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ABSTRACT SECTION

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Oral presentations

A. THE 5 BEST ORAL PRESENTATIONS

001

INCREASES OF RESIDENT HEPATIC MACROPHAGES AND CIRCULATION-DERIVED MONOCYTES IN THE LIVERS OF PATIENTS WITH CHRONIC LIVER DISEASES

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Background. Resident macrophages and infiltrate monocytes have been demonstrated to contribute to tissue damage and play a role in the regulation of fibrosis. A marked increase in hepatic macrophages and infiltrate monocytes are observed in experimental models of liver injury and fibrosis. However, much less is known about macrophages and monocytes in patients with chronic liver diseases (CLD). **Material and methods.** A total of 93 patients with different types of chronic liver disease (chronic HBV infection, autoimmune hepatitis, alcoholic liver disease and primary biliary cirrhosis) were enrolled in our study. Seventeen normal liver tissues were included as control. The degree of hepatic inflammation and fibrosis of liver fibrosis in patients with chronic hepatitis B virus infection was graded using the modified histology activity index described by Scheuer. Resident hepatic macrophages (CD68+) and circulation-derived monocytes (MAC387+) were determined by immunohistochemistry in the formalin-fixed, paraffin-embedded liver tissues of CLD patients. **Results.** The density of resident hepatic CD68+ macrophages was significantly increased in the livers of CLD patients (117.51 ± 41.78/HPF) compared with normal tissues

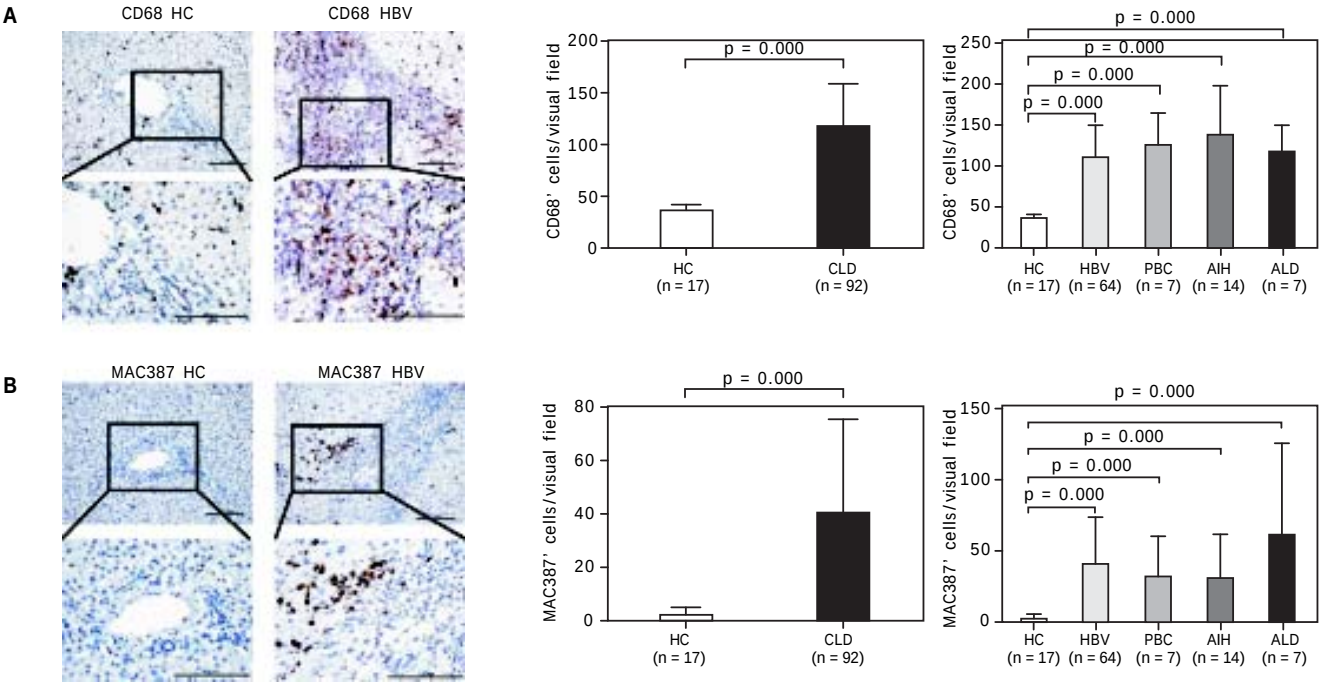

Figure 1. Immunohistochemical analysis of resident hepatic macrophages and circulation-derived monocytes in chronic liver diseases. AIH: autoimmune hepatitis. ALD: alcoholic liver disease. CLD: chronic liver diseases. HBV: chronic hepatitis B virus infection. HC: healthy controls. PBC: primary biliary cirrhosis.

(37.45 ± 4.79/HPF, P < 0.001) (Figure 1A). A larger number of MAC387+ monocytes infiltrated livers of CLD patients (40.45 ± 35.17/HPF) than normal tissues (2.45 ± 2.78/HPF, P < 0.001) (Figure 1B). In different etiologies of CLD patients, the CD68+ macrophages and MAC387+ monocytes were all significantly increased (P < 0.001). In addition, chronic HBV infected patients with higher G scores had more CD68+ macrophages and MAC387+ monocytes in their livers compared to those with lower G scores. Significantly more MAC387+ monocytes were found in the liver tissues of chronic HBV infected patients with higher S scores compared to those with lower S scores. CD68+ macrophages also showed a trend of positive association with S score in these patients. CD68+ macrophage numbers were positively correlated with serum ALT (r = 0.298, P = 0.005), AST (r = 0.361, P = 0.001) and total bilirubin (r = 0.278, P = 0.008) levels. MAC387+ monocyte numbers were negatively correlated with serum albumin (r = -0.247, P = 0.02). **Conclusions.** Resident hepatic CD68+ macrophages and circulation-derived MAC387+ monocytes may play a pathological role in exacerbating chronic liver inflammation and fibrosis in CLD patients. Thus, inhibition of macrophages and monocytes would be a potential therapeutic option for CLD patients.

002

TYPE 2 DIABETES MELLITUS IS DIRECTLY ASSOCIATED WITH A FIRST EVENT OF CLINICAL DECOMPENSATION IN HCV-RELATED COMPENSATED CIRRHOSIS

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Background. The association between hepatic cirrhosis and type 2 diabetes mellitus (T2DM) has been previously described in several studies. However, the impact of the presence of different categories of glucose impairment, including T2DM, on the clinical outcomes indicating disease progression has not been prospectively investigated. Thus, our study was aimed to identify the association between different categories of glucose abnormalities and the occurrence of first episode of clinical decompensation in HCV-related cirrhotic patients. **Materials and methods.** Two hundred and fifteen patients with compensated HCV-related cirrhosis were prospectively recruited in a tertiary academic center, National Institute of Gastroenterology, Havana, Cuba. At admission, overall patients were screened for T2DM. To do that, fasting glucose and/or oral glucose tolerance test (OGTT) were performed. Subjects were followed at 4 months intervals during six years to identify a first event of clinical decompensation. It was defined as the time to a first event of ascites, variceal bleeding and encephalopathy. Patients who developed hepatocellular carcinoma during the follow-up were censored at the same time when they occurred. The cumulative probability of clinical decompensation was assessed by Kaplan-Meier curves. Multivariable Cox regression models were computed to determine factors associated with a first episode of clinical decompensation. Results: Over a median of 182 weeks, the cumulative proportion of any clinical liver-related decompensation was 22.8%, being ascites (10%), variceal bleeding (6%) and hepatic encephalopathy (4.2%) the most frequent recorded. Seven patients developed hepatocellular carcinoma over time. T2DM was diagnosed in 105 subjects (49%), impaired glucose tolerance in 22 subjects (10%) and impairment fasting glucose in 9 subjects (4.6%). The cumulative proportion of patients with any clinical episode of decompensation was 43% (95% CI: 32-56%) in patients with T2DM as compared to 7% (95% CI: 4-16%) in those without T2DM (P < 0.01). The risk of clinical decompensation increased in 4.1 (95% CI: 1.35-12.7) fold for those individuals with T2DM. At the multivariable analysis, MELD and Child Pugh scores, presence of varices, elevated 2-h plasma glucose in OGTT, INR for prothrombin, platelet count and T2DM were significantly associated with any event of clinical decompensation. **Conclusions.** The presence of type 2 diabetes mellitus significantly increases the probability of a first episode of clinical decompensation in HCV-related compensated cirrhotic patients.

003

BENEFICIAL EFFECTS OF MINERALOCORTICOID RECEPTOR BLOCKADE IN EXPERIMENTAL NON-ALCOHOLIC STEATOHEPATITIS

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Background. Currently, the therapeutic armamentarium to treat Non-alcoholic steatohepatitis (NASH) is limited. Aldosterone plays a role in hepatic fibrogenesis and its modulation could be beneficial for NASH. **Aim.** To investigate whether eplerenone, a mineralocorticoid receptor antagonist, modulate liver damage in experimental NASH. **Material and methods.** C57bl6 mice were fed a choline-deficient amino acid-defined (CDAA) diet for 22 weeks with or without eplerenone supplementation. Serum levels of aminotransferases and aldosterone were measured and hepatic steatosis, inflammation, and fibrosis scored histologically. Hepatic triglyceride content (HTC) and hepatic mRNA levels of pro-inflammatory (TNF-α and MCP-1), pro-fibrotic (TGF-β, α-SMA, Col1α1 and TIMP-1), oxidative stress-associated genes (NRF2, HOX-1, glutathione reductase-1 and gamma-*glutamylcysteine synthase)* and of the mineralocorticoid receptor (MR) were also assessed. Results: CDAA diet effectively induced NASH, and increased the hepatic expression of pro-inflammatory, pro-fibrotic genes and oxidative stress-associated genes. Hepatic MR mRNA levels were increased in NASH and significantly correlated with the expression of pro-inflammatory and pro-fibrotic genes. Epleronone administration was associated to a reduction in the hepatic mRNA levels of the MR and significantly reduced HTC and steatosis and attenuated the development of liver fibrosis, which was associated to a significant decrease in the expression of pro-fibrogenic genes and of the oxidative stress-associated Nrf2 up-regulation. Eplerenone did not influence hepatic inflammation in the setting of NASH. **Conclusion.** the expression of MR correlates with inflammation and fibrosis development in experimental NASH. MR blockade with eplerenone has hepatic anti-steatotic and anti-fibrotic effects. Considering its safety and FDA-approved status, eplerenone, alone or in combination with other agents, should be tested in human NASH.

004

THE NUCLEAR RECEPTOR FXR, BUT NOT LXR, UPREGULATES BILE ACID TRANSPORTER EXPRESSION IN NONALCOHOLIC STEATOHEPATITIS

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NAFLD is the most common cause of chronic liver disease worldwide and comprises a wide spectrum of liver damage ranging from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis. Recently, hepatic nuclear receptors have been associated with progression of NAFLD because of their important regulatory functions in bile acid and lipid homeostasis. The aim of our study was to investigate the role of nuclear receptors farnesoid X receptor (FXR) and liver X receptor (LXR) and other known mediators of bile acid homeostasis and transport including the nuclear orphan receptor small heterodimer partner (SHP) and bile acid transporters (Na+/taurocholate cotransporter pump [NTCP] and bile salt export pump [BSEP]). Forty patients with biopsy-proven NAFLD were enrolled. Liver biopsies were collected between 2009 and 2012 and classified as simple steatosis (N = 20) and nonalcoholic steatohepatitis (N = 20). Gene expression of FXR, LXR, NTCP, SHP, and BSEP was analyzed by real-time reverse transcription-quantitative polymerase chain reaction and protein expression was assayed by western blotting. Gene expression of FXR, SHP, NTCP, and BSEP was significantly upregulated in nonalcoholic steatohepatitis *vs.* simple steatosis ($P < 0.01$). Protein expression of FXR and SHP protein was decreased in patients with nonalcoholic steatohepatitis compared with patients with simple steatosis and the control group ($P < 0.05$), while LXR protein content remained unchanged between the groups. Nuclear receptor FXR seems to upregulate expression of SHP, NTCP, and BSEP in patients with nonalcoholic steatohepatitis, which could be related to the degree of progression of nonalcoholic fatty liver disease. FXR may also influence lipid and glucose metabolism via SHP signaling within both the liver and elsewhere.

005

ETIOLOGY, PROGNOSTIC INDICATORS AND OUTCOME FOR 129 CONSECUTIVE ADULT PATIENTS WITH ACUTE LIVER FAILURE IN CHILE

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Introduction. Acute liver failure (ALF) is a severe acute disease with high morbimortality. Liver transplantation (LT) has improved its prognosis. An early prognostic assessment is critically important for optimum clinical management. **Aims.** To describe the clinical features, etiology, prognostic indicators and outcomes of Chilean adults with ALF. **Material and methods.** Observational study of a prospectively followed cohort of consecutive adult patients referred to two liver transplant units in Chile (2000-2012). We assessed the MELD and Kings College criteria (KCC) in relation to outcome. **Results.** 129 adult patients with ALF. Most were women (78%), mean age 37.6 years-old (15-83 years-old). The most frequent causes of ALF were: a) Indeterminate (26%); b) Drug induced (26%); c) Autoimmune (15%); d) Fatty liver of pregnancy (10,8%); e) Viral hepatitis A and B (13%); f) Other causes (9.2%). Out of 129 patients with ALF, 77 (60%) were listed for LT due to severity of disease. Finally 34 patients (34/77; 44%) were transplanted, 29 died while awaiting LT (29/77; 37%), and 14 survived with medical support (14/77; 18%). 34 patients received LT with good overall outcome (only 7 died during first 6 months: 79,4% survival). Overall 52 patients were not listed for LT (40%) due to: a) Non severe disease (n = 24, only 8.2% of them died); b) Severe infection (n = 14, where 50% died); advanced age (n = 3, 66% died); d) Severe neurologic impairment and cerebral edema (n = 4 cases, 100% died); f) other causes (n = 7; 42% died). A MELD score > 33 predicted mortality/LT with a sensitivity (Se) and specificity (Sp) of 76% and 44%, respectively, and positive predictive value (PPV) and negative predictive values (NPV) of 72% and 50% respectively [Diagnostic accuracy (DA): 65%)]. The KCC (> 3 minor or > 1 major criteria) was a better predictor of mortality/LT with Se and Sp of 97% and 57%, respectively and PPV and NPV of 81 and 93% respectively (DA: 83%). **Conclusions.** The main causes for ALF in our country are drug induced and autoimmune (41%). ALF affects mainly women (78%). 62% of ALF cases were listed for LT and half of them were transplanted. Only 18% of ALF patients listed for LT survived spontaneously. Of those not listed for LT, 63% survived spontaneously. KCC and MELD criteria can be considered both reasonable criteria to decide for LT listing. It is important to select patients with severe disease to decide their early transfer to a liver transplant unit.

B. VIRAL HEPATITIS

001

THE INFLUENCE OF DIFFERENT TREATMENT PROTOCOLS ON HBSAG KINETICS IN PATIENTS WITH CHRONIC HEPATITIS B

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Background. Serum HBsAg represents an important serological marker of chronic hepatitis B virus (HBV) infection in HBeAg-negative patients under treatment. We aim to determine whether HBsAg decline may predict on-therapy and off-treatment remission. **Material and methods.** We studied a cohort of patients with HBeAg-negative/positive compensated CHB treated with peginterferonum alpha 2a-15 patients (3 e positive/12 e negative)-group A, tenofovir disoproxil fumarate (TDF)-12 patients (2 e positive/10 e negative)-group B and Entecavir-18 patients (2 e positive/16 e negative)-group C for at least 12 months. Stored serum samples taken before and at 6 and 12 months of therapy were tested for HBsAg, HBV-DNA and HBeAg. Results: Before treatment, group A, B and C patients had a mean value of HBV DNA 40,000 IU/mL, 45,000 IU/mL and 55,000 IU/mL, HBsAg 3.5, 3.4 and 3.2 log10 IU/mL respectively. Virologic remission rates at 12 months (HBV DNA undetectable by PCR) were 6.66% in group A, 8.33% in group B and 5.55% in group C. Compared to before treatment, levels of HBsAg decreased by a median of 0.06, 0.30 in

group A, 0.04, 0.20 in group B and 0.035, 0.15 in group C at 6 and 12 months, respectively ($p < 0.0030$). No patient cleared HBsAg at 12 months of therapy. **Conclusions.** In treatment naïve HBV patients, peginterferonum alpha 1 a, TDF, ETV therapy significantly decrease serum HBsAg levels, but the rate of HBsAg decline is slower in ETV therapy.

002

THE RESTING ENERGY EXPENDITURE AND METABOLIC SYNDROME IN PATIENTS WITH CHRONIC HEPATITIS C

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Background and aim. Liver diseases of different etiologies and severity present an elevated variability in resting energy expenditure (REE). In hyperinsulinemic patients has been observed a REE reduction. However, it is unknow if change of REE is related to metabolic syndrome (MS) in patients with chronic hepatitis C virus (CHC). The study evaluated the REE of the patients with CHC and the relationship with MS. **Material and methods.** A cross-sectional study included patients with CHC histologycal before the any treatment. The measurement of REE was done by indirect calorimetry. MS was defined according to the criteria of the IDF (2005). The patients with CHC were classified in 2 groups: G1-CHC patients with MS (HCV + MS); G2-CHC patients without MS (HCV-MS). Clinical and nutritional characteristics were compared between the 2 groups. Classification of REE was categorized in eumetabolic, hypometabolic or hypermetabolic according the measured energy expenditure and energy expenditure estimated. **Results.** A total of 34 patients with CHC were included. The mean age was 46.8 ± 10.1 years old and 64.7% were women. The histologic analyzes showed in 29.4% of the cases of CHC association with steatosis. All (100%) patients were Child-Pugh A and 79.4% were genotype 1. In G1 were included 32.4% patients, and 54.5% of them were hypometabolic. In G2 43.5% of the patients were hypometabolic ($p > 0.05$). There was not association between REE and MS or for any specific parameters (IDF/2005) of the MS ($p > 0.05$). The two groups also were similar regarding gender and age ($p > 0.05$). In G1 the value of the BMI was higher than in the G2, 32.5 ± 7.1 kg/m^2 and 25.2 ± 3.6 kg/m^2, respectively ($p = 0.001$). The HOMA-IR was higher in the G1 compared to G2, 3.3 ± 1.8 and 1.9 ± 1.6, respectively ($p = 0.016$). **Conclusion.** The resting energy expenditure in patients with chronic hepatitis C virus did not present association with metabolic syndrome. The MS in CHC patients had a positive association with increased BMI and IR.

003

POLYMORPHISMS NEAR IL28B AND SEROLOGIC RESPONSE TO INTERFERON IN HBeAg-POSITIVE PATIENTS WITH CHRONIC HEPATITIS B GENOTYPE F

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Background and Aim. There is a strong association between the polymorphisms near of IL28B gene and response to antiviral treatment with interferon alfa (IFNa or PegIFNa) in chronic hepatitis C. This drug is also used in chronic infection with hepatitis B virus (HBV) and some IL28B polymorphisms studies have shown that there is also a clear association with response to therapy, but depending on viral genotype. In Chile the predominant HBV genotype is F and there are no studies linking it with the IL28B polymorphisms. We investigated the association between polymorphisms near IL28B gene and response to treatment with IFNa or PegIFNa in chronic HBV genotype F. **Material and methods.** Serum samples were studied retrospectively in 29 HBeAg-positive patients chronically infected with HBV genotype F that had received antiviral therapy with IFNa or PegIFNa. 18/29 patients were responders to therapy, as evidenced by seroconversion of HBeAg to antiHBe. To study the IL28B polymorphisms rs12979860, rs12980275 and rs8099917, polymerase chain reaction and restriction fragment length polymorphim were used. **Results.** The IL28B rs12979860 CC, rs12980275 AA and rs8099917 TT genotypes were more frequently found in patients with serologic response compared to non responders (61, 61 and 72% *vs.* 27, 27 and 36%, respectively), although these differences were not statistically significant. **Conclusions.** In patients with chronic hepatitis B genotype F, there is a trend in the association between IL28B polymorphisms and the success of therapy. However, it is necessary to increase the number of cases studied, to confirm this results.

004

EFFICACY OF BOCEPREVIR AND TELAPREVIR FOR TREATMENT OF GENOTYPE 1 HEPATITIS C VIRUS INFECTION: SYSTEMATIC REVIEW AND META-ANALYSIS OF 12 RANDOMIZED CLINICAL TRIALS

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Background. Hepatitis C virus (HCV) infection still the main cause of decompensated cirrhosis in USA. Protease inhibitors (PI), boceprevir (BOC) and telaprevir (TLR) showed sustained viral response (SVR) of 73% in naive patients, 88% in previous relapsers, and 33% non-responders when added to dual therapy with PEG-interferon and ribavirin (PR). The WHO guidelines for the screening, care and treatment of persons with HCV infection suggest triple therapy as moderate quality of evidence, so scientific community have made an attempt to validate these results. The objective of this study was to assess the efficacy of BOC and TLR in the treatment of genotype 1 HCV infection. **Material and methods.** Electronic research was made in the supplements of the main international meetings of liver diseases (The Liver Meeting, The International Liver Congress, DDW and Annual Scientific Meeting of the American College of Gastroenterology), Pubmed and EMBASE. Randomized clinical trials (RCT) in English reporting the use of BOC and TLR plus PR in genotype 1 HCV infected patients that report SVR, published from January 2009 to November 2013 were included. Two authors identified every abstract of original articles published and unpublished; extracted the data and assessed of risk of bias the

Cochrane Collaboration's risk of bias. Outcomes were expressed using risk ratios (RR) and 95% CIs. A meta-regression for the assessment of adjusted variables such as previous treated, co-infected with HIV and use of BOC or TLR was made. **Results.** A total of 356 studies were found in the first research, 342 were excluded. Twelve RCT with a total of 5,293 patients were analyzed. SVR was higher for PI + PR (RR 2.07; 95% CI 1.72-2.50; I2 77%). SVR for BOC + PR is higher than PR (RR 2.07; 95% CI 1.80-2.37; I2 72%), also for TLR + PR (RR 1.94; 95% CI 1.75-5.71; I2 81%). In meta-regression the previous treated patients shown more benefit from PI + PR (RR 3.47; 95% CI 2.78-4.33, I274.8%); with no difference in co-infection with HIV, or the type of PI (Table).

Table. (004) Factors associated with sustained viral response.

Variable	RR	95% CI	*P*-value
Pretreated	3.47	2.78-4.33	0.000
Co-infection HIV	1.22	0.78-1.91	0.36
BOC *vs.* TLR	1.03	0.87-1.22	0.68
PI	2.07	1.72-2.50	0.000

Conclusion. The use of BOC and TLR has improved the SVR rate when used in combination with PR, no difference between each PI was detected, and the greater benefit was found in patients previously treated.

005

BOCEPREVIR FOR CIRRHOTIC PATIENTS HCV GENOTYPE 1 INFECTION

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Introduction. A new number of high quality of clinical trails have been published examining the efficacy of Protease Inhibitors to Standard of care treatment in hepatitis c virus infection, cirrhotic patients is a kind of population difficult to treat with a poor response to conventional hepatitis C treatment. The aim of the study was determinate safety, tolerance and antiviral response with triple therapy in a cirrhotic population with hepatitis C virus in a Mexican population. **Materials and methods.** Open clinical trial, Treatment group received pegylated interferon alpha 2a 180 mcg/week plus ribavirin 1,000 mg/day < 75 kg and 1,200 mg/day > 75 kg, in 4 week lead-in-period, follow by pegylated interferon alpha 2a, plus ribavirin plus boceprevir 800 mg/day for 44 weeks. Plasma HCV RNA levels were measured with the use of the TaqMan 2.0 assay (Roche Diagnostics) in 4, 8, 12, 48 and 60 weeks. **Results.** Twenty-nine cirrhotic patients, 18 men (62.1%) and 11 women (37.9%). Mean age 43 + 14.5 years. Genotype 1 in 100%; 1a in 9 (31%) 1b in 18 (62.1%), coinfeccion 1a + 1b in 2 patients (6.9%). IL28B CC in 4 patients(13.8%), CT in 15 (51.7%) and TT in 10 (34.5%). 8 Naïve (27.6%), 21 treatment experienced patients (72.4%): null responders 15 (51.7%), breakthrough 2 (6.9%), 1 partial responders (3.4%) and 3 relapse (10.3%). Six patients were retired during the trial: 4 were retired in week 4 (Lead-in period) by thrombocytopenia (13.8%); 1 in week 12 (3.4%) and 1 in week 24 (3.4%) by stopping rules. The rates of sustained virological response are in 10 patients (34.4%). Naïve cirrhotic patients SVR 12 in 5/8(62.5%) and cirrhotics treatment experienced patients 5/21 (24%), 6 null responders (20.6%), 2 relapsed (6.8%), 1 breakthrough (3.4%), 3 partial responders (10.3%) and 2 reported serious adverse events and were discontinued treatment because of sepsis. Three have SVR12 with triple therapy and were previous relapser patients (10.4%) and 2 null responders (6.8%). Adverse events: anemia in 22 patients (75.9%), 16 (55.2%) grade II (8 - < 9.5 g/dL), anemia grade III in 5, 6.5 - < 8 g/dL (17.2%); and 1 with grade IV < 6.5 g/dL (3.4%), EPO use in 22 (75.9%), 11 (37.9%) reduction in ribavirin dose and 1 patient required blood transfusion. Neutropenia was detected in 22 patients (75.8%), 11 required reduction in a peginterferon dose, and 11 required dose reduction plus G-CSF during the treatment. Dysgeusia in 3 patients and anorectal symptomatology in 1 patient (3.4%). **Conclusions.** The triple therapy in cirrhotic patients with close surveillance is well tolerated, safe, and increase viral response specially in naive patients. Relapser treatment experienced patients treated with triple therapy, show better response rate compared with null responders, in whom the response probability was minimal.

006

PERCEPTION OF SLEEP QUALITY FOR PATIENTS UNDERGOING TREATMENT FOR CHRONIC HEPATITIS C: MINI SLEEP QUESTIONNAIRE AS A SCREENING TOOL

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Introduction. Sleep disturbances often occur during treatment for chronic hepatitis C (CHC) with interferon (IFN) α plus ribavirin. Poor sleep quality is related to the onset of depression and impaired quality of life in patients receiving treatment. Therefore, it is necessary to perform early diagnosis of sleep disorders. The aims of this study were to test the Mini Sleep Questionnaire (MSQ) how screening tool, not yet utilized in this profile of patient, to assess the self-reported sleep quality and the prevalence of sleep disorders. **Material and methods.** This is a transversal observational descriptive-analytical study was conducted in the city of Ipiaú, Bahia, Brazil, comprising 41 subjects with CHC, divided into two groups, treatment (n = 16) and control (n = 25). A structured questionnaire was used to collect sociodemographic clinics variables. For the assessment of sleep quality was applied the MSQ. The inferential statistics were performed by applying the chi-square test to compare sleep quality among groups. **Results.** Significant difference between groups in the classification of sleep variable was observed ($p < 0.05$), being observed higher frequency of sleep disorders in patients of treatment group, 62.5%, while in the control group the frequency was 12%. **Conclusions.** This study identified higher prevalence of sleep disorders and self-reported poor sleep quality in CHC patients in treatment, in agreement with the frequencies published literature, suggesting an association between both events. Thus, the MSQ can be used as a screening tool for sleep disorders in CHC patients during the treatment with IFN-α plus ribavirin.

007

LOW PRESENCE OF RESISTANCE-ASSOCIATED VARIANTS Q80K TO HEPATITIS C VIRUS PROTEASE INHIBITORS IN NAÏVE DAA PATIENTS FROM SÃO PAULO, BRAZIL

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Background. Several new direct-acting antiviral (DAA) drugs are being developed or are already approved for the treatment of chronic hepatitis C virus (HCV) infection. HCV variants presenting drug-resistant phenotypes were observed both in vitro and during clinical trials. Our group previously demonstrated that the Q80K variant was the most prevalent mutation of subtype 1a, present in36% of the sequences of Los Alamos databank.The aim of this study was to characterize amino acid changes at positions previously associated with resistance in the NS3 protease in treatment-naïve brazilian patients with HCV genotypes 1a and 1b. **Material and methods.** Plasma samples from 171 treatment-naïve HCV 1a (N = 54) and 1b (N = 117) infected patients were obtained from the Liver Clinic at Department of Gastroenterology at University of São Paulo School of Medicine in São Paulo, Brazil. Nested PCR and Sanger sequencing were used to obtain genetic information on the NS3 protein. Bioinformatics was used to confirm subtype information and analyze frequencies of resistance mutations. **Results.** The results from the genotype analysis using non-NS3 targeted methods were at variance with those obtained from the NS3 protease phylogenetic analyses. It was found that 7.4% of patients infected with HCV genotype 1a showed the resistance-associated mutations V36L, T54S, Q80K, and R115K, while 5.1% of patients infected with HCV genotype 1b had the resistance-associated mutations V36L, Q41R, T54S, and D168S. Interestingly, the mutation Q80K was only found in 1 out 54 (1.9%) of genotype 1a patients. **Conclusions.** The low level frequency of Q80K mutations on genotype 1a found in high levels on other studies appears to be a characteristic of the Brazilian population. The resistance mutations present in treatment-naïve HCV patients biased by geographical location warrant closer examination, due to different susceptibility to different oral antiviral agents.

C. NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND ALCOHOLIC LIVER DISEASE (ALD)

001

THE ROLE OF CELL-CELL INTERACTIONS IN LIPID ACCUMULATION AND ACTIVATION PATHWAYS IN AN *IN-VITRO* MODEL OF NASH

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Background. Non-alcoholic steatohepatitis (NASH) is characterized by lipid accumulation and inflammation both involved in the development of fibrosis. Previous data suggest that FFA intracellular accumulation in hepatocytes induces an inflammatory response due to the up-regulation in pro-inflammatory cytokines and generation of reactive oxygen species which constitutes the initial step of the "two-hits theory". The activation of hepatic stellate cells (HSC) is a key factor for extracellular matrix remodeling (ECM) where metalloproteinases (MMPs) and its tissue inhibitors (TIMPs) play a determinant role. **Aim.** This study was designed to evaluate the interplay between hepatocytes and HSC in an *in vitro* cell model of NASH, in terms of activation and ECM gene expression markers. **Material and methods.** We determined TIMP1, TIMP2 and MMP2 mRNA expression in a hepatocyte (HuH7) and HSC (LX2) human cell lines loaded with FFA (1,200 μM palmitic-oleic mixture). Three different experimental strategies were used: a) HuH7 and LX2 were cultivated separately and loaded with FFA; b) Transwell system in which only HuH7 were loaded with FFA; and c) Simultaneous coculture of HuH7 and LX2 loaded with FFA. HSC activation was also assessed by mRNA expression of actin-alpha1 skeletal muscle (ACTA). Gene expression was determined by RT-PCR. Intracellular lipids accumulation was determined by fluorescent microscopy (Nile red staining) and flow cytometry. **Results.** Intracellular fat accumulation induces significant TIMP1 up-regulation in HSC (1.57 ± 0.13 folds, $p < 0.02$) but not in hepatocytes in strategies A and B (1.20 ± 0.17). TIMP2 showed a non-significant increased in HSC (strategy A) and hepatocytes in strategy B (1.28 ± 0.32); meanwhile, MMP2 expression levels were unchanged in HSC during all experimental strategies, whereas its expression was undetectable in hepatocytes. HSC were activated in the simultaneous co-culture (strategy C) due to high ACTA mRNA expression (2.7 ± 0.06 folds, $p < 0.003$), associated with a marked intracellular lipids accumulation (3.0 ± 0.2 folds $p > 0.01$) quantified by Spectrofluorimeter. In transwell system HSC showed an important increased (32%) of lipid droplets accumulation. **Conclusion.** Intracellular accumulation of FFA induces TIMP1 gene expression in HSC which is apparently hepatocyte-independent. However, cell-cell interactions and paracrine mediators promotes HSC activation as well as lipid intracellular accumulation, which are masterpieces in the development of fibrosis.

002

A GENETIC RISK SCORE CONSTRUCTED USING PNPLA3, GCKR, LYPLAL1 AND PPP1RB POLYMORPHISMS IS ASSOCIATED WITH LIVER FAT CONTENT AND STEATOHEPATITIS IN MEXICANS WITH MORBID OBESITY

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Background. Genome-wide association studies have identified single nucleotide polymorphisms (SNPs) near/in PNPLA3, NCAN, GCKR, LYPLAL1 and PPP1R3B genes associated with hepatic steatosis (HS) mainly in individuals of European ancestry. Here were tested whether these genetic variants and a genetic risk score (GRS) are associated with elevated liver fat content and non-alcoholic steatohepatitis (NASH) in Mexicans with morbid obesity. **Material and methods.** 130 morbidly obese Mexican individuals were genotyped for six SNPs. Hepatic fat content [triglyceride (HTG) and total cholesterol (HTC)] was quantified directly in liver biopsies and NASH was diagnosed by histology. A GRS was tested for association with liver fat content and NASH using logistic regression models. **Results.** PNPLA3, LYPLAL1 and PPP1R3B polymorphisms were associated with higher alanine aminotransferase levels (ALT), higher HTG content and steatosis stage, although only the association with PNPLA3 reached statistical significance ($P < 0.05$). GCKR also showed significant association with higher HTC content ($P = 0.034$), although the association was abolished when adjusting for Diabetes status ($P = 0.133$). The GRS was significantly associated with higher HTG and HTC content ($P = 0.002$ and 0.030, respectively), steatosis stage ($P = 0.042$), and higher ALT levels ($P = 9.7 \times 10^{-5}$). Subjects with GRS ≥ 6 showed a significantly increased risk of NASH (OR = 2.51, $P = 0.046$) compared to those with GRS ≤ 5. However, the GRS did not predict NASH status, as AUC of ROC curves was 0.56 ($P = 0.219$). **Conclusions.** Nonalcoholic fatty liver diseases (NAFLD) associated loci in Europeans and a GRS based on these loci contribute to the accumulation of hepatic lipids and NASH in morbidly obese Mexican individuals. Nevertheless, available genetic information cannot currently be used as predictive of NASH.

003

DEVELOPMENT OF A SIMPLE CLINICAL PREDICTION MODEL TO IDENTIFY PATIENTS WITH NONALCOHOLIC STEATOHEPATITIS RESOLUTION AFTER 52 WEEKS OF LIFESTYLE MODIFICATION

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Background. Clinical and laboratory predictors for nonalcoholic steatohepatitis (NASH) resolution after therapeutic intervention are need to avoid unnecessary liver biopsies. Thus, our study identified predictors of NASH resolution after 52 weeks of lifestyle modification. **Material and methods.** A total of 293 patients with histologic diagnosis of NASH were treated in the clinical practice with lifestyle modification during 52 weeks. A second liver biopsy was performed at 52 weeks to detect NASH resolution with no fibrosis impairment. Clinical data and laboratory determinations were obtained at baseline and at the end of the intervention. **Results.** NASH resolution was detected in 93 of 293 patients. Of the candidate predictors of NASH resolution, percentage of weight loss (OR, 1.51; 95% CI, 1.33-1.71; $P < 0.0001$), type 2 diabetes mellitus (OR, 0.19; 95% CI, 0.07-0.49; $P = 0.001$), body mass index (OR, 0.85; 95% CI, 0.77-0.94; $P = 0.002$), steatosis at baseline > 33% (OR, 0.42; 95% CI, 0.19-0.88; $P = 0.002$), chronic portal inflammation at baseline = 2 (more than mild) (OR, 0.19; 95% CI, 0.05-0.75; $P = 0.02$) and mean uric acid change from baseline (OR, 1.01; 95% CI, 1.005-1.04; $P = 0.005$) were independently associated to NASH resolution. The area under the ROC curve (AUC) of the selected model was 0.91 (95% CI, 0.87-0.94), and a risk score threshold of ≥ -0.332 corresponding with a predicted probability of NASH resolution of 42% showed 81% sensitivity and 88% specificity. **Conclusions.** A simple clinical prediction model may help to identify patients with NASH resolution after 52 weeks of lifestyle modification. The external validation is required in further studies.

004

NONALCOHOLIC FATTY LIVER DISEASE AND HEPATOCELLULAR CARCINOMA: BRAZILIAN SURVEY

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Background. The majority of the cases of hepatocellular carcinoma (HCC) have been related with cirrhosis associated with hepatite C and B virus and alcohool abuse. However, patients with nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatoepatitis (NASH) have increased the prevalence of HCC around the world. In 2000, one of the first cases of HCC related with NASH was reported in Brasil, and the present study aimed to evaluate the relevance and characteristics of HCC in patents with NAFLD/NASH throughout the country at the moment. **Material and methods.** Members of the Hepatology Brazilian Society were invited to complete a survey regarding patients with HCC related with NALFD/NASH. The questionnaire included clinical and histological

data from chart review and also prospectively. Patients with history of alcohol intake (> 20 g/day) and other liver diseases were excluded. HCC diagnosis was performed by liver biopsy or image methods according to HCC-AASLD Guideline/2011. **Results.** The survey included 110 cases with diagnosis of HCC and NAFLD from Hepatology Unit of six Brazilian States. The mean age was 67 ± 11 years and 65.5% (72) were male. Obesity was observed in 52.7% (58) ot the cases, diabetes in 73.6% (81), dyslipidemia in 41.0% (45), arterial hypertension in 60% (66) and metabolic syndrome in 57.2% (63) Histological diagnosis of HCC was performed in 52 (47.2%) patients: NASH without fibrosis was observed in 3.8% (2) cases, NASH with fibrosis (grades 1-3) in 27% (14), and cirrhosis in 61.5% (32). In 7.7% (4) of the cases of NALD the histological diagnosis was only HCC. A total of 58 patients had diagnosis of HCC by ultrasound confirmed by CT or MRI: 55% have 1 nodule; 17%, 2 nodules and 28% ≥ 3 nodules. All of them presented cirrhosis. **Conclusions.** The Survey suggests that HCC in Brazil is also associated with NASH and it was observed in non-cirrhotic NASH patients with and without fibrosis. These results showed that further investigations are required in this country to establish strategies for early diagnosis and treatment of HCC in patients with NAFLD/NASH.

005

COFFEE CONSUMPTION IS A PROTECTOR FACTOR FOR SEVERE OBESE PATIENTS WITH NONALCOHOLIC STEATOHEPATITS

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Background and aim. The relationship between caffeine consumption and some liver diseases, such as chronic hepatitis C virus and nonalcoholic fatty liver disease (NAFLD) has been suggested. However, the relevance of coffee consumption (CC) and histologycal grades of NAFLD in severe obese patients needs to be established. The present study evaluated the association between CC with insulin resistance, and CC and severity of NAFLD in these obese patients. **Material and methods.** Obese patients (BMI ≥ 35 kg/m^2), who undewent bariatric surgery, and had NAFLD diagnosis on liver biopsy from September/2013 to April/2014 were included. The histological diagnosis of NAFLD (steatosis and NASH) was done according the NASH Clinical Research Network (2011) criteria. A questionnaire was applied to quantify CC and the following variables were study: gender, age, BMI, coffee consumption history and liver histology. Insulin resistance (HOMA-IR ≥ 3) was performed in non diabetic patients. The patients were classificated according coffee consumption in 3 groups: G1-CC < 200 mL/day; G2-CC ≥ 200-400 mL/day and G3-CC > 400 mL/day. Data were presented as mean ± standard deviation or median (Md) and interquartile range (IQR). **Results.** A total of 100 obese patients were evaluated from September /2013 to April/2014. The mean age of the MOP was 37.4 ± 9.5 years, 69% of them were female, and mean BMI was 41.6 ± 4.8 kg/m^2. The CC was reported by 77.8 % of these 100 obese patients: 53.5% in group (G) 1, 25.3% in G2, and 21.2% in G3. The mean of insulin resistance index was similar in all groups {HOMA-IR [Md: 4.2 (II Q: 3.08-6.15) *vs.* Md: 3.7 (IIQ: 2.7-7.19) *vs.* Md: 4.5 (3,05-5,7), p = NS]}. Histological analysis, evaluated in 80 patients, observed in 17.5% (14) of the cases normal histology; in 18.8% (15) steatosis and 63.7% (51) steatohepatitis and fibrosis (grade 1 or 2). The relationship with coffee consumption and severity of NAFLD (NASH and fibrosis) was observed in 69% (29) patients in G1 (coffee consumption CC < 200 mL/day; in 63.2% (12) in G2 (CC ≥ 200-400 mL/day), and in 52.6% (10) patients in G3 (CC > 400 mL/day), (p = 0,465). **Conclusion.** The diagnosis of NASH and fibrosis was less frequent in severe obese patiens, who had more elevated coffee consumption. The results suggest that obese coffee drinkers may have lower chance to developing more severe NAFLD/NASH.

006

A NEW NON-INVASIVE METHOD TO EVALUATE OXIDATIVE STRESS IN PATIENTS WITH NAFLD

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Background/AIM. Oxidative stress (OXS) has a relevant participation in the pathogenesis of nonalcoholic fatty liver disease (NAFLD). Some studies has suggested that fatty acids increased inside the mitochondria can lead to generation of Reactive Oxygen Species (ROS) and consequent OXS. It may has influence for the NAFLD progression from steatosis to steatohepatitis (NASH). The present study evaluated a new methodology to quantifier ROS as a serum biomarker in patients with steatosis or NASH. **Material and methods.** Severe obese patients (BMI ≥ 35 kg/m^2) who underwent bariatric surgery (BAS) and liver biopsy from September/2013 to April/2014 were included. Serum simple of healthy volunteers also were included for results comparasion. NAFLD/NASH diagnosis was done according NASH Clinical Research Network (Kleiner/2011). The study participants were classificated according histologic diagnosis in 3 groups: G1-patients with steatosis; G2-patients with NASH and G3-healthy volunteers. Data were presented as mean ± standart deviation or median (Md) and interquartile range (IIQ). The ROS production in fresh whole blood of the patients and volunteers was measured by chemiluminescence in real time using a sensitive photon counter and L-012 (Wako Pure Chemical Industries Osaka, Japan) used as secondary emitter light. The nature of ROS was characterized using specific inhibitors: hydralazine and desferroxamine as inhibitors of peroxynitrite; superoxide dismutase and sodium azide as inhibitors of myeloperoxidase. **Results.** The simple included 18 healthy volunteers and 26 severe obese. In cases and volunteers the mean age was 36.7 (SD = 10.2) and 45.7 (SD = 9.9) years respectively. The mean BMI in obese patients was 43.3 (SD = 3.9) kg/m^2 and 53.8% were women. Steatosis isolate (G1) was observed in 22.7% (10) patients, NASH (G2) in 36.4% (16). In obese patients with NASH, 31.3% (5) of them presented fibrosis (grades 1-2). Patients in G2 (NASH) had higher levels of ROS when compared to G1 (steatosis) and G3 (healthy volunteers) [Md1: 13893 (IIQ: 10731-17820) *vs.* Md2: 2662 (IIQ: 2169-3420) *vs.* Md3: 201 (IIQ: 111-259), p < 0.001]. The same was observed when compared ROS between the groups 1 and 2 (p < 0.001). **Conclusion.** ROS serum levels, an oxidative stress marker,

in this simple of severe obese patients, were more elevated in patients with NASH and fibrosis than those with steatosis. These results suggest that this new methodoloy could be useful to identify severe obese patients with steatosis or NASH before de bariatric surgery in the pratical clinic.

D. HEPATIC CIRRHOSIS

001

GLUCOSE INTOLERANCE-A PREDICTIVE FACTOR IN PATIENTS WITH LIVER CIRRHOSIS

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Introduction. Glucose intolerance is a relative frequent characteristic in patients with liver cirrhosis. Clinical and laboratory data highlight diabetes in 15-30% of patients with liver diseases. We aim to evaluate whether oral glucose tolerance test can be considered as a predictor factor of prognosis. **Mateiral and methods.** 165 patients with liver cirrhosis were included in this study and were followed up for 5 years. Glucose tolerance was diagnosed by a 75 g oral glucose tolerance test (OGTT). WE investigated the relationship between clinical variables of cirrhosis prognostic using univariate and multivariate regression models. **Results.** In 66 patients (40%) we found normal glucose tolerance. Diabetes mellitus was diagnosed in 55 patients (33.33%) and impaired glucose tolerance in 44 patients (26.66%). The survival rates are significantly differed in patients with liver cirrhosis and diabetes mellitus versus patients with liver cirrhosis and normal glucose tolerance (95% at 5 years *vs*. 65 at 5 years). In univariate analysis the highly significant factors were serum albumin, glucose intolerance, total bilirubin, prothrombin activity, Child-Pugh score. In multivariate analysis only serum albumin and diabetes mellitus were the most significant negative predictors factors of survival. **Conclusion.** Oral glucose tolerance test can be considered an important predictive factor of survival in liver cirrhosis. We recommend performing this test as early as possible when dealing with a potential impaired glucose tolerance, in order to prescribe the necessary lifestyle chances that would improve the patients' outcomes.

002

NOSOCOMIAL INFECTIONS IN LIVER CIRROSIS

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Background. Bacterial infections in cirrhotic patients are reported mainly in community infections, however the nature of the germs involved in nosocomial infections is poorly understood. **Aims.** We aim to study the carriage of Methicillin Resistant Staphylococcus aureus (MRSA) in hospitalized patients and also to describe the frequency and etiology of infections in cirrhotic patients. **Material and methods.** We studied the carriage of MRSA in the nose and the stool in a group of 748 cirrhotic patients treated in-hospital; we also studied the nature of the germs responsible for spontaneous bacterial peritonitis (SBP), bacteriemia and urinary infections occurring during hospitalization. **Results.** The characteristics of the patients were: 481 males, age 54.4 ± 11.7 years, Child Pugh score 9.5 ± 2.3, average hospitalization period 37.1 ± 27.4 days. We identified 106 episodes of SBP, 84 episodes of bacteriemia, 194 episodes of urinary tract infections. The enterobacteria were responsible for the largest number of urinary infections, while Gram positive cocci accounted for 64% of all cases of SBP and 76% of all cases of bacteriemia. 125 patients were carriers of MRSA (16.7%). MRSA carriage increased the risk of MRSA infection more than 10 times. In multivariate analysis, Child Pugh score, age, the portage of MRSA and bacteriemia were independent factors associated with a higher mortality. **Conclusion.** Nosocomial infections in cirrhotic patients are characterized by a predominance of gram-positive cocci causing spontaneous ascites infection and bacteremia. MRSA carriage is a factor of poor outcome.

003

THE NATURAL HISTORY OF HCV-RELATED CIRRHOSIS AND ITS TEMPORAL PROGRESSION ACROSS THE DIFFERENT CLINICAL STAGES

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Background. The clinical course of HCV-related cirrhosis and its temporal progression across the different clinical stages has not been completely investigated. Our study evaluated the cumulative incidences (CIs) of clinical outcomes marking disease progression across the different clinical stages. **Materials and methods.** At baseline, 660 patients were classified as compensated (absence [294], or presence [108] of gastroesophageal varices) or decompensated (ascites [144], variceal bleeding alone [45] or in combination with ascites [17] and encephalopathy alone or together with bleeding and/or ascites [52]). Subjects were followed during 6 years to identify time to a first event marking disease progression. **Results.** Among compensated patients without varices, the 6-year CIs for developing varices, ascites, and encephalopathy were 37.4, 13.6 and 3.5%, respectively. The 6-year CIs of development of ascites, bleeding and encephalopathy were 24, 12.5 and 9.9% for compensated subjects with varices, respectively. Among patients with ascites, the 6-year CIs of bleeding, liver-related deaths/transplant and encephalopathy were 23.5, 27.8, and 47.3%, respectively. The 6-year CIs of ascites, liver-related deaths/transplant and encephalopathy were 22.5, 14.7 and 5.7% among patients with bleeding; however, CIs of liver-related deaths were significantly higher in those with ascites plus bleeding (77.6%). Patients with encephalopathy alone or in combination with ascites and/or bleeding displayed the highest rates of deaths (6 years, 90%). **Conclusions.** Among compensated patients, the presence of varices suggests a more accelerated course of the disease. Decompensated patients show the most severe clinical course, particularly in those with a combination of two or more clinical events.

004

ULTRA-SENSITIVE PROCALCITON IN MAY HELP RULE OUT BACTERIAL INFECTIONS IN PATIENTS WITH CIRROSIS

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Background. Bacterial infections are frequent complications in patients with cirrhosis. Since they are associated with poor outcomes, antibiotics are frequently overprescribed. Surrogate markers of bacterial infections, like procalcitonin, are needed to better discriminate between infected and not infected patients. **Aims.** To evaluated the diagnostic accuracy of an ultra-sensitive procalcitonin assay for the diagnosis of bacterial infections in patients with cirrhosis. **Material and methods.** In a single-center prospective study, we determined the basal levels of procalcitonin in 106 episodes of admissions to the Emergency Department in 84 cirrhotic patients. Patients were classified as infected or not infected by two independent hepatologists blinded to the procalcitonin result. **Results.** The prevalence of bacterial infection was 28% (29 episodes). The median procalcitonin was significantly higher in the infected group than in the not infected group (0.45 ng/mL *vs.* 0.061 ng/mL, $p < 0.001$). The diagnostic accuracy of procalcitonin for bacterial infection estimated by the ROC curve was 0.95 (CI 95%, 0.91-0.99). When selecting a cutoff value of 0.098 ng/mL a sensitivity of 97% and a negative predictive value 98% were found. **Conclusions.** The use of an ultra-sensitive procalcitonin assay identifies patients with cirrhosis at very low risk of bacterial infections.

005

DYSGEUSIA IN CIRRHOSIS: AN EXPERIMENTAL ANALYSIS

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Introduction. Protein-energy malnutrition (PEM) is a common complication of cirrhosis, where the zinc (Zn) and the change of taste can be determining factors. **Materials and methods.** We used 14 male Wistar rats (± 250 g) were divided into two groups: (CO-control) received 0.5 mL of mineral oil and (CCl4-cirrhosis) received 0.5 mL of CCl4 dissolved in mineral oil 1:6, 2x/week. At week 16, blood was taken for measurement of Zn and tongue for histological analysis (H/E) and immunohistochemical staining with PGP 9.5 antibody and T1R2 and T1R3 receptors. The morphology was studied by scanning electron microscopy (SEM). We used the Student t-test with $p < 0.05$. **Results.** Zn in CCl4 were lower than CO. CCl4 tongue showed changes in filiform papillae. In both groups there was immunoreactivity for type II and III cells and T1R2. CCl4 showed no immunoreactivity for T1R3. CCl4 by SEM showed uniform taste buds, base tapering papilla (CO: 43.93 ± 3.138; CCl4: 28.37 ± 4.231) and width of the apex of the papilla (CO: 16:13 ± 2.644; CCl4: 11.67 ± 1.794) ($p < 0.05$). The taste buds showed abnormalities between groups, with higher average area of 3.69 ± 0.439 and a diameter of 73.72 ± 12.63 in the CO ($p < 0.05$). There was a reduction in the number of taste buds in CCl4. **Conclusion.** The Study data may help elucidate the physiological mechanisms of taste alterations in cirrhotic patients.

006

TYPE 2 DIABETES MELLITUS AS A RISK FACTOR FOR HEPATIC ENCEPHALOPATHY IN PATIENTS WITH LIVER CIRRHOSIS

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Objectives. To determine the type 2 diabetes mellitus (T2DM) is a risk factor for the development of Hepatic Encephalopathy (HE) in patients with liver cirrhosis. **Material and methods.** A cross-sectional, retrospective, case-control study in patients with liver cirrhosis admitted to hospitalization for decompensation, regardless of etiology, was included. We divided 2 groups, the first group (cases) corresponds to patients with EH and the second group (control) patients without EH. Analysis bivariate with χ^2 Pearson was conducted, variables studied were presence of T2DM, use of diuretics, constipation, gastrointestinal hemorrhage, infection, electrolyte imbalance, acute renal failure (ARF), use of drugs potentially precipitating EH and alcohol intake. **Results.** 174 patients were included, of which 76 (43.7%) correspond to the cases, and 98 patients (56.3%) to the controls; 69 male patients (39.7%) and 105 women (60.3%); average age 55 years, the three leading causes of cirrhosis were viral (HCV, HBC) alcoholic and cryptogenic. HE group had higher Child Pugh score (Child Pugh C: 28.7% *vs.* 11.5% compared to controls) and higher MELD score (21.37 *vs.* 14.01). A significant association between the use of diuretics (OR 6.75, 95% CI 3.04-14.96, $p \leq 0.001$), infection (OR 3.078, 95% CI 1.62-5.83, $p \leq 0.001$), presence of T2DM (OR 2.018, 95% CI 1.07-3.80, $p = 0.029$), electrolyte imbalance (OR 3.23, 95% CI 1.63-6.41, $p = 0.01$) and acute renal failure (OR 6.75, 95% CI 3.047-14.9, $p \leq 0.001$) with the development of HE in patients was found. The same analysis with uncontrolled glucose, regardless associated to T2DM (defined this by increased glucose 130 mg/dL) was conducted, also found a significant association (OR 2.797, 95% CI 1.45-5.38, $p = 0.002$). **Conclusions.** T2DM and the use of diuretics, electrolyte imbalance, ARF, infections and elevated serum glucose was associated with the development of EH in patients with liver cirrhosis. Prospective and of greater magnitude studies are needed to corroborate the association of T2DM with HE.

007

EVALUATION OF SURVIVAL IN CIRRHOTIC PATIENTS WITH REFRACTORY ASCITES: THERAPEUTIC PARACENTESIS x TIPS x LIVER TRANSPLANTATION

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Introduction. Refractory ascites (RA) is observed in 5-10% of advanced cirrhosis and has a one year mortality rate of 20-50%. Controlled trials have compared TIPS with therapeutic paracentesis in the management of RA; however the survival results in liver transplantation versus TIPS and therapeutic paracentesis (TP) are controversial. **Aims.** The purpose of study was to evaluate the survival of cirrhotic patients with RA, comparing those submitted to TIPS and or to liver transplantation (LT) *vs*. those that used only TP for ascites control. **Material and methods.** From March 2009-April 2014, at the Clinic for Refractory Ascites of the Division of Gastroenterology and Hepatology in Brazil, 83 cirrhotic patients with RA were consecutively and prospectively enrolled. Ascites of other etiology was excluded. Patients withdrawn from the protocol of conventional treatment of ascites were followed-up by TP and patients who required this procedure up to twice a month, the insertion of TIPS was then proposed. During the follow up 16 patients underwent to LT. In all patients Child-Pugh and Meld score were evaluated. The mortality rate was individualized according to the modality of treatment and the cause of death (related or not to liver disease). The survival rate was calculated in patients who died or remain at follow-up from the diagnosis date of RA to death or until the last medical visit, respectively. **Results.** Of 83 RA, 71.1% were male with a mean age of 55.8 ± 9.3 y.o. with alcoholic etiology in 42.2%. The Meld score was 13.5 ± 3.8 and 68.7 and 31.3% were Child-Pugh B and C respectively. 42 (50.6%) remain in clinical follow-up while 41 (49.4%) died. Of patients at follow-up, 30 (71.4%) control ascites with TP; 8 (19.0) underwent TIPS, while 4 (9.5%) underwent LT. Of the total deaths, 21(51.2%) controlled the ascites with TP, and within this group the death was not related to liver cirrhosis (LC) in 76.19%; 11 (26.8%) underwent LT and in these, the death was related to LC in 54.5%; 8 (19.5%) underwent TIPS with 62.5% of causes of death related to LC and 1 (2.4%) underwent TIPS and LT with the LC-related death. The survival rate of according to the type of treatment given was: TP 219.2 ± 224.4 x 448.3 ± 467.0 ($p < 0.04$); TIPS 454 ± 396.3 x 561.3 ± 456.1 ($p = 0.62$); LT and TIPS 169.5 ± 138.3 x 103.3 ± 88.7 ($p = 0.39$) and LT 486 x 0 days, for patients who died or are still in the clinical follow-up respectively. **Conclusions.** RA led to a high mortality rate and survival was statistically lower in the control of ascites by TP; however not related directly to liver disease in most cases.

008

EFFECTS OF HYPERAMMONEMIA ON GLUTAMINE AND BRANCHED-CHAIN AMINO ACID METABOLISM: EXPERIMENTAL STUDIES UNDER *IN VIVO* AND *IN VITRO* CONDITIONS

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Background. Hyperammonemia, hyperglutaminemia, and decreased levels of branched-chain amino acids (BCAA; valine, leucine and isoleucine) are characteristic findings in patients with liver cirrhosis and play a major role in pathogenesis of hepatic encephalopathy. Two separate studies were performed using male Wistar rats in which the effects of hyperammonemia on glutamine (GLN), BCAA, and protein metabolism were estimated. **Material and methods.** In the first, *in vivo* study, the hyperammonemia was induced by infusion of ammonium acetate/bicarbonate mixture. The parameters of leucine and protein metabolism were measured under steady state conditions using L-[1-14C] leucine infusion. Statistical comparisons were performed using ANOVA and Bonferroni test. In the second, *in vitro* study, soleus (SOL, slow-twitch, red muscle) and extensor digitorum longus (EDL, fast-twitch, white muscle) muscles were incubated in a medium with or without 0.5 mM ammonia. We measured the exchange of amino acids between the muscle and the medium, amino acid concentrations in the muscle, leucine oxidation, total and myofibrillar proteolysis, and protein synthesis. Paired t-test was used for the analysis of the data. **Results.** Ammonium infusion increased ammonia and GLN, and a decreased BCAA and alanine levels in blood plasma, increased whole-body BCAA oxidation, and decreased protein synthesis in skeletal muscle. Under *in vitro* conditions, hyperammonemia enhanced GLN and decreased BCAA release from muscle, and increased leucine oxidation and GLN concentration in muscles. The effect of ammonia on intracellular BCAA concentration, protein synthesis and on total and myofibrillar proteolysis was insignificant. **Conclusions.** The results indicate that hyperammonemia directly affects the BCAA metabolism in skeletal muscle which results in decreased levels of BCAA in the extracellular fluid. The effect is associated with activated synthesis of GLN and BCAA oxidation. The effect of ammonia is more pronounced in muscles with high content of white fibres. Supported by PRVOUK P37/02.

009

EXERCISE CAPACITY IN HEPATOPULMONARY SYNDROME

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Introduction. Hepatopulmonary syndrome (HPS) is characterized by a clinical triad of liver disease and/or portal hypertension, intrapulmonary vascular dilatation and abnormal arterial oxygenation. These conditions can worsen muscle strength, exercise capacity and functionality in the affected population. The objective of this study was to compare exercise capacity, functional condition and respiratory muscle strength in cirrhotic patients diagnosed with HPS and

cirrhotic patients without this diagnosis. **Material and methods.** This cross-sectional study used a convenience sample consisting of 178 patients (92 patients with HPS and 86 patients without HPS) with a diagnosis of liver cirrhosis caused by either alcohol consumption or the hepatitis C virus (HCV). Peak oxygen consumption (VO_2 peak) was used to verify exercise capacity, the six-minute walk test (6MWT) was used to test functionality, and manovacuometry was used to evaluate the strength of the respiratory muscles. The Kolmogorov-Smirnov test and Student's t-test were used for the statistical analysis. The data were analyzed using SPSS 16.00, and $p < 0.05$ was considered significant. **Results.** The group of patients with the diagnosis of HPS exhibited a lower VO_2 peak (14.2 ± 2.3 *vs.* 17.6 ± 2.6, $p < 0.001$), shorter distance walked in the 6MWT (340.8 ± 50.9 *vs.* 416.5 ± 91.4, $p < 0.001$), lower maximal inspiratory pressure (-49.1 ± 9.8 *vs.* -74.2 ± 13.9, $p = 0.001$) and lower maximum expiratory pressure (60.1 ± 12.2 *vs.* 76.8 ± 14.7, $p = 0.001$). **Conclusion.** The group of cirrhotic patients diagnosed with HPS exhibited lower values for VO_2 peak, distance walked in the 6MWT and respiratory muscle strength than the cirrhotic patients not diagnosed with HPS.

010

FUNCTIONAL CAPACITY, RESPIRATORY MUSCLE STRENGTH, AND OXYGEN CONSUMPTION PREDICT MORTALITY IN PATIENTS WITH CIRRHOSIS

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Introduction. Liver diseases influence musculoskeletal functions and may negatively affect the exercise capacity of patients with cirrhosis. **Aim.** To test the relationship between the Six-Minute Walk Test (6MWT), maximal inspiratory pressure (MIP), and exercise capacity (VO_2peak) measures and the survival rate of patients with cirrhosis. **Material and methods.** This prospective cohort study consisted of 86 patients diagnosed with cirrhosis with the following aetiology: hepatitis C virus (HCV), hepatitis B virus (HBV), and/or alcoholic cirrhosis (AC). All patients were followed for three years and submitted to the 6MWT, pressure measurements with a compound gauge, and an exercise test (VO_2peak). **Results.** The study included 66 males and 20 females, with 40 patients in the HCV group, 30 patients in the AC group, and 16 patients in the HBV group. The survival rate analysis showed that the individuals who covered a distance shorter than 410 m during the 6MWT had a survival rate of 55% compared with a rate of 97% for the individuals who walked more than 410 m ($p = 0.0001$). Individuals with MIPs below -70 cmH_2O had a survival rate of 62% compared with a rate of 93% for those with MIPs above -70 cmH_2O ($p = 0.0001$). The patients with VO_2peak values below 17 mL/kg had a survival rate of 55% compared with a rate of 94% for those with VO_2peak values above 17 mL/kg ($p = 0.0001$). **Conclusion.** The 6MWT distance, MIP, and oxygen consumption are predictors of mortality in patients with cirrhosis.

011

EFFECT OF *ROSMARINUS OFFICINALIS* IN OXIDATIVE STRESS AND EPIGENETIC CHANGES OF RBP1 GENE IN EXPERIMENTAL ALCOHOLIC LIVER CIRRHOSIS

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Attempt to avoid the transition of alcoholic cirrhosis to hepatocellular cancer (HCC), brings a pharmacological promise, being one of these cases the uses of *Rosmarinus officinalis* (Rosemary) extract which has shown hepatoprotective and antioxidants properties, among others. An important event in alcoholic cirrhosis, as well as the different etiology, is the oxidative stress as a really important manner, which promotes the inflammatory and fibrotic injury, enabling the stellar cells, responsible for the storage of retinoids (among other processes), through binding to the cellular protein of union of retinol 1 (cellular retinol-binding protein-1, CRBP-1). There are unknown genetic and epigenetic mechanisms regulating the RBP1 gene expression; however, this has been associated with the progression to HCC. Following this principle, we evaluate epigenetic changes, particularly methylation to DNA and oxidative damage in experimental alcoholic cirrhosis treated with R. officinalis leaf extract. Male Wistar rats (180 ± 5 g) were used to induce liver cirrhosis by ethanol (3 g/kg, VO) up to 24 weeks. We studied preventive and reversion effect of *R. officinalis* (10 mg/kg, VO), measuring metabolic indicators (glycogen and bilirubin), enzymes [alanine aminotransferase (ALT) and gamma-glutamyltranspeptidase (γ-GTP)], lipoperoxidation (LPox) and total antioxidant capacity (TAC); and furthermore the RBP1 methylation gene expression. From the epigenetic point of view because the small number of studies on methylation of RBP1 gene, specific methylation primers were designed (through software Methprimer results); extraction and DNA methylation was conducted with FFPE gDNA (Promega) and Cells-to-CpGTM Bisulfite (Applied Biosystems). The results showed that in cirrhosis increased bilirubin and also ALT and γ-GTP; liver glycogen decreased (60%); LPox increased 1.5 times, and TAC decreased by 65%. In the treatment of prevention R. officinalis regulated metabolic and enzymatic indicators. It also prevented LPox increase; TAC avoided the decrement, bringing on the 14% more over control value. Reversion therapy, showed partial recovery suggesting benefit in liver function. Methylation of the RBP1 gene was evident in cirrhosis; was showed in both melting curves by real time PCR and agarose gels. Treatment with *R. officinalis* avoided this methylation suggesting protective effect. Alterations were treated with *R. officinalis,* modifying the course of cirrhosis, making possible the use of an alternative phytotherapy and specifically phytoepigenetic therapy. Funded by SEP-CONACYT, CB-2008-01-105986.

012

EFFECT OF SUSTAINED VIROLOGICAL RESPONSE ON THE INCIDENCE OF HEPATOCELLULAR CARCINOMA IN HCV CIRRHOTIC PATIENTS

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Background. There is evidence of decreased incidence of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C virus (HCV) infection who achieve a sustained virological response (SVR). The aim of this study was to compare the rate of HCC among HCV cirrhotic patients with and without SVR. **Material and methods.** In this retrospective cohort study, 357 HCV cirrhotic patients that received interferon based therapy between 2005 and 2012 in Hospital de Clinicas de Porto Alegre, Brazil, were divided in two groups: a) Patients with SVR, and b) Patients without SVR. At baseline, all patients were Child A with no previous history of hepatic decompensation and no evidence of HCC on abdominal ultrasound (US). SVR was defined as negative HCV-RNA 24 weeks after end of treatment using molecular amplification method with a limit of detection of 15 IU/mL. Patients were followed every 6 months with US until HCC, death, or liver transplantation. HCC was diagnosed using dynamic imaging method (computerized tomography and/or magnetic resonance) showing a liver nodule with typical vascular pattern with wash-in on arterial phase and wash-out on portal phase. The protocol was approved by the Institution Ethics Committee and all patients signed informed consent. Statistical analysis was based on Fisher's Exact Test and Kruskall-Wallis (alpha < 0.05). **Results.** Among 357 treated HCV cirrhotic patients, 125 (35%) achieved SVR (group A) and 232 (65%) did not (group B). Mean follow-up was 49.9 ± 30.0 months in those with SVR *vs.* 33.4 ± 24.0 months in those without SVR. During follow-up, HCC was diagnosed in 15 (12%) of 125 SVR patients and 48 (21%) of 232 non-SVR patients (P = 0.04). Baseline characteristics were similar among SVR and non-SVR patients, with the exception of age (51.7 *vs.* 54.3 years; P = 0.01) and platelets (138,000 ± 53,000/mm^3 *vs.* 112,000 ± 54,000/mm^3; P < 0.0001), respectively. **Conclusions.** There was a significantly higher incidence of HCC among HCV cirrhotic patients without SVR. However it is important to notice that a fairly large proportion of patients with SVR were still able to develop HCC. These findings support the fact that cirrhotic patients need indefinite follow-up, regardless of HCV RNA eradication status.

013

EFFECTS OF NOCTURNE SUPPLEMENTATION WITH BRANCHED-CHAIN AMINO ACIDSON BODY COMPOSITION AND HANDGRIP STRENGTH IN PATIENTS ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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Background. Protein-energy malnutrition (PEM) is highly prevalent (20 to 85%) in patients with chronic liver disease who are candidates for orthotopic liver transplantation (OLT) with extreme depletion of both muscle and fat stores. PEM has been associated withthe presence of comorbidities andcomplications at the time of liver transplant and after it, leading to an increase in hospital stay; increased risk of infections and mortality. Providing adequate nutrition to OLT candidates would seem particularly important and it has been suggested that the overnightsupplementation with carbohydrates and branched chain amino acids (BCAA) can improve the nutritional status and decrease muscle wasting of the subjects. But this recommendation stills controversial. **Aim.** Assess the impact of the nocturne supplementation-daily, during 1 month-with BCAA on the body composition and handgrip strengthin patients on the waiting list for liver transplant. **Material and methods.** Eighthy of 23 subjects on the waiting list for OLT received a food supplement with BCAA and calories (1 bag of Enterex Hepatic®, 110 g). Patients with PEM were included using the following criteria: phase angle < 5.4º measured by bioelectrical impedance, grade B or C in the subjective global nutritional assessment or handgrip strength < 30 in men and < 20 in women (measured by dynamometry). Patients with hepatorenal and hepatopulmonary syndrome were excluded. Body composition were analyzed using body plethysmography (fat and free mass) and by anthropometric parameters [weight, height, body mass index (BMI), mean arm circumference (MAC), muscle arm area (MAA) and tricipital skinfold]. Themuscle strength was measuredthrough no dominant handgrip strengthat beginning and after 30 days of nocturne supplementation. Adherence to treatment was measured by a 24-h recall and a food questionnaire. Statistical analysis was made using SPSS v.17. Changes were considered as significant at p < 0.05. **Results.** Thirteen women and 5 men were enrolled in a non-controlled clinical trial, the mean age was 47.18 ± 11 years. Daily Supplementation with BCAA and calories significantly improve the Mid-arm circumference, tricipital skinfold thickness, body fat mass and the handgrip strength of patients on the waiting list for OLT (p < 0.05). The main adverse effects reported were satiety and nausea. **Conclusions.** Supplementation with BCAAand calories improves body composition and muscle strength of patients on the waiting list for OLT. A controlled clinical trial with placebo group, and bigger sample size is needed.

E. HEPATOCELLULAR CARCINOMA

001

EPIDEMIOLOGY OF HEPATOCELLULAR CARCINOMA. MULTICENTER STUDY IN ARGENTINE

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Background. Nowadays, the epidemiological information in Argentine about hepatocellular carcinoma (HCC) is very poor. Our aim is to know and describe epidemiological variables of the HCC in our country and compare the results with worldwide papers. **Material and methods.** A multicentric, descriptive, retrospective and observational study was taken since June 2007 up to February 2014. We analyze: sex, age, cirrhosis etiology, distribution based on BCLC Staging System and used therapies. Patients were registered in a unique data base from 21 publics and private centers, all around 11 cities of 9 states from Argentine. **Results.** 316 patients with HCC were registered. 72.78% male with a relation between sexes of 2.67/1. Average age was 63.4 year (20-86). Cirrhosis etiologies found were: CHV 39.8%; alcohol 27.5%; cryptogenic 13.3%; NASH 7.6%; non specified 5.86%; BHV 3.16%; hemochromatosis 0.6%; CHV + OH 0.3%; NASH + OH 0.3% and autoimmune 1.58%. Distribution according BCLC staging was: A 40.2%; B 32.9%, C 18.6% and D 8.3%. 258 patients have had some treatment, leaving a 18.4% untreated. 274 therapies were implemented: TACE 25.9%, sorafenib 21.5%, combined therapies 14.9%, surgery 12.7%, transplant 11%, RF 2.5% and palliative cares 11.5%. **Conclusions.** We found similar results with worldwide information in the distribution and the average age, and also in the cirrhosis etiology. We have observed that most of our patients belong to the A and B stages in Barcelona which leads us to the conclusion that screening methods are efficient. However, we have also found a lot of treatments for advanced stages, which leads us to investigate this relation in near future.

F. LIVER TRANSPLANT

001

DIABETES AND CHRONIC KIDNEY DISEASE AFTER LIVER TRANSPLANTATION: A 5-YEAR RETROSPECTIVE COHORT STUDY

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Background. Liver transplantation is a therapeutic tool for patients with liver cirrhosis; however, it requires the use of immunosuppressants that can lead to metabolic alterations in the post-transplant period. **Objective.** To identify the prevalence of comorbidities in patients submitted to orthotopic liver transplantation (OLT), as well as to establish the association between these alterations and calcineurin inhibitors. **Material and methods.** Retrospective cohort study performed by reviewing the records patients subjected to OLT –for different etiologies– at the Santa Casa de Misericordia Hospital Complex of Porto Alegre, in Porto Alegre, Brazil, between 2000 and 2008. Clinical, laboratory and anthropometric parameters were reviewed, both pre-operative (evaluation on the transplant admission day) and post-operative (6 months, first through third and fifth year). The following definitions for the classification of metabolic alterations were utilized: diabetes mellitus (DM): fasting blood sugar > 126 mg/dL, utilization of oral or injectable hypoglycemic agents, clinical diagnosis; dyslipidemia: CT ≥ 240 mg/dL or LDL > 160 mg/dL; chronic kidney disease (CKD): glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2, calculated with the MDRD6 formula. **Results.** The data from 193 patients who were submitted to OLT between 2000 and 2008 was retrospectively analyzed; of these, 88.6% (n = 171) were accompanied for five years. The male sex predominated with 63.7% (n = 123) and the average age was 51.9 + 10.5 years. 73.1% (n = 141) of the patients had their transplants performed by the public health system. Cyclosporine was significantly associated with the prognostic scores (Child-Pugh C and MELD > 20) and with the following metabolic changes: hyperglycemia and DM –in the pre- and post-transplant periods– and hypertriglyceridemia, dyslipidemia, and increased creatinine only post-transplant. A modification in the immunosuppressant scheme (from tacrolimus to cyclosporine) showed an association with CKD (GFR < 60 L/min/1.73 m^2). **Conclusion.** There was an increase in the prevalence of DM and CKD, when comparing data prior to hepatic transplantation with the follow-up period after the surgical procedure. It should be noted that these alterations were observed early on, a fact that highlights the importance of action directed to the prevention and/or treatment of metabolic complications, contributing to lower morbidity among patients.

002

CYTOKINES, CHEMOKINES, AND COLLAGEN TYPE I AND III IN LIVER TISSUE FROM END STAGE OF LIVER DISEASE

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Introduction. Cytokines play a critical role in communication and cellular activation, the liver is a source of cytokines involved in the development of liver disease. These proteins are key molecules in most acute and chronic liver disease. **Objective.** To evaluate gene expression of TNF-α, IL-10, CXCL-8, CXCL-10, TGFβ-1, and collagens type I and III in hepatic tissue from children with end stage of liver disease. **Material and methods.** We included 7 patients with end stage of liver disease (ESLD) of different etiologies: biliary atresia (3) fulminant hepatitis (3) and tyrosinemia (1), who underwent liver transplantation at Mexico City's Children's Hospital (Hospital Infantil de México). Five patients received a liver allograft from living relatives and two from deceased donors, informed consent was obtained and a liver biopsy from each subject. In each of the samples was carried out RNA extraction and obtaining cDNA and determined the gene expression of TNF-α, IL-10, CXCL-8, CXCL-10, TGFβ-1, Col-I and Col-III by real time PCR. Data analysis was performed a Student t-test. **Results.** Patients with ESLD (3 girls and 4 boys) were 3 ± 2 years. A control group of 7 people was included with mean age of 31 ± 14 years, (3 women and 4 men). The expression of the genes was TNF-α (ng/mL) in ESLD = 3 ± 2 and CT = 2 ± 0.8 ($p = 0.778$). IL-10 (ng/mL) at ESLD = 6 ±5 and CT = 0.3 ± 0.2 ($p = 0.025$) CXCL-8 was 53 ± 21 and 0.4 ± 0.3 for ESLD and CT, respectively ($p = 0.048$), CXCL-10 (pg/mL) was ESLD = 3 ± 0.4 and CT = 0.8 ± 0.2 ($p = 0.043$), TGFβ-1 (ng/mL) was ESLD = 7 ± 1 y CT = 1 ± 0.50 ($p = 0.002$), Col-I expression (pg/mL) was ESLD = 15 ± 8 and CT = 8 ± 1 pg/mL (NS) and Col-III (pg/mL) was ESLD = 35 ± 2 and CT = 2 ± 1 pg/mL (0.032). **Conclusions.** In liver tissue of liver transplant recipients, the gene expression of proinflammatory cytokines and chemokines was increased, with higher transcriptional activity of CXCL8. Also the expression of genes related to the fibrogenic process is 7 times in the terminal stage of liver disease, regardless of etiology and patient age.

003

RADIOLOGIC-PATHOLOGIC CORRELATION OF HEPATOCELLULAR CARCINOMA TUMOR SIZE IN LIVER EXPLANTS

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Introduction. The Milan and San Francisco criteria for orthotopic liver transplantation (OLT) are based on hepatocellular carcinoma (HCC) tumor size. CT and MR imaging represent the primary tools for assessment of tumor size, preoperative decision-making, and treatment planning. The purpose of this study is to evaluate the performance of cross-sectional imaging in characterizing and staging HCC by comparing liver explant histopathology results to preoperative imaging findings. **Materials and methods.** This IRB approved study (#20090093) evaluated 59 hepatomas from 42 patients who underwent OLT for HCC at Jackson Memorial Hospital between 2008 and 2011. Tumor sizes on pre-operative CT or MR were correlated to size of gross pathologic specimens from hepatic explants using linear regression analysis, and descriptive statistics were calculated. Inter-group differences were assessed using the Wilcoxon rank sign test. Cases in which tumor under- or over-estimation resulted in a deviation from ideal surgical management were identified. **Results.** The median age was 58 years. Thirty-seven of 44 patients were infected with viral hepatitis; the remaining five patients suffered from alcoholic liver disease. Ten cases were imaged with MRI; the remaining 32 cases were imaged with CT. Radiographic and pathologic sizes of HCC lesions were positively correlated ($r = 0.87$). The median radiographic size was 2.3-cm (range 1.2-7). The median pathologic size was 2.3-cm (range 0.7-7.0). The median difference was 0.7-cm. Wilcoxon ranked sign test showed no significant difference between the two groups ($p = 0.06$). There were 3 cases (7%) in which imaging underestimated tumor size resulting in excess hepatic transplants per the Milan criteria. There were no cases in which imaging tumor overestimated tumor size which would have prevented a patient from receiving a liver transplant. No change in management would have occurred if using the San Francisco criteria. **Conclusions.** Imaging and gross pathologic measurements of hepatomas are sufficiently similar that CT and MR can be confidently used for the preoperative assessment of OLT candidates. The imaging findings in this series never prevented surgery due to overestimation of tumor size, while underestimation of size affected management in only 6% of patients. CT and MR appear to be reasonably adequate tools when applying the Milan or San Francisco criteria to OLT candidates.

004

LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA IN URUGUAY: OUTCOMES AND CORRELATION BETWEEN IMAGING AND PATHOLOGICAL FINDINGS

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Introduction. Liver transplantation (LT) is the best therapeutic option for patients with cirrhosis and early stage hepatocellular carcinoma (HCC). The aim of this study is to describe clinical-epidemiological characteristics of patients who underwent LT with HCC, in last 5 years. We evaluated results according to international standard criteria and performed a correlation between imaging and pathological findings in explants. **Material and methods.** Descriptive, observational, retrospective study of patients evaluated and transplanted with HCC (14/07/2009-14/05/2014) We analyzed epidemiological aspects and used as references Milan, University of San Francisco criteria (UCSFc), Up to 7, an Total Tu-

mor Diameter (TTD), and estimated specificity and sensibility of TC and RNM regarding pathological findings. **Results.** 90 LT were performed, 28 had HCC at time of evaluation and were studied according actual standards of care. All performed dynamic CT, 13 dynamic RNM. Four don't apply for transplant. Nine exceeding Milan and meeting UCSFc, all were downstaged with chemoembolization, 2 were not effective, and 7 were effective. 22/28 were listed: 3 delisted, one for progression, 2 for others contraindications. Five were chemoembolized as bridging therapy. 19/22 were transplanted: 14 within Milan, 5 downstaged. Gender: 21/22 male. Cirrhosis' most frequent etiologies were alcohol and HCV. Age 54 (33-68). MELD 13 (6-22), prioritized to 22 points. Explants: pTNM: T1:32%, T2:36,5%, T3:27%, NoHCC: 4.5%. There were 3 incidental cases: one met Milan and 2 were beyond UCSFc. Of 10/14 were actually in Milan. Of 5 with effective downstaging: 2 were within UCSFc, and 3 beyond UCSFc. Overall analysis: 50% were transplanted within Milan, 14% between Milan and UCSF, 32% beyond UCSFc and 4% were not HCC. 76% were within Up to 7 and 71% had TTD < 10. 2 perioperative deaths unrelated to HCC. Recurrence: 4 post-transplant recurrence: 3 patients exceeded UCSF and one was between Milan and UCSFc. 1 isolated nodular liver lesion and 3 systemic dissemination. Sensitivity/Specificity of imaging: we evaluated accuracy of image techniques regarding, HCC found with ultrasound and number of found/missed lesions for CT and RNM. Ultrasound: sensitivity 83% specificity 95%. CT sensitivity 41.5%, specificity 93%. RNM sensitivity 77%, specificity 95%. **Conclusions.** Our results are comparable to the region, despite there were too many cases exceeding UCSF and T3. Taking account that all these cases were evaluated only with CT and given the low sensibility of this method, it was decided to evaluate all patients with MRI pre transplant in our program.

005

ANTIPHOSPHOLIPID ANTIBODIES: AN UNDER-RECOGNIZED CAUSE OF MORBIDITY AND MORTALITY IN PATIENTS TRANSPLANTED FOR END-STAGE LIVER DISEASE

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Introduction. Antiphospholipid antibodies (aPL-ab) are often detected in liver disease. **Aim.** To establish prevalence of aPL-ab in patients transplanted for cirrhosis and assess their impact in outcome at 1 year post-OLT. **Materials and methods.** Between Jan/2006 and Dec/2010, 150 patients transplanted for cirrhosis were screened for aPL-ab and lupus anticoagulant activity. Clinical and Doppler-ultrasound evaluations were performed before OLT and at different timepoints post-OLT. Results were compared with aPL-ab negative patients. Immunosuppressive regimen: calcineurin inhibitors+ mycophenolate-mofetil + steroids. All patients received aspirin and/or low weight heparin post-OLT. Median follow-up: 26 months (12-56). **Results.** 39/150 patients (24%) evidenced increased levels of aPL-ab pre-OLT. Child C patients had lower prevalence of aPL-ab than Child B (21 *vs.* 32 %, NS). No difference was observed in renal or liver function tests, except for bilirrubin levels which were higher in aPL-ab + patients (5.9 *vs.* 3.6 mg/dL, p = 0.04). Seven thrombotic complications were observed in 6/36 aPL+ patients post-OLT (humeral thrombosis, n = 1, cerebrovascular ischemia n = 3, HAT n = 1, retinal thrombosis = 1, intestinal ischemia n = 1) resulting in one graft loss and one death, compared to nine thrombotic complications in 8/114 patients aPL negative (cerebrovascular ischemia n = 3, deep vein thrombosis n = 2, hepatic artery thrombosis n = 1, intestinal ischemia n=1, humeral thrombosis n=1, femoral thrombosis n = 1) resulting in one graft loss and re-transplantation (p < 0.05). Five patients in the ApL+ group developed catastrophic antiphospholipid syndrome and 4/5 died in spite of plasmapheresis and anticoagulation. No differences were observed between both groups in infection rates, thrombocytopenia, acute cellular rejection or bleeding complications. **Conclusions.** Patients with end-stage liver disease have a high prevalence of aPL antibodies. Their presence is associated with higher risk of morbidity and mortality post-OLT Pre-OLT screening for anticardiolipin and lupus anticoagulant, and a high index of suspicion of ApL associated vascular complications post OLT is recommended to improve outcome.

006

METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: A 5-YEAR RETROSPECTIVE COHORT STUDY

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Background. Liver transplantation is a therapeutic tool for patients with liver cirrhosis; however, it requires the use of immunosuppressants that can lead to metabolic alterations in the post-transplant period. **Objectives.** To identify the prevalence of metabolic syndrome (MS) and of metabolic alterations in patients submitted to orthotopic liver transplantation (OLT), as well as to establish the association between these alterations and calcineurin inhibitors. **Material and methods.** Retrospective cohort study performed by reviewing the records patients subjected to OLT –for different etiologies– at the Santa Casa de Misericordia Hospital Complex of Porto Alegre, in Porto Alegre, Brazil, between 2000 and 2008. Clinical, laboratory and anthropometric parameters were reviewed, both pre-operative (evaluation on the transplant admission day) and post-operative (6 months, first through third and fifth year). Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the International Diabetes Federation (IDF). **Results.** The data from 193 patients, 63.7% male, with an average age of 51.9 + 10.5 years, was evaluated. Over a period of 5 years, 62.7% of the patients presented PTMS. There was a significant increase in the prevalence of systemic arterial hypertension (6.7% pre-transplant *vs.* 57.9% fifth year), hypertriglyceridemia (7.8% pre-transplant *vs.* 34.5% fifth year), obesity (18.7% pre-transplant *vs.* 22.8% fifth year). The use of cyclosporine was associated pre-transplant with prognostic scores (Child-Pugh C-p = 0.022 and MELD > 20-p = 0.018), hyperglycemia (p = 0.035) and MD (p = 0.047)-and post-transplant with hypertriglyceridemia (p = 0.002), hypercholesterolemia (p < 0.001) e CKD (p = 0.031). After adjusting with the Poisson multivariate regression model (PR), age (PR = 1.03-p = 0.001), the use of cyclosporine (PR = 1.26-p = 0.049) and obesity prior to transplantation (PR = 1.35-p = 0.018) remained independently associated with PTMS. **Conclusion.** The prevalence of MS, was greater in the post-liver transplant period when compared to

the data prior to the surgery, highlighting the importance of action directed to the prevention and/or treatment of metabolic complications related to the post-liver transplant period.

007

LIVER TRANSPLANT IN ECUADOR: EARLY EXPERIENCE

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Introduction. There was a highly unmet need for treating end-stage liver diseases in Ecuador, the development of a liver transplant program was necessary. Liver transplantation activity started in 2009 and has been growing progressively over time. We present the report of the first four years of liver transplantation in Ecuador. **Materials and methods.** We performed a retrospective chart review of all patients who underwent liver transplant from December 2009 to April 2014 in the largest transplant center in the country. Demographic features, MELD scores, complications and mortality rate were also included. **Results.** A total number of 71 cadaveric liver transplants were performed over the past four years. The mean age of liver transplant recipient was 50 years old (range, 11-65). From all the liver recipients 55% of them were male and 44.9% were females. The most common cause for liver transplantation was: cryptogenic cirrhosis (30%), followed by autoimmune hepatitis (28.9%), alcoholic liver disease (10%), secondary biliary cirrhosis (7%). The mean MELD score for transplantation was 17 ± 3. Complication included: neurological (27%), vascular (10%) and biliary (7%) as the most common. From all the transplanted patients 76% were still alive to the last follow up and 24% have died. The most common causes of dead were intraoperative bleeding (27%) cardiovascular disease (22%) and sepsis (11%). Interestingly, the intraoperative mortality rate improved over the years, in 2010 was 10.5% and in 2013 to the date intraoperative mortality has dropped to 0%. The retransplant rate was 4,1%. **Conclusions.** This is the report about the situation of liver transplantation in Ecuador. It's clear that as time has progressed our intraoperative mortality rate has dropped significantly, demonstrating that interdisciplinary efforts combined with adequate center support good outcomes can be achieve. These findings suggest that developing a well established liver transplantation center in a limited resource country is feasible.

G. AUTOIMMUNE AND CHOLESTATIC LIVER DISEASE

001

AUTOIMMUNE HEPATITIS IN MEN: DISTINCTIVE CLINICAL PRESENTATION, BIOCHEMICAL FEATURES AND OUTCOME

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Background. Autoimmune hepatitis predominantly affects women. Little is known about presentation and long term prognosis among males. **Aim.** To evaluate clinical features and outcome of male patients with autoimmune hepatitis compared with females. **Material and methods.** We evaluated 245 consecutive patients with diagnosis of AIH between January 2000 and June 2008 (48 men, 197 women). Diagnosis was established according to the recommendations of the International Autoimmune Hepatitis Group. Prognostic factors of "bad evolution" (death or requirement of liver transplantation) among men were evaluated. Mean follow up: 3.2 years (0.4-7.5). **Results.** Compared with females, males have higher frequency of fulminant hepatic failure (14.8 *vs.* 6.3%, $p < 0.05$) and of acute hepatitis as initial presentation (42 *vs.* 27%, $p < 0.05$), and lower overlap with primary biliary cirrhosis (6.57 *vs.* 13.19%, NS). Males presented with lower frequency of "definitive" diagnosis of AIH according to the score of the IAHG (36 *vs.* 63.9%, $p < 0.05$), lower gammaglobulin levels (1.79 ± 0.64 *vs.* 2.23 ± 1.02 g/dL), lower frequency of autoantibodies (67 *vs.* 86%), lower titers of antinuclear antibodies and higher transaminases levels at presentation (398 (48-2980) *vs.* 273 (52-2,740) UI/mL, NS). Mean age at presentation was similar (42 ± 23 *vs.* 44 ± 19 years, NS), though females presented a bimodal distribution (1st-2nd and 4th-5th decades) compared to men (2nd to 4th decades) Women more frequently presented with cirrhosis at initial biopsy (21 *vs.* 8%, $p < 0.01$) and had associated autoimmune conditions (64 *vs.* 17%, $p < 0.01$). Complete response to steroid treatment was lower among males at 3 and 6 months post treatment. A bad evolution was observed in 25% of men (n = 12) and 17% of women (n = 34). Factors associated with bad prognosis were fulminant presentation, no "definitive" diagnosis of AIH, absence of autoantibodies and no steroid response at 3 months of treatment. **Conclusion.** AIH in males compared to females has a distinctive clinical presentation and inmunological profile, with less response to steroid therapy and a worst prognosis.

002

PRIMARY SCLEROSING CHOLANGITIS HAS A SPECIFIC HEMODYNAMIC BEHAVIOUR THAT IS NOT OBSERVED IN OTHER CHOLESTATIC OR HEPATOCELLULAR LIVER DISEASES

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Background. It has been suggested that microcirculatory disturbances in the peribiliary vascular plexus may contribute to ischemia and result in ductal injury in PSC. These disturbances might be associated with hemodynamic changes in the liver vascular flow. **Aim.** To evaluate hemodynamic parameters of hepatic flow measured with Doppler US in patients with PSC in relation with other cholestatic and non-cholestatic diseases. **Material and methods.** Group 1: patients with PSC confirmed by cholangiogram (n = 16), group 2: patients with PBC (antimitochondrial antibody+ and florid bile duct lesions) (n = 20). Group 3: patients with histologically proven PCR-HCV+ chronic hepatitis, naive of antiviral therapy (n=20). Within group 1, hemodynamic parameters were compared between patients with or without cirrhosis. Patients were referred for measurements of hemodynamic parameters by Doppler US (hepatic artery and portal diameter, portal velocity, hepatic artery systolic peak and end of dyastole velocity, suprahepatic velocity). Hepatic artery resistance index was calculated. To avoid observer variations, all cases were evaluated by two blinded operators in two different occasions, with 8 h fasting. Results were averaged. **Results.** No significant

differences were observed between groups in portal diameter, portal or suprahepatic velocity. A larger diameter of the hepatic artery was observed in group 1, but reached no statistical significance (5.1 ± 0.7 mm, 4.4 ± 0.5 mm, 4.6 ± 0.7 mm, p = 0.7). Patients with PSC presented a significant lower hepatic artery resistance index in comparison with patients in group 2 (0.5 ± 0.1 *vs.* 0.9 ± 0.1, p = 0.005) and group 3 (0.5 ± 0.1 *vs.* 0.8 ± 0.1, p = 0.006). Lower intrahepatic resistance in group 1 was mostly dependent of a higher hepatic artery end of dyastole velocity (23.0 ± 8.2, 18.7 ± 8.3, 19.1 ± 9.1 mm/sec, p = NS). Within group 1 all patients with (n = 7) or without cirrhosis (n = 9), presented the same hemodynamic behaviour. In the subgroup with cirrhosis, a lower suprahepatic vein velocity was observed compared to patients with PSC without cirrhosis (34.8 ± 7.3 *vs.* 46.8 ± 6.7 cm/sec, p = 0.006). **Conclusions.** PSC is associated with a specific hemodynamic behaviour characterized by low hepatic artery resistance index that is not observed in other cholestatic or hepatocellular diseases. This finding is not modified by the development of cirrhosis. Phisiopathological relevance of this observation should be further clarified.

H. MISCELLANEOUS

001

MANAGEMENT NUTRITIONAL AND LYSOSOMAL PATIENTS IN COLOMBIA: MANUAL STUDY

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Background. Lysosomal storage diseases are considered orphan disorders, like Niemann-Pick C (NP-C) and Mucopolysaccharidoses type VI (MPS-VI). Little is known about the nutritional status of these diseases, and how nutritional interventions may alter the natural of this disease. Thus, it is of utmost importance to propose adequate nutritional guidelines that enhance health and life quality of these patients. NP-C is considered a quite heterogeneous disorder that affects organs like liver and spleen; and presenting progressive neurological manifestation. MPS-VI has a multisystem involvement that include clinical manifestations like skeletal dysplasia that severely affects linear growth along with other findings like hepatosplenomegaly. Both diseases has liver affectation as well as nutritional affectations. **Aim.** To describe the anthropometrical status of colombian patients with two types of lysosomal diseases: NP-C or MPS-VI, both belonging to MANUAL study (MAnagement NUtritional And, Lysosomal patients). Methods: Observational and descriptive study. Patients were recruited in a nutritional practice. A thorough nutritional assessment was conducted, including anthropometrical assessment. Pediatric patients were classified according to the Growth Standards of the World Health Organization (WHO). Using weight and height, indicators as height for age, weight for height, and body mass index (BMI) for age were created and compared to the WHO standards. Adult patients were assessed on the basis of height and BMI. For patients with height for age below -2DS, weight was also assessed on the basis of bone age (age that corresponds to actual height on the 50thpercentile). **Results.** Thirty-eight patients were recruited. Fifteen NP-C patients with Miglustat therapy were recruited, nine were men. Average age was 11.4 ± 9.4-years-old. Five out of 13 pediatric patients had adequate nutritional status, 15.4% suffered emaciation and 46.2% were stunted, 33.3% of these patients suffered from emaciation too. Emaciation might be even higher in NP-C considering that weight may seem unaffected due to hepatomegaly and splenomegaly; thus, body composition assessment is more reliable. Twenty-three MPS-VI patients with enzyme replacement therapy were recruited; 56.5% were men. The average age was 12.2 ± 4.7-years-old. Average height was 101.5 ± 7.9 cm (range 83-121 cm). Every patient suffered growth retardation (height for age z-score -6.5 ± 2.1), thus the anthropometrical assessment was done using the age according to their height instead of chronological age. 8.7% had adequate weight; 91.3% suffered overweight or obesity. **Conclusion.** Growth retardation is presenting in both diseases. The overweight or obesity is a typical feature in MPS-VI patients, likewise that NP-C patients is usual the adequate nutritional status followed of emaciation.

002

THE VARIANT I148M IN PNPLA3 IS ASSOCIATED WITH THE DEVELOPMENT OF CHOLESTEROL POLYPS IN MEXICAN PATIENTS

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The most common of the non-neoplastic lesion in gallbladder is the cholesterol polyp. These result when the lamina propria is infiltrated with lipid-laden foamy macrophages in a process called cholesterolosis. Adiponutrin encoded by PNPLA3 has been to have both lipolytic and lipogenic properties; the PNPLA3 rs738409 polymorphism has been found to be associated with susceptibility to non-alcoholic fatty liver disease and hepatocellular carcinoma in various cohorts. The aim of this study was to investigate the association of the variant I148M/PNPLA3 in a cohort of Mexican adults with cholesterol polyps. We analyzed a total of 70 biopsy-proven cholesterol polyps patients (F/M = 44/26, average age = 44.2, average BMI = 25.8) and 35 controls (F/M = 10/25, average age = 44, average BMI = 25.9). Samples were genotyped for PNPLA3 gene polymorphism (rs738409 C > G) using TaqMan assays. The biopsy specimens were histologically diagnosed by a qualified pathologist. Anthropometric and demographics data were collected. We observed an association of G allele with the presence of cholesterol polyps (OR 3.61, 95% CI 1.59-8.22, p < 0.005), adjusting in a multivariate logistic regression analysis by sex, gender and body mass index. The frequency of risk allele (GG) in cholesterol polyps patients was 29%. Overall, the rs738409 G allele is associated with the presence of cholesterol polyps. These data suggest that this polymorphism could be playing an important role in cholesterol polyps susceptibility in our population such as occurs with NAFLD. Despite genetics cannot be modifiable, dietary and lifestyle factors modifications could improve the metabolic condition in susceptible subjects avoiding the development of metabolic-related diseases such as cholesterol polyps in gallbladder.

003

TRANSIENT ELASTOGRAPHY (FIBROSCAN): DATA ANALYSIS WITH 4000 STUDIES AT THE ITALIAN HOSPITAL OF BUENOS AIRES, ARGENTINA

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Objectives. To present the characteristics of the studies, their implications on liver biopsy and to assess the association with mortality. **Material and methods.** Data from October 2009 to January 31th was analyzed. Diffuse liver biopsies in patients with hepatitis C virus as well as the available medical records of patients evaluated through 2011 were evaluated to obtain mortality data. **Results.** 4,101 studies were done. Of these studies: 16% were made until 2010, 24% in 2011, 26% in 2012 and 34% in the last period. The percentage of studies demanded by physicians from others hospitals was 14% until 2011, 39% by 2012 and 63% from 2013. Etiologies were hepatitis C (38 %), NAFLD (27%), hepatitis B (21%) and others (14%). 22% of patients had paired liver biopsy and fibroscan until 2011 actually both studies are in 9% of the patients. The failure rate of the study was 4.2% through 2010, 8.3% up to 2011, 12% in 2012 and 14.3 % today. The number of liver biopsies in patients with hepatitis C decreased by 66.5% from 2010 to the present. From 147 patients with hepatitis C who performed fibroscan from 2009 to 2011 mortality data to 2014 was obtained retrospectively. In the group up to 7 kPa (n: 61) 4% died, between 7.1 and 11.9 kPa (n: 51) 3% died, between 12 and 25 kPa (n: 24) 8% died and those with more than 25 kPa (n:11) 24% died. **Conclusions.** The number of annual studies ordered by physicians from others hospitals has been increased progressively. The hepatitis C virus is the main reason for the request but steatosis is an important source of orders. The failure rate increased probably associated with the acceptance of the method and therefore intended to perform the fibroscan in more patients. The number of patients with hepatitis C who are delivered to liver biopsy is progressively going down as happens in other parts of the world. Finally, although a retrospectively small group was analyzed, the higher the result of baseline elastography, the higher the mortality at 2 years.

Ha. DILI

001

EVALUATION OF *LUTEOLIN* IN AN EXPERIMENTAL MODEL OF ACUTE TOXIC HEPATITIS

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Background. Nowadays, there are not many options for treat acute hepatitis, and the few treatments have different side effects in patients. The research of new drugs is always necessary in order to reduce or avoid those effects. Luteolin is an abundant flavonoid in plants worldwide that demonstrates a broad spectrum of biological activities like antioxidant and anti-inflammatory. The aim of this study was to evaluate the pharmacologic effect of Luteolin in an acute toxic hepatitis (ATH) model induced by CCl4 administration. **Material and methods.** Thirty-two male Wistar rats (150 g) were divided into 4 groups (n = 8): 1. Control: PBS 0.5 mL i.p. 3-times per week for 1-week; 2. Luteolin: 50 mg/kg oral 3-times per week during 1-week; 3. ATH: CCl4 4.0 g/kg oral once per week for 1-week; 4. ATH + Luteolin: doses mentioned above. At the end of experimental protocol, rats were sacrificed using CO2 chamber. Serum ALT, GGT and liver MDA were analyzed by a spectrophotometric method. Three-micron-thick sections of the liver were stained with H&E for morphologic analysis. **Results.** ATH had an increase in serum ALT (6.2-fold), GGT (10.1-fold) and hepatic MDA 5.7-fold), alterations in parenquima (necrosis, macro/microvesicular steatosis) and portal structures with inflammatory cells were observed, all compared with control group ($p < 0.05$). Rats with ATH treated with Luteolin had a reduction of serum ALT (39.0%), GGT (45.7%) and hepatic MDA (33.4%); morphologic analysis showed a reduction in portal structures alterations, a reduction in necrosis and macrovesicular steatosis. It was observed a lower presence of inflammatory cells, all compared with ATH group. No statistical difference was observed between control group and Luteolin group, no changes were observed in parenquima and portal structures in Luteolin group (Table). **Conclusions.** The treatment with Luteolin reduced liver necrosis and inflammatory cells by reduction of oxidative stress, resulting in a decrease of acute toxic hepatitis.

Table. (001).

ALT (UI/L)	GGT (UI/L)		MDA (nmol/mg protein)
Control	60.24	4.47	40.83
Luteolin	75.68	3.22	37.77
ATH	373.47*	45.15*	232.73*
ATH + Luteolin	227.83*,**	24.83*,**	155.93*,**

Two different experiments run in triplicate. *$p < 0.05$ compared with control group. **$p < 0.05$ compared with ATH group.

002

HEPATOTOXICITY DUE TO HERBALS AND DIETARY SUPPLEMENT (HDS) PRODUCTS: A GROWING CONCERN

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Introduction. HDS products including androgenic anabolic steroids (AAS) is a growing cause of drug-induced liver injury (DILI). We aimed to determine HDS-DILI incidence and the phenotype and outcome of AAS hepatotoxicity. **Material and methods.** AAS-induced DILI cases included in the Spanish and Latin-American DILI Registry were analyzed for demographic, clinical-biochemical parameters and outcome. **Results.** Sixty-four out of 1023 DILI cases included in the registry over 20 years were attributed to HDS, 25 (39%) by AAS and 39 (61%) by other HDS. Eighty percent (20/25) of the AAS and 41% (16/39) of the other HDS cases were identified in the last 4 years. All AAS cases were male with a mean age of 32 years (range: 20-49). Classified into type of liver injury (60% hepatocellular and 40% cholestatic), the main causative agents were stanozolol in both groups followed by methylepitiostanol. The mean peak total bilirubin (TBL) value in the hepatocellular group was 21 x ULN (range: 2-37) and 32 x ULN (range: 6-54) in the cholestatic group ($p = 0.029$). Six patients with cholestatic injury and high TBL values (22-54 x ULN) developed acute renal impairment (AKI) with serum creatinine 1.6-8.50 mg/dL. A TBL value > 21.5 x ULN was found to be associated with AKI (serum creatinine ≥ 1.5 mg/dL) (AUROC: 0.87, sensitivity: 100% and specificity: 63%) in cases with cholestatic damage. **Conclusions.** HDS use is a rapidly growing cause of DILI and represents a major health concern. AAS-induced liver injury presents a characteristic phenotype in which hepatocellular damage with high TBL values predominates. Cholestatic damage and high TBL values increase the risk of renal impairment during AAS hepatotoxicity.

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INFLUENCE OF BODY MASS INDEX AND METABOLIC RISK FACTORS ON THE PHENOTYPE AND CLINICAL EXPRESSION OF DRUG INDUCED LIVER INJURY

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Introduction. Drug-induced liver injury (DILI) is a complex condition, with undefined underlying mechanisms, believed to be affected by drug properties, genetic variations and environmental factors. It has been suggested that excess weight and metabolic risk factors (MRFs) may play a role in DILI presentation. Hence, the aim of this study was to determine the influence of body mass index (BMI), diabetes, hypertension and dyslipidemia in the clinical profile of DILI. **Material and methods.** All DILI patients enrolled in the Spanish Dili Registry until December 2013 were analysed. The study inclusion criteria were available information on BMI, absence of previous hepatic disease and no history of high alcohol consumption (≥ 30 g/day male or ≥ 20 g/day female). Clinical presentations were compared between patient groups classified by presence or absence of MRFs (diabetes, hypertension and dyslipidemia) and BMI (< 25 or ≥ 25). Hypersensitivity features (HPS) included rash, fever, eosinophilia, lymphopenia and arthralgia. Autoantibodies included antinuclear, anti-smooth muscle, anti-mitochondrial and liver kidney microsomal type 1 autoantibodies. **Results.** 457 patients (51% females) fulfilled the inclusion criteria. 53% of the patients were ≥ 55 years old. Anti-infectives were the main causative drug group (39%). The total incidence of overweight and obesity (BMI ≥ 25), diabetes, hypertension and dyslipidemia were 56.7, 11.4, 20.8 y 16.0%, respectively. The presence of positive autoantibodies ($p = 0.003$) and HPS ($p = 0.03$) differed significantly between the analysed groups. Positive autoantibody titres were significantly more frequent in patients with MRFs (30 *vs.* 14%, $p = 0.003$), while hypersensitivity features were significantly more common in overweight and obesity DILI patients (48 *vs.* 35%, $p = 0.030$). In view of these results, the presence of autoantibodies were examined in DILI patients with any of the three MRFs. Presence of autoantibodies was significantly associated with dyslipidemia ($p = 0.039$) and hypertension ($p = 0.002$), in particularly positive antinuclear antibody titres ($p = 0.001$ and $p = 0.007$, respectively). Furthermore, the presence of autoantibodies was significantly associated with age ≥ 55 years ($p < 0.001$) independently of the presence or absence of MRFs. HPS were found to be associated with overweight and obesity ($p = 0.010$), particularly lymphopenia ($p = 0.028$). **Conclusions.** BMI and other MRFs appear to be related with the presentation of different clinical profiles in DILI. The presence of dyslipidemia, hypertension and age ≥ 55 years could be factors favoring an immunological response in DILI.

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