Introduction and Objectives: Chronic infection with hepatitis C virus (HCV) still affects millions of people around the world despite the recent development of very effective direct-acting antiviral (DAA) treatment. Even after a high cure rate, patients with advanced fibrosis should remain under surveillance due to the high risk of developing hepatocellular carcinoma. This study aimed to evaluate the prevalence and risk factors for hepatocellular carcinoma development in previously treated chronic HCV patients in an outpatient hepatology clinic at Clinic Hospital of the University of São Paulo of School Medicine in the city of São Paulo.

Materials and Methods: This is a retrospective, observational and descriptive study of a series of cases in which 410 HCV patients were treated with three different antiviral regiments: Interferon plus Ribavirin (INF + RBV) or Protease Inhibitors (PI) or DAA, were followed for up to ten years (2011-2021). Demographic, clinical and laboratory data were obtained for electronic medical records.

Results: the total sample of this study consists of 402 patients. Table 1 shows the patient demographic and clinical data. Of the 35 patients who developed HCC, 26 (74%) had F4-degree fibrosis. Logistic regression model was performed with the following variables: BMI (p=0.005), positive anti-HBC IgG (p=0.015), combination fibrosis and CHIILD-PUGH score A (p=0.001), B (p=0.012) and C(p< 0.001).

Conclusions: In our cohort, obesity and anti-HBc IgG were significantly associated with a high risk of developing HCC. The type of antiviral treatment (IFN or DAA-based) was not associated with the risk of HCC.

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P- 43 PIRFENIDONE PREVENTS NEOPLASTIC LESIONS DEVELOPMENT BY OXIDATIVE, FIBROGENIC, ANTIPROLIFERATIVE AND EPIGENETIC MECHANISMS REGULATION IN A MODEL OF CHEMICAL HEPATOCARCINOGENESIS

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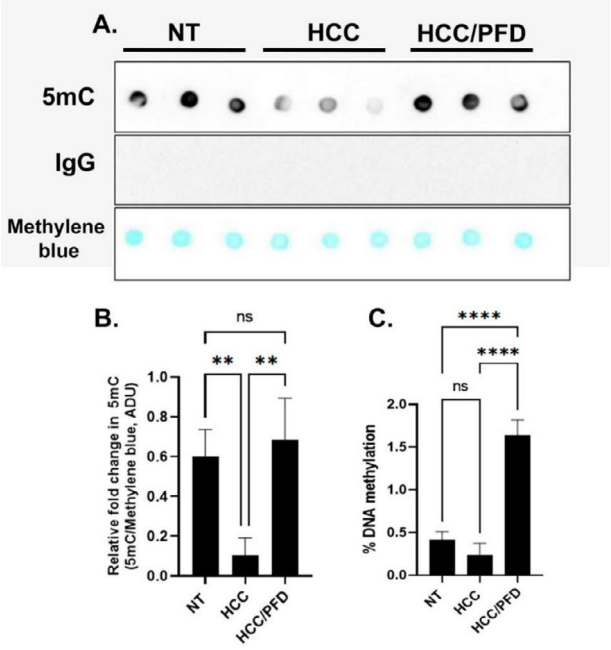
Introduction and Objectives: Hepatocellular carcinoma (HCC) is the most frequent hepatic neoplasia, where oxidative, fibrogenic, proliferative, and epigenetic processes are altered. Pirfenidone (PFD) has been shown to have important hepatoprotective properties. However, its efficacy in HCC development is unknown. This study aimed to 1) To determine whether PFD has antioxidative, antifibrogenic and antiproliferative effects. 2) To determine PFD effects on epigenetic regulation mechanisms.

Materials and Methods: Male Fischer-344 rats were divided into three groups. Group 1. Control, NT; Group 2. Damage, HCC, generated by diethylnitrosamine weekly administration; (50mg/kg, i.p.) and 2-acetylaminofluorene (25mg/kg, p.o.) for 12 weeks; and Group 3. HCC/PFD: with the same treatment as Group 2, plus PFD (300 mg/kg, p.o./day). Liver enzyme activity was quantified in serum; lipoperoxidation and GSH levels were evaluated in liver tissue samples; histopathological analyzes were performed. In addition, fibrogenic, antioxidant, anti-proliferative and epigenetic regulation markers were determined by Western blot. Finally, global DNA methylation was determined by Dot-blot and ELISA. The data obtained were analyzed using one-way ANOVA and a Tukey post hoc test.

Results: We demonstrate that PFD treatment reduces the number and size of neoplastic lesions, prevents damage to hepatic architecture and collagen deposition, and decreases the presence of the histopathological marker Glypican-3. On the other hand, it positively regulates antioxidant markers such as GSH, MDA, Nrf2, GSTP1 and Catalase. It was also effective to decrease c-Myc expression and β-catenin redistribution from the nucleus to the cytoplasm. Finally, PFD stimulated the nuclear transfer of several isoforms of PPARs, SIRT1 and DNMT1, increasing epigenetic mechanisms of global DNA methylation (figure 1).

Conclusions: PFD prevents neoplastic lesions development by modulating antifibrogenic, antioxidant, and antiproliferative processes and modulating epigenetic marks to reverse global DNA hypomethylation.

Figure 1. Analysis of global DNA methylation. A) Representative dot blot using anti-5mC which recognizes global methylated DNA, anti-IgG as negative control and methylene blue staining as total DNA loading control. B) Graphs shows mean ± standard deviation of 5mC densitometry brand intensity of study groups. C) Graph that represents the percentage of global methylation of the DNA analyzed with ELISA.A one-way ANOVA statistical test and a Tukey post hoc test were performed. Group NT: only received vehicle; Group HCC: damage group induced by weekly administration of DEN and 2-AAF for 12 weeks; and Group HCC/PFD: which received the same treatment as Group HCC, plus PFD (300 mg/kg) (**p<0.005)



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P- 44 HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS IN A PARAGUAYAN LIVER REFERENCE CENTER: CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS

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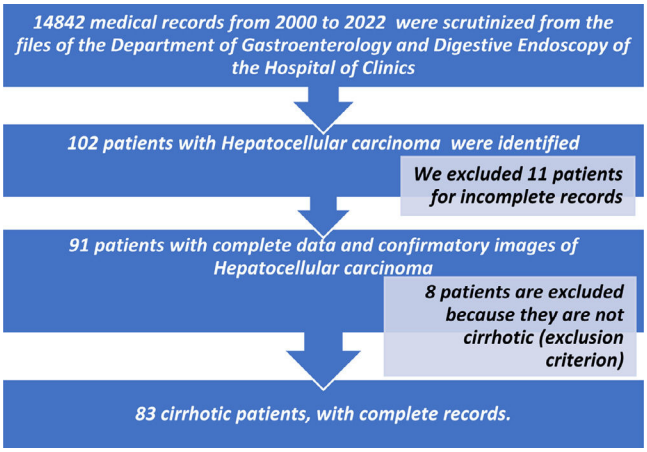
Introduction and Objectives: Hepatocellular carcinoma (HCC) is a disease with an important variability according to the geographic location; worldwide is the second cause of cancer-related death. It is most frequently associated with VHB, VHC and alcoholism. Paraguay is a low-incidence country, but it is still an important cause of morbimortality, especially in cirrhotic patients. This study aimed to establish the epidemiologic and clinical characteristics of cirrhotic patients with hepatocellular carcinoma, as well as the staging, the characteristics of the tumor and the treatment received.

Materials and Methods: Observational, descriptive, retrospective study. We used and Excel spreadsheet to gather data. The variables were expressed in frequency, mean and percentage. *Graphic 1.*

Results: 83 patients were included, and 40% of them were diagnosed in the last four years. 83% were males; the average age was 63 years, range 38 to 82. The etiology of cirrhosis was alcoholism in 34 cases, nonalcoholic fatty liver disease in 15, cryptogenic in 13, VHB in 13, VHC in 4, autoimmune, PSC, PBC and hemochromatosis in 1 each. In 28% of cases, the diagnosis was first suspected by screening ultrasound. 60% of diagnosed cases were outside the Milan criteria. There was a solitary lesion in 59% of patients. Only 24% of the principal nodule was smaller than 3 cm. 2 patients were diagnosed at a very early stage according to the BCLC staging system (0); 31 in stage A; 16 in stage B, 20 in stage C and 14 in stage D. 49% received treatment, being the most frequent chemoembolization (17 cases).

Conclusions: This Paraguayan study of hepatocellular carcinoma shows that although HCC has been much more frequently seen in the last years, a low percentage of HCC are diagnosed at an early stage or as the result of routine screening and that half of the patients do not receive treatment.



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P- 45 ENDOSCOPIC ULTRASOUND SHEAR-WAVE ELASTOGRAPHY OF THE RIGHT AND LEFT HEPATIC LOBE PREDICTS LIVER CIRRHOSIS: A DIAGNOSTIC TRIAL

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Introduction and Objectives: The diagnostic work-up of chronic liver disease includes less invasive procedures such as transient elastography (TE), abdominal ultrasonography, esophagogastroduodenoscopy, and more invasive procedures, mainly portal gradient pressure measurement and liver biopsy. Endoscopic ultrasound (EUS) recently included shear-wave elastography (tissue elasticity), defined as the elastic modulus by measuring shear-wave velocity. This study aimed to evaluate EUS shear-wave of the liver to predict liver cirrhosis.

Materials and Methods: a single-center, diagnostic cohort study. Consecutive patients with a history of chronic liver disease were evaluated with an EUS shear-wave elastography of the right and left hepatic lobes. Patients without any medical condition history despite subepithelial lesions were included as a control. A TE was performed to study and control patients to correlate with elastography. We calculated the overall accuracy of EUS shear-wave elastography of the liver in the prediction of liver cirrhosis.

Results: Among the 28 patients included, 14 had liver cirrhosis. Baseline data is described in table 1. EUS shear-wave elastography of the right hepatic lobe has a direct, proportional and significant correlation (r=0.693 [95% CI 0.431 – 0.847; P<0.001]) as well as left hepatic lobe (r=0.460 [95% CI 0.105 – 0.711; P =0.014]). EUS shear-wave of the right and left hepatic lobe reached an area under the receiver operating characteristics curve (AUROC) of 0.98 and 0.96, respectively. For identifying patients with cirrhosis, EUS shear-wave elastography of the right hepatic lobe with a cut-off value of ≥10.7 kPa had a sensitivity, specificity, PPV, and NPV of 100%, 93%, 93%, 100%, respectively. In the left hepatic lobe using a cut-off value of ≥14.0 kPa, EUS shear-wave had a sensitivity, specificity, PPV, and NPV of 93%, 93%, 93%, and 93%, respectively.

Conclusions: EUS shear-wave of the liver accurately diagnoses patients with liver cirrhosis. EUS shear-wave of the right and left hepatic lobe correlates with TE measurements of the liver.

Table 1. Baseline characteristics of the patients included in the study.

	Overall (n=28)	Cirrhosis (n=14)	Controls (n=14)	P-value
Age (years), n (%)	65.5 (35 – 84)	65 (50 – 84)	66 (35 – 78)	0.5035[a]
Young adults (18-39 y/o)	5 (17.9)	-	5 (35.7)	
Adult (40-64 y/o)	9 (32.1)	8 (57.1)	1 (7.1)	
Elder (≥65 y/o)	14 (50.0)	6 (42.9)	8 (57.1)	
Gender (female), n (%)	18 (64.3)	8 (57.1)	10 (71.4)	0.6933[b]
BMI (kg/m^2), n (%)				0.7793[b]
Underweight	1 (3.6)	-	1 (7.1)	
Normal weight	8 (28.6)	4 (28.6)	4 (28.6)	
Overweight	11 (39.3)	6 (42.9)	5 (35.7)	
Obese class I	8 (28.6)	4 (28.6)	4 (28.6)	
Cirrhosis cause, n (%)				n/a
NASH	-	7 (50.0)	-	
Alcohol	-	5 (35.7)	-	
Med-related	-	1 (7.1)	-	
Cryptogenic	-	1 (7.1)	-	
Child-Pugh, n (%)				n/a
A	-	13 (92.9)	-	
B	-	1 (7.1)	-	
MELD score, n (%)	-	8.8 (6.4 – 17.4)	-	n/a
0 – 9	-	7 (50.0)	-	
10 – 19	-	7 (50.0)	-	
>19	-	-	-	
TE (kPa), n (%)				0.4038[b]
F0-1 (0 – 7.6)	16 (57.1)	2 (14.3)	14 (100.0)	
F2 (7.7 – 9.4)	2 (7.1)	2 (14.3)	-	
F3 (9.4 – 14.0)	2 (7.1)	2 (14.3)	-	
F4 (>14.0)	8 (28.6)	8 (57.1)	-	

BMI, body mass index; **y/o**, years old; **AST**, aspartate transaminase; **ALT**: alanine transaminase, **MELD**, Model for End-Stage Liver