with severe cirrhosis who are admitted for hepatic encephalopathy and receive corticosteroid treatment have a higher risk of developing a bacterial infection during their hospitalization than other cirrhotic patients.

#### THE RISK OF VARICEAL BLEEDING AFTER STOPPING NON SELECTIVE BETA-BLOCKERS IN CIRRHOTIC PATIENTS WITH REFRACTORY ASCITES

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**BACKGROUND:** The non selective beta-blockant (NSBB) treatment in cirrhotic patients has several limitations regarding side effects, as arterial hypotension or bradicardia. Caution should be taken in cirrhotic patients with refractory ascites, hyponatremia or arterial hypotension, as NSBB could precipitate the development of the acute kidney injury. The aim of this study was to evaluate the risk of variceal bleeding after the NSBB treatment is stopped in patients with refractory ascites.

**METHODS:** All consecutive patients with liver cirrhosis and refractory ascites admitted to the Institute of Gastroenterology and Hepatology from January 2017 to December 2017 were included in this study. The diagnosis of refractory ascites was established according to the current guidelines.

**RESULTS:** During the study period a total of 57 patients were diagnosed with refractory ascites. In more than half of them, 29 patients (50.8%), the NSBB treatment was stopped, the main cause of stopping the treatment being systolic blood pressure less than 90 mmHg. The majority of the patients were receiving propranolol (86.2%), and only 4 patients (3.8%) received carvedilol. Out of the 29 patients that stopped the treatment, 21 (72.4%) were Child-Pugh class C, and 5 patients (17.2%) developed variceal bleeding. The risk of variceal bleeding was not increased in cirrhotic patients with refractory ascites that stopped the NSBB treatment (OR 1.207, Cl 0.361-4.039, p=0.796).

**CONCLUSION:** Stopping the NSBB treatment in patients with refractory ascites is not associated with an increased risk of variceal bleeding , despite the severity of liver disease.

#### STANDARD COAGULATION CUT-OFFS FOR INTERVENTIONAL PROCEDURES IN CIRRHOSIS - IS THROMBOELASTOGRAPHY RENDERING THEM OBSOLETE?

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**BACKGROUND:** Patients with cirrhosis have frequent abnormalities in standard coagulation tests (SCTs). Despite not providing an adequate hemostasis assessment, cut-offs based on SCTs still frequently guide interventional procedures and blood product transfusions. Thromboelastography (TEG) provides a global assessment of coagulation, including clotting factors (R-time), fibrinolysis (Ly30), platelet (maximum amplitude-MA), and fibrinogen (K-time, alpha-angle) function.

AIM: To investigate whether conventional cut-offs based on SCTs are associated with TEG abnormalities.

**METHODS:** A consecutive series of patients with cirrhosis and at least one abnormal SCT (using standard cut-offs: INR>2, platelet count< $50.000/\mu$ L, fibrinogen<200 mg/dL) was analyzed using TEG.

**RESULTS:** 106 patients were included, of which 62 (58.5%) were in the Child-Pugh C class. Of the 50 (47.1%) patients with an INR>2, no patients met the criteria for fresh frozen plasma transfusion, while 25 (n=50%) had a hypercoagulable status. Patients with thrombocytopenia <50.000/ $\mu$ L (n=36, 33.9%) had a higher rate of TEG-based platelet dysfunction compared to patients without thrombocytopenia (20% vs. 2.8%, p=0.01), yet overall, only 8 (7.5%) met the TEG-based criteria for platelet transfusion. Regarding fibrinogen, of the 55 patients (51.8%) had values<200 mg/dL, 13 (23.6%) met the criteria for cryoprecipitate transfusion, compared to 3 (5.8%, p=0.01) in patients with fibrinogen>200 mg/dL. Overall, 69 (64.4%) patients had at least one hypercoagulable feature on TEG. The INR-R, platelet count-MA, fibrinogen-K, and fibrinongen-alpha-angle correlation coefficients were all <0.5.

**CONCLUSIONS:** TEG provides a significantly better risk stratification than conventional SCT cut-offs in patients with cirrhosis and might significantly reduce blood product use.

#### <u>PP-15</u>

#### LONG-TERM TRANSPLANT-FREE SURVIVAL IN PATIENTS WITH TIPS: A ROMANIAN SINGLE-CENTER EXPERIENCE

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**BACKGROUND:** Transjugular intrahepatic portosystemic shunt (TIPS) is an established bridge to transplantation procedure for portal hypertension (PHT)-related complications.

**AIM:** We primary aimed at assessing transplant-free survival (TFS) after TIPS placement for variceal bleeding or refractory ascites. Secondly, we evaluated the role of TIPS dysfunction in predicting outcome.

**METHODS:** All consecutive patients who underwent TIPS for PHT-related complications were included. Hemodynamic dysfunction was defined as systematic 6-week after TIPS first revision portal pressure gradient (PPG)  $\geq$ 12 mmHg. Subgroup analysis was performed in patients surviving  $\geq$ 6 months after TIPS. Time-dependent Cox regression analysis was used to estimate the effect of TIPS dysfunction in TFS.

**RESULTS:** 196 eligible patients were analyzed. Recurrent variceal bleeding was the main indication for TIPS placement (73.9%), while 26.1% had refractory ascites. The median initial and post-TIPS PPG were 17 mmHg (9–31) and 7.5 mmHg (2–17), respectively. Five patients (0.02%) received liver transplantation. 6 months TIPS dysfunction rate was 48.4% and hemodynamic dysfunction was assessed in the majority (66.7%) of these cases. 10 patients presented with recurrence of symptoms, four of which had rescue TIPS. Overall 6 months survival was 78.9%. In subgroup analysis(n=130), TFS at median follow-up of 19.5 months (6–88) was 84.6%. TFS was significantly impaired by the occurrence of TIPS dysfunction (HR 3.5;95%CI 1.01–12.25;p=0.04).

**CONCLUSIONS:** TIPS is an effective treatment in the setting of PHT-related complications, with good TFS. Interestingly, systematic hemodynamic revision of TIPS may be a valuable predictive tool in the absence of clinical recurrence.

#### INCIDENCE, RISK FACTORS AND IMPACT OF OVERT HEPATIC ENCEPHALOPATHY ON LIVER TRANSPLANTATION WAITING LIST MORTALITY IN A HIGH VOLUME CENTER IN ROMANIA

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**BACKGROUND:** Overt hepatic encephalopathy (OHE) negatively affects prognosis of patients with cirrhosis on the liver transplantation (LT) waiting list. The MELD-HE score was proposed to address this inequality.

**AIM:** Our aim was to assess the incidence and risk factors for the development of OHE and its impact on waiting list mortality.

**METHODS:** We analyzed 108 patients included on the waiting list for LT between 2019-2022 including demographics, cirrhosis etiology, severity of liver disease and pharmacotherapy, along with biological and clinical status.

**RESULTS:** The mean age of 52,6 yo, 35,2% with alcoholic etiology of liver disease and an incidence of OHE of 49,1%. The median MELD 3.0 score was 18 and 30,6% of patients has associated HCC. The main predictors of OHE were the alcoholic ethiology (p=0.001) and the treatment with PPI (p=0.012). The predictors of death in patients with OHE in the univariate analysis were MELD-HE score (p=0.013), PPI treatment (p=0,044), infections (p=0,003), MELD score (p=0,03), MELD 3.0 (p=0,01), MELD-Na (p=0,008), renal dysfunction (p=0,02) and the neutrophil to lymphocyte ratio (NLR) (p=0,02). In the multivariate analysis the only two predictors of death were found to be the presence of infections (p=0,02) and the NLR (p=0,02).

**CONCLUSIONS:** The incidence of OHE in patients included on the waiting list for LT is high, especially in patients with alcoholic cirrhosis and patients with chronic PPI treatment. The presence of OHE increases mortality especially with the association of infections and increased NLR so the prioritization of these patients in the allocations systems is essential.

#### <u>PP-17</u>

#### SIMILAR INCIDENCE OF HEPATOCELLULAR CARCINOMA (HCC) IN CHRONIC HEPATITIS C (CHC) PATIENTS AFTER HCV CURE AND IN TREATED CHRONIC HEPATITIS B(CHB) PATIENTS: RESULTS FROM A REAL-WORLD COHORT OF PATIENTS WITH CIRRHOSIS

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**METHOD:** We conducted a retrospective study on 535 consecutive patients with cirrhosis from 2 Departments of Clinic Fundeni Institute (Gastroenterology Department and Internal Medicine Department): 224 with treated CHB cirrhosis and 311CHC cirrhosis patients with HCV cure with DAAs.

**RESULTS:** Compared to patients with HCV cure, treated CHB patients were younger (53±11 vs. 66±11) and more likely male (68% vs.43%). The majority of CHB patients received entecavir (94%) with the remaining receiving tenofovir, while the majority of CHC patients received Ombitasvir/ Paritaprevir/ritonavir + Dasabuvir + Ribavirin(76%). By 5-year on HBV treatment or post HCV cure, occurrence of a new HCC was 27 among treated CHB patients (12%) and 30 among HCV cure patients (9.5%) (p= 0.374). Overall, number of new HCC cases was higher in HCV cure patients compared to treated CHB patients among patients with decompensated cirrhosis (7/160- 4.4% vs 5/143-3.5%) (p<0.001) with no differences observed among those with compensated cirrhosis. However, on multivariable Cox regression analysis there was no significant difference in the risk for HCC development between treated CHB cirrhosis and CHC cirrhosis patients with HCV cure (adjusted hazard ratio [aHR] 0.84, P=0.21), which factors independently associated with HCC development included age (aHR1.03, P<0.001), sex (aHR 1.41, P=0.003), platelet (aHR 0.98, P=0.03) and albumin (aHR 0.59, P<0.001).

**CONCLUSION:** Though antiviral therapy for CHB is only suppressive and not curative, there was no significant difference in the risk for HCC development among CHB cirrhosis patients treated with first-line oral antiviral medications and CHC cirrhosis patients after HCV cure.

#### HEPATOCELLULAR CARCINOMA TREATED BY TRANSARTERIAL CHEMOEMBOLIZATION BEFORE LIVER TRANSPLANTATION, A FIVE-YEAR SINGLE CENTER EXPERIENCE

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**BACKGROUND and AIM:** The number of patients with hepatocellular carcinoma (HCC) listed for liver transplant (LTx) has increased significantly and many of them are now receiving transarterial chemoembolization (TACE) to prevent disease progression. The aim of the study is to analyze the course of disease in patients with HCC who received TACE before LTx.

**METHODS:** Patients and tumor characteristics were compared between recipients who received TACE and those who did not. Kaplan–Meier method was used to compare patient survival.

**RESULTS:** Thirty-one patients treated with sequential TACE of a total of 63 patients with proven HCC that underwent LTx between 2013 and 2018 were included in the study. Altogether, 51 TACE procedures were accomplished (range 1–6). Twenty two patients (70.9%) received TACE with Lipiodol while the rest were treated with Debdox. Forty patients were within the Milano criteria and twelve patients (19.04%) had a complete response after TACE. Follow up duration was 72.3 months (62-114) and thirteen patients (20.6%) developed HCC recurrence after LTx. The recurrence free survival was 85.7%, 69.6% and 58.9% at 1, 3 and 5 years, respectively. There was no significant difference in survival in patients that received TACE compared to those that did not (p=0.455). In the univariate analysis an AFP value greater than 100ng/mL, absence of tumor tissue at the time of LTx and a tumor within Milan criteria were found to be predictive factors for survival but only Milan criteria was significantly associated with survival in multivariate analysis (p=0.007; Cl 95%: 0.1262 to 0.7266).

**CONCLUSION:** TACE is an effective method for the therapy of the HCC before LTx in selected patients Milano criteria is the best predictive factor for survival in HCC patients undergoing liver transplant.

#### IMPROVED RECURRENCE-FREE SURVIVAL RATES IN PATIENTS WITH HCV-RELATED HEPATOCELLULAR CARCINOMA WITH SUSTAINED VIROLOGICAL RESPONSE TO DIRECT-ACTING ANTIVIRALS

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**BACKGROUND:** Despite the high efficacy of direct-acting antivirals (DAAs) in chronic HCV infection, a more aggressive pattern of hepatocellular carcinoma (HCC) in patients previously treated with DAAs, has been reported. Tumor aggression in HCV-related HCC after DAAs has been linked to impaired outcome.

**AIM:** On this basis, we aimed to assess the pattern of HCC and survival rates in patients previously treated with DAA therapy.

**METHODS:** This is a case-control study investigating the features of HCC and survival rates in patients with chronic HCV infection whom were previously treated with DAAs versus naïve patients. Patients were matched for sex and age in a 1:3 fashion. HCC infiltrative pattern, portal vein thrombosis (PVT), metastases, Milan criteria, Barcelona Clinic Liver Cancer (BCLC) staging, tumor-node-metastasis (TNM) staging, Cancer of the Liver Italian Program (CLIP), as well as the recurrence and overall survival (OS) rate at 18 months of follow-up, were compared in the 2 groups. This research was carried out in the Institute of Gastroenterology lasi, Romania, between January 1st, 2017 and December 31, 2019.

**RESULTS:** The study included 124 patients that were divided into two groups according to DAA status: 31 DAAs-treated HCC patients and 93 non-DAAs HCC patients. The mean age in the non-DAA group (58.9 $\pm$  6.8 years) was higher than that of the HCC patients with DAA treatment. There was no significant difference between groups regarding sex distribution. The mean values of APRI and Fib-4 scores were significantly higher in the DAA-treated group than in naïve patients (p<0,001). The frequency of the infiltrative HCC pattern, PVT, and metastasis was higher in the non-DAA group (p=0,002). According to BCLC, CLIP, and TNM, HCC patients in the non-DAA group had more advanced stages and limited treatment options (p<0,001). Furthermore, HCC recurrence rate was higher in naïve patients than in those DAA-treated (16,2% versus 8,6%, p=0,002). The 18-months OS rate was 73.3% in the DAA-treated group and 43.7% in non-DAA group (p=0,008).

**CONCLUSIONS:** Our study indicates a better recurrence-free OS rate in patients with HCV-related hepatocellular carcinoma with SVR to DAAs compared with naïve patients, demonstrating the beneficial impact on the outcome of these patients.

#### ALPHA-FETOPROTEIN LEVEL, PROGNOSTIC FACTOR FOR HEPATOCELLULAR CARCINOMA

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**BACKGROUND:** Alpha-fetoprotein reliability in the diagnosis of hepatocellular carcinoma (HCC) has been debated.

AIM: To assess correlations between alpha-fetoprotein (AFP) levels and HCC stage at diagnosis.

**METHODS:** We retrospectively studied the patients diagnosed with HCC in a tertiary center, during one year. We correlated AFP values and survival rates with the stage at diagnosis, according to BCLC classification.

**RESULTS:** 48 cirrhotic patients with HCC were analyzed, 6 patients being diagnosed in the early (A), 11 in the intermediate (B), 11 in the advanced (C), and 20 in the terminal (D) BCLC stage. The distribution of AFP levels was: 4 cases (66%) within the range 0-20 ng/mL, 1 case (17%) with a FP > 200 ng/mL in the A stage group; 8 cases (73%) within the range 0-20 ng/mL, 1 case (17%) with AFP > 200 ng/mL in the A stage group; 8 cases (73%) within the range 0-20 ng/mL, 1 case (9%) within the range 20-200 ng/mL, 2 cases (18%) with >200 ng/mL in the B stage group; 5 cases (45%) within the range 0-20 ng/mL, 2 cases (18%) within the range 20-200 ng/mL, 4 cases (36%) with >200 ng/mL in the C stage group; 7 cases (35%) within the range 0-20 ng/mL, 1 case (5%) within the range 20-200 ng/mL, 12 cases (60%) with >200 ng/mL in the D stage group. 2-year survival rates were 40% in A, 32% in B, 20% in C, and 12% in D stage.

**CONCLUSIONS:** Higher AFP values correlate with more advanced HCC, and with poorer survival rate. AFP may be considered as prognostic factor for HCC.

## NOVEL AUTOMATED INVESTIGATIONAL ALGORITHM "THE INTELLIGENT TEST FOR DETECTING FATTY LIVER DISEASE" IN PRIMARY CARE SETTINGS

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**BACKGROUND:** Diagnosing NAFLD remains an enduring challenge, A lack of consensus on whether to screen for NAFLD in high-risk patients further complicates this issue.

**AIM:** Developing an automated investigational algorithm for primary care providers (PCPs) that helps identify patients at risk for fatty liver disease (FLD).

**METHODS:** A panel comprising 6 specialists in liver disease, internal medicine, primary care medicine, and information technology, based on a non-invasive predictive model named "Index for Fatty Liver Disease" (IFLD), developed an automated investigational algorithm for primary care providers (PCPs).

**RESULTS:** We developed a simple automated investigation algorithm, named "The Intelligent Test for Detecting Fatty Liver Disease," helpful for identifying risk factors for FLD. Before visits to PCPs, patients with obesity or type 2 diabetes, abnormal liver tests should be evaluated by a nurse with IFLD. The physician determines if the patient may have FLD. In cases of IFLD > 58, it is important to determine the risk of advanced hepatic fibrosis and cardiovascular risk (FIB-4 and SCORE-2). Patients at high risk for advanced fibrosis and cardiovascular events should be referred to specialists (hepatologist, cardiologist).

**CONCLUSIONS:** This novel algorithm may raise awareness of risk factors for FLD in primary care settings, resulting in more effective use of specialist consultations and improved patient outcomes.

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#### ASSESSMENT OF LIVER FIBROSIS IN INDIVIDUALS WITH METABOLIC SYNDROME OR TYPE 2 DIABETES MELLITUS USING NON-INVASIVE TESTS

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**INTRODUCTION:** Individuals with metabolic syndrome (MS) or type 2 diabetes mellitus (T2DM) are at high risk for developing non-alcoholic fatty liver disease and advanced liver fibrosis. Although, there are currently no recommendations for screening patients with MS or T2DM. This study aimed to assess the diagnostic accuracy of non-invasive tests in predicting advanced liver fibrosis (≥F3) in patients with MS or T2DM using vibration-controlled transient elastography (VCTE) as a reference quantification method.

MATERIALS AND METHODS: We prospectively enrolled patients with MS or T2DM which have been evaluated using non-invasive tests such as aspartate aminotransferase to platelet ratio index (APRI) score, fibrosis-4 (FIB-4) index, and NAFLD fibrosis score (NFS), in the Gastroenterology and Hepatology Institute lasi, between December 2021 to April 2022. We calculated the area under the receiver operating curve (AUROC), specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) for each of these biomarkers in the detection of advanced liver fibrosis (≥F3) compared with liver stiffness measurements (LSM).

**RESULTS:** Among 96 patients with T2DM and MS enrolled with a mean BMI of 27.82 ±4.62 kg/m<sup>2</sup>, 58 (60.4%) were females. According to LSM measurements, 28 (29.2%) individuals had at least advanced fibrosis ( $\geq$ F3) using a cut-off  $\geq$ 9.7 kPa. A significant correlation was found between LSM measurements and FIB-4 index (r=0.576), NFS (r=0.587), and APRI score (r=0.644) (p <0.001). The FIB-4 index had the highest NPV (90.38%) followed by the NFS score (87.84%). Although, all the biomarkers had relatively low specificity (<80%) and PPV (<75 %), the major finding of our analysis was that all these biomarkers had relatively high NPV (>85%) and accuracy (>83%) for predicting advanced liver fibrosis.

**CONCLUSION:** FIB-4 index and NFS score appear to be the most appropriate surrogate biomarkers of VCTE for the barring of advanced fibrosis in MS and T2DM patients. Utilization of these non-invasive and cost-effective screening tests in the routine practice of primary care settings may suggest a call for action for further evaluation of liver fibrosis in a tertiary care center for populations at risk.

#### IMPACT OF USING ORAL SEMAGLUTIDE IN PATIENTS WITH TYPE 2 DIABETES AND NON-ALCOHOLIC FATTY LIVER DISEASE

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**INTRODUCTION:** Patients with type 2 diabetes mellitus (T2DM) frequently have non-alcoholic fatty liver disease (NAFLD). It is common knowledge that NAFLD therapeutic options are minimal. Semaglutide, a GLP-1 receptor agonist authorized for the treatment of T2DM, plays an important role in weight control. Additionally, may represent a novel therapeutic choice for patients with T2DM who have NAFLD. This study uses vibration-controlled transient elastography (VCTE) with controlled attenuation parameter (CAP) to examine the effects of semaglutide medication on liver steatosis and fibrosis in T2DM patients.

**Material and methods:** From August to February 2022, thirty-seven consecutive patients with T2DM and NAFLD receiving oral semaglutide were enrolled and assessed utilizing VCTE with CAP. All patients' clinical and laboratory information was documented. According to the diabetologist's recommendations, oral semaglutide was started at a dose of 3 mg once daily, and the dose was gradually increased to 7 mg at 4 weeks and 14 mg at 8 weeks.

**RESULTS:** VCTE examination revealed that 26 diabetic individuals (70.3%) had significantly better CAP levels from baseline to 24 weeks. Only 12 (32.4%) diabetic patients experienced a decrease in liver fibrosis. Regarding body mass index (BMI), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), have improved significantly compared to the baseline (mean BMI 28.72±5.43 kg/m<sup>2</sup> to 25.67±6.11 kg/m<sup>2</sup>, mean AST 58.17 ± 16.33 IU/L to 34.54 ± 13.8 IU/L, mean ALT 63.31 ± 12.66 IU/L to 39.17 ± 14.3 IU/L). Hemoglobin A1c (HbA1c) values significantly decreased from baseline to 24 weeks (mean HbA1c 8.9% to 7.4%). Changes in CAP values were significantly associated with fasting plasma glucose ( $\beta$ =0.234, p=0.017), AST ( $\beta$ =0.198, p=0.046), and BMI ( $\beta$ =0.362, p< 0.001). The two most frequent side effects that were experienced were nausea and fatigue.

**CONCLUSION:** Oral semaglutide therapy has improved glycemic control, liver enzymes, body weight, and liver steatosis in patients with T2DM with NAFLD. Since these results raise the prospect that semaglutide may be helpful in the therapy of NAFLD patients, further research concerning liver fibrosis are required.

#### PLANE-WAVE VISCOSITY ULTRASOUND FOR EVALUATION OF LIVER INFLAMMATION IN HEPATOCITOLYSIS SYNDROME

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**BACKGROUND:** It is well-known that liver necroinflammation plays a significant part in the process of hepatic fibrogenesis, so there are various studies that analyzed several methodologies for the measurement of necroinflammatory activity in liver illnesses. Viscosity Plane-Wave UltraSound (Vi.PLUS) 2D imaging mode, a parameter integrated in 2D - ShearWave Elastography (2D-SWE) ultrasound machine permits the assessment of tissue viscosity, which has been found to be is related with liver inflammation owing to shear wave dispersion.

**AIM:** Therefore, we sought to evaluate the necroinflammatory activity in hepatocitolysis syndrome patients.

**METHODS:** Between September 2022 and February 2023, we prospectively included consecutive patients referred to the Institute of Gastroenterology and Hepatology, Iaşi with elevated transaminase values (ALT or AST 50 U/L). All participants were evaluated with an Aixplorer MACH 30 (Supersonic Imagine, Aix-en-Provence, France) ultrasound machine equipped with 2D-SWE.PLUS for quantifying liver fibrosis (LSM), Sound Speed Plane-wave UltraSound (SSp.PLUS) in conjunction with Attenuation Plane-wave UltraSound (Att.PLUS) for liver steatosis, and Vi.PLUS for assessing liver viscosity.

**RESULTS:** Our research comprised a total of 103 patients (59.3% females, mean age 54.8±13.15 years, and BMI 26.69±3.72 kg/m<sup>2</sup>). In accordance with the criteria, valid measures were acquired from 98 (95.1%) patients, and these were included in the final analysis. 15 patients (15.3%) reported chronic alcohol usage (> 30 g/day), and 4 patients (4.1%) tested positive for viral hepatitis (1.1% HBsAg and 3% HCV antibodies). 44.2% were identified as having hepatic steatosis (SSp.PLUS 1537 Pa.s), with a mean SSp.PLUS of 1436±32.81 m/s and an Att.PLUS of 0.42±0.03 dB/cm/MHz. Regarding LSM, 72 (73.5%) patients were F0-1 (8 kPa), 16 (16.3%) were F2-3 (8-12.4 kPa), and 10 (10.2%) were F4 (12.5 kPa), with a mean 2D-SWE.PLUS of 8.6± 6.24 kPa. 61 (62.2%) patients had an elevated liver viscosity (1.8 Pa.s) with a mean Vi.PLUS of 2.14±0.56 Pa.s, which is closely connected with ALT (r =0.488, p <0.001), AST (r = 0.412, p 0.001), BMI (r=0.314, p =0.005), LSM (r =0.753, p <0.001), ), SSp.PLUS (r = 0.644, p <0.001), and Att.PLUS (r = -0.284, p = 0.004). Participants with chronic alcohol intake had a higher Vi.PLUS [2.51±0.63 vs. 1.74 ± 0.55 Pa.s (p = 0.006)] and a higher risk of liver necroinflammation (OR 2.43, 0.41–7.01; p <0.001) than nonalcoholic participants. In addition, individuals with an aberrant AST level had an elevated risk of liver inflammation (OR 1.81, Cl 0.58 – 3.24, p = 0.024), while an AST value of 70 U/L may moderately predict a ViPLUS score > 2.2 Pa.s (moderate liver inflammation) (ROC curve = 0.656, Sp = 68, Ss = 61%).

**CONCLUSION:** Vi.PLUS parameter is a unique technique for non-invasive evaluation of liver inflammation that correlates with both fibrosis and steatosis ultrasonography parameters, making it a potential and extremely intriguing strategy for disease staging in patients with NAFLD and abnormal liver enzymes.

#### SCREENING FOR ADVANCED FIBROSIS IN PATIENTS WITH ALCOHOL CONSUMPTION USING TRANSIENT ELASTOGRAPHY

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**BACKGROUND:** Alcoholic liver disease (ALD) represents a major health problem worldwide, frequently diagnosed at advanced stages when the prognosis is severe.

**AIM:** This study aimed to evaluate the prevalence of significant fibrosis in adult population with chronic alcohol consumption.

**METHOD:** Using transient elastography we analyzed the patients with day hospitalization in our Institute between January 2022 and December 2022 who admitted harmful alcohol consumption (men  $\geq$ 3 drinks/day, women  $\geq$ 2 drinks/day) without known hepatic disease. Based on uni and multivariate statistics, the approach correlated clinical and laboratory parameters with the level of hepatic fibrosis.

**RESULTS:** The study included 689 patients with an average age of 49,32±14,31 years, a proportion of 66,5% represented by men (p=0.003). Establishing a cut-off at 12,1 kPa for advanced fibrosis (≥F3), we observed that 17,85% could be included in this category. Using multiple equations of regression by stepwise method, predictors involved in the dynamic of fibrosis were identified. Empirical findings suggested a positive correlation between the level of GGT and advanced fibrosis ( $\beta$ =0,373, p=0,001). Moreover, a negative correlation was noticed between liver damage and platelet count ( $\beta$ =-0,428, p<0,001), albumin ( $\beta$ =-0,215, p<0,001), fibrinogen ( $\beta$ =-0,188, p=0,003). In order to estimate elastography's efficiency, we considered the level of sensitivity and specificity through ROC analysis. Statistical results indicated that AUROC=0,904 for a cut-off 12,1kPa.

**CONCLUSION:** Screening using transient elastography represents an approach that could provide early diagnosis of advanced liver fibrosis in asymptomatic population, with possibility to prevent the evolution of ALD and the development of complications of cirrhosis.

#### ANTICOAGULATION FOR ATRIAL FIBRILLATION IN PATIENTS WITH LIVER CIRRHOSIS

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**BACKGROUND:** Atrial fibrillation is frequently diagnosed in patients with liver cirrhosis, especially in those with non-alcoholic steatohepatitis or alcoholic etiology. Anticoagulant treatment is recommended for stroke prevention in patients with atrial fibrillation. Considering the impaired coagulation balance in liver cirrhosis, predisposing the patients to bleed or thrombotic events, the anticoagulant treatment is still a matter of debate. The aim of this study was to compare direct oral anticoagulants (DOACs) with acenocoumarol in patients with nonvalvular atrial fibrillation and liver cirrhosis.

**METHODS:** In this prospective study we included patients with atrial fibrillation and liver cirrhosis treated with oral anticoagulation and followed-up for 1 year. We analyzed the risk of ischemic stroke, intracranial hemorrhage, gastrointestinal bleeding, major bleeding, and all-cause death.

**RESULTS:** A total of 64 patients receiving a DOAC and 66 patients receiving acenocoumarol were included, mosta of the patients were Child-Pugh class B, and had alcoholic liver cirrhosis. DOACs were associated with lower risks for ischemic stroke (hazard ratio [HR]: 0.55; 95% confidence interval [CI]: 0.320-0.0.680), intracranial hemorrhage (HR: 0.57; 95% CI 0.394 -0.581), gastrointestinal bleeding (HR: 0.819; 95% CI: 0.619 -0.949), major bleeding (HR: 0.66; 95% CI: 0.577 -0.739), all-cause death (HR: 0.698; 95% CI: 0.568-0.869), and the composite outcome (HR: 0.63; 95% CI: 0.567-0.656) than acenocoumarol).

**CONCLUSIONS:** Patients with atrial fibrillation and liver cirrhosis, DOACs showed better effectiveness and safety than acenocoumarol.

#### <u>PP-27</u>

#### THE GENOTYPIC PROFILE OF PATIENTS WITH WILSON'S DISEASE IN THE REPUBLIC OF MOLDOVA

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**BACKGROUND:** Wilson's disease (WD) is a monogenic disorder associated with the disturbance of copper metabolism. It is characterized by extraordinary mutational heterogeneity and phenotypic diversity.

**AIM:** The study aims to evaluate the genotypic presentation in patients with Wilson's disease in the Republic of Moldova.

**METHODS:** There were evaluated retrospectively 60 patients (29 women and 31 men) suspected of WD, between 2006 and 2021. The Leipzig score was used to specify the diagnosis. Genetic testing was performed in 25 cases (14 women and 11 men) by the Sanger sequencing method. Exons with a high and moderate frequency of mutations were examined.

**RESULTS:** The mean age was 29 years (range 3-69 years). In 14 patients (56%) pathogenic variants were detected on both alleles, in 7 patients (28%) - a single pathogenic variant, in 2 patients (8%) - benign variants and in 2 patients (8%) - no mutation was identified. In 9 patients (36%) the homozygous recessive p.H1069Q mutation was detected, in 6 patients (24%) compound heterozygous mutations with different associations were observed, and in 8 patients (32%) only 1 mutation was identified. The most frequent p.H1069Q mutation is associated with a hepatic onset in 35 % of cases.

**CONCLUSIONS:** The most frequent variants detected in patients of Moldovan origin are identified at exons 8, 14, and 20. In the presence of a clinical and biochemical picture suggestive of WD, it is necessary to evaluate all the exons and areas outside the exons.

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