Methods: This randomized controlled trial included 141 HCV who received double dose (40ug) or standard dose (20ug) and 70 healthy volunteers who received standard dose (20ug) at 0, 1 and 6 months. Anti-HBs titers were measured at 1 month after last dose. Vaccine response was defined by anti-HBs ≥10 U/L. Non-responders received the fourth dose according to the group that were previously randomized. Multivariate regression was modeled as a logistic regression.

Results: 128 completed the study. Median age 51 years, 61% female, 52% White, 40% F2-3, and 75% GT1, median 6 log10 HCV RNA. Overall seroconversion rate was 76.7% (n=60) in double dose and 73.5% (n=68) in standard dose, compared to 91.2% in controls (n=68). 23 patients received the fourth dose; 7 seroconverted (30.4%) and seroconversion rate for double and standard doses were 42.9% and 11.1%, respectively (p=0.18). Controlling for confounders, only older age (p<0.001) and GT1 (p=0.005) were associated with a decreased anti-HBs response.

Conclusion: In HCV-infected patients without cirrhosis, responses to HBV vaccination are significantly impaired and this reduced response cannot be overcome by the use double dose. Besides that, 4th dose HBV vaccination can be a strategy efficacious this vulnerable population.

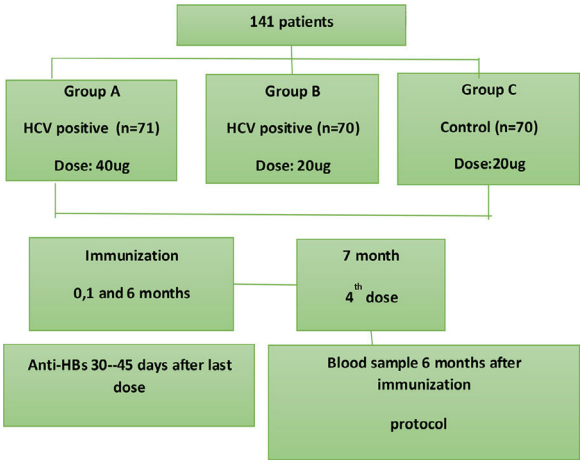

Figure 1- A randomized study comparing two doses of anti-HBV vaccination.

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O-19 INCIDENCE, PATTERN OF PRESENTATION AND RISK FACTORS FOR HEPATOCELLULAR CARCINOMA AFTER DIRECT ACTING ANTIVIRAL TREATMENT IN PATIENTS WITH HEPATITIS C VIRUS CIRRHOSIS

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Background: Brazilian public health system currently provides universal free all oral direct-acting antiviral (DAA) therapy for patients with hepatitis C virus (HCV) infection. Despite high rates of sustained virological response (SVR), patients with cirrhosis remain at risk for hepatocellular carcinoma (HCC).

Objectives: The aim of this study was to investigate incidence, risk factors and tumor pattern at presentation in a cohort of Brazilian HCV-related cirrhotic patients treated with DAAs.

Methods: This prospective cohort study included patients with HCV-related cirrhosis treated with DAAs and followed for at least 24 weeks after therapy at the Viral Hepatitis Outpatient Clinic of Hospital de Clinicas de Porto Alegre, Brazil, between August 2016 and November 2017. Ultrasound screening was performed within 24 weeks before DAA therapy and patients with presumed past or current HCC were excluded. Primary outcome was HCC incidence. Secondary outcomes were risk factors for HCC ocurrence and tumor pattern at presentation. Multivariate analysis was used to identify independent variables associated with HCC development.

Results: A total of 234 patients with HCV cirrhosis were included. Fifty-six percent were males with a mean age of 61.2±10.9 years. Overall SVR was 97.4%. Child-Turcotte-Pugh (CTP) A, B and C at baseline was found, respectively, in 89.3%, 9.4% and 1,3%. Mean Model for End Stage Liver Disease (MELD) score was 9.17 ± 2.82. Esophageal varices were found in 43.6% of the patients. Type 2 diabetes was present in 18.8%. *De novo* HCC was diagnosed in 9% (21/234) of the patients during follow-up. Tumor pattern at presentation according to BCLC staging was 0, A, B, C and D in 19,1%, 47.6%, 4.8%, 28.6% and 0%, respectively. Multivariate analysis showed significant relative risk (RR) for HCC occurrence associated with the following variables: baseline MELD score ≥10 (RR: 1.8; p=0.05); absence of SVR (RR: 6.9; p=0.04); baseline platelet count <120 × 10^9/L (RR: 5.0; p=0.04) and baseline albumin level <3.5 mg/dL (RR: 4.6.

Conclusions: A high incidence of HCC was found after DAA therapy compared to the literature, particularly among patients with more advanced cirrhosis, particularly those with baseline albumin levels < 3.5 g/dL plus platelets < 120 × 10^9/L. Absence of SVR was also significantly associated with HCC development. The majority of patients presented with very early (BCLC 0) or early (BCLC A) HCC, although a significant proportion showed advanced stage (BCLC C) at presentation.

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O-20 ASSOCIATION BETWEEN UNCOUPLING PROTEIN 3 POLYMORPHISMS AND NONALCOHOLIC FATTY LIVER DISEASE AND METABOLIC SYNDROME

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Introduction: Genetic variants in the uncoupling protein 3 (*UCP3*) gene have been associated with obesity, type 2 diabetes and atherogenic lipid profile, with conflicting results.

Objective: Our study evaluated the possible association between *UCP3* single nucleotide polymorphisms (SNPs) with nonalcoholic steatohepatitis (NASH) and metabolic syndrome (MetS) in NAFLD patients.

Methods: *UCP3* SNPs rs1726745, rs3781907 and rs11235972 were genotyped in 158 biopsy-proven NAFLD patients. Patients were evaluated according to the presence of nonalcoholic fatty liver (NAFL) or NASH and, according to the absence or presence of MetS. Statistics were performed with JMP, R and SHEsis software's.

Results: The TT genotype of rs1726745 was protective for MetS (OR=0.18; 95% CI=0.05-0.61; p=0.006) and was associated with lower body mass index (BMI) in the general sample (p=0.01) and in the NASH group (p=0.02). The rs1726745-T was associated with lower values of AST (p=0.001), ALT (p=0.0002), triglycerides (p=0.01) and total cholesterol (p=0.02) in the general sample. There were lower values of aminotransferases strictly in individuals with NASH (AST, p=0.002; ALT, p=0.0007) and with MetS (AST, p=0.002; ALT, p=0.001). The rs3781907-G was associated with lower GGT values (p=0.002) in the general sample and in the NASH group (p=0.004) and with MetS group (p=0.003) and, with protection for advanced fibrosis (OR=0.25; 95% CI=0.08-0.69; p=0.01).The rs11235972-A was associated with lower GGT values (p=0.006) in the general sample and in the NASH group (p=0.01) and with MetS group (p=0.005), with fibrosis absence (OR=0.34; 95% CI=0.14-0.80; p=0.01) and protection for advanced fibrosis (OR=0.17; 95% CI=0.03-0.56; p=0.01). The TAA haplotype was protective for NASH (OR=0.01; 95% CI=0.00-0.12; p=0.002) and TGG haplotype was protective for MetS (OR=0.22; 95% CI=0.07-0.69; p=0.01).

Conclusion: *UCP3* variants were associated with protection against NASH and MetS, in addition to lower values of liver enzymes, lipid profile, BMI and, lesser fibrosis severity in the studied population.

Table 1
Genotype frequencies of *UCP3* polymorphisms according to the presence of metabolic syndrome

UCP3 SNPs 5'->3'	With MetS	Without MetS	OR (CI 95%)	*P value*
rs11235972			-**	0.99
GG	0.706	0.815		
GA	0.254	0.185		
AA	0.040	0.000		
MAF	0.167	0.092		
rs3781907			0.51 (0.05 – 3.88)	0.52
AA	0.609	0.556		
AG	0.313	0.333		
GG	0.078	0.111		
MAF	0.234	0.277		
rs1726745			0.18 (0.05 – 0.61)	0.006*
CC	0.323	0.231		
CT	0.472	0.346		
TT	0.205	0.423		
MAF	0.441	0.596		

OR (odds ratio) for the minor allele in a recessive model obtained in logistic regression analysis adjusted for sex, age, type 2 diabetes mellitus and dyslipidemia. *$P \leq 0.02$.
**OR [2428148 (9.9×1015 – -)]: due the AA genotype absence among Without MetS individuals, it was not possible to calculate precisely the OR.
MAF, minor allele frequency; MetS, metabolic syndrome; SNPs, single nucleotide polymorphisms; *UCP3*, uncoupling protein 3 gene.

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O-21 SOLUBLE CD163 PERFORMANCE AS A NON-INVASIVE BIOMARKER OF DIFFERENT LIVER CONDITIONS

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Introduction: Development of noninvasive tests to predict liver injury represents a current goal. Soluble CD163 (sCD163) is a specific plasma biomarker of macrophage activation with promising clinical relevance in estimating damage severity and predicting the outcome in different liver conditions.

Aim: To evaluate sCD163 performance as a non-invasive marker of liver damage.

Materials and Methods: sCD163 was quantified by enzyme-linked-immunosorbent assay in plasma from 123 patients (57 HCV, 20 HCV/HIV, 10 HBV, 36 MAFLD) obtained at time of liver biopsy. 20 healthy donors were included as controls. sCD163 values were compared among disease conditions and related to histological parameters of liver damage. Diagnostic performance was assessed by the area under the receiver operating characteristic curves (AUROC).

Results: Patients' sCD163 levels [0.579g/L (0.034 -3.596)] were higher than controls' [0.221g/L (0.116-0.549)] ($p<0.0001$, Mann-Whitney). However, in a detailed analysis according to disease etiology, only viral conditions showed significantly higher sCD163 levels [HCV+ 0.7520g/L (0.168-3.468), $p<0.0001$; HCV+/HIV+ 0.964g/L (0.345-3.596), $p<0.0001$; HBV+ 0.526g/L (0.199-0.802), $p=0.0375$, Dunn's-multiple-comparisons]. MAFLD patients displayed similar sCD163 levels to the control group [0.345g/L (0.0338-1.804)]. HCV mono- and HIV-coinfected patients shared the highest sCD163 levels. In relation to liver injury, HCV+ and HCV+/HIV+ patients specifically displayed a profile with higher sCD163 levels associated with more severe hepatitis. Remarkably, just in HCV+/HIV+ cases these differences were significant ($p=0.0097$ Mann-Whitney) and the AUROC analysis demonstrated a good performance in predicting hepatitis severity [AUROC=0.875; cutoff: 0.672g/L (91.67% sensitivity, 83.33% specificity)]. Concerning fibrosis, only HCV+ and HCV+/HIV+ patients with significant fibrosis displayed a profile with high sCD163 level; however, the AUROC analysis showed good performance just for HCV +/HIV+ patients [AUROC=0.825); cutoff: 0.9640g/L (100% sensitivity, 60% specificity)].

Conclusion: Plasmatic sCD163 is elevated in patients with several liver conditions but it can be particularly used as a marker of liver inflammation and fibrosis in HCV/HIV co-infected patients.

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