infiltration of immune cells that activate collagen-producing hepatic stellate cells (HSCs), leading to excessive ECM production, and causing uncontrolled scarring. Maresin1 is a derivative of -3 docosahexaenoic acid (DHA), which has been shown to have pro-resolving and anti-inflammatory effects in various organs like those observed for DHA. This study aimed Mar1+DHA supplementation would prevent the development of fibrosis and promote regeneration in an animal model of chronic liver damage.

Materials and Methods: FH was induced in Sprague-Dawley rats by injections of diethylnitrosamine (DEN, 50 mg/kg) and treated with MaR1 (4ng/g) and/or DHA (375 mg/kg) for five weeks. Transaminases, liver histology, and proteins were analyzed by western blot.

Results: the DHA+ MaR1 group showed a greater positive response (significant) than MaR1 in terms of normalization of AST and ALT levels, and architecture of the liver. Reducing inflammation and necrosis. Furthermore, both MaR1 and DHA reduced the levels of TGF-, its receptor TGFRII, and TIMP1, increasing MMP1. Results that coincide with the quantification of type I collagen fibers in tissue. On the other hand, they would promote liver regeneration by increasing Cyclin D1.

Conclusions: Both MaR1 and MaR1/DHA improve regeneration and DEN-induced liver fibrosis parameters, promoting regeneration and acting as an antifibrotic agent. Results that open the possibility that MaR1/DHA are potential therapeutic agents in fibrosis and other liver pathologies.

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O-16 DIFFERENCES IN HEPATOCARCINOMA IN PATIENTS WITH CIRRHOSIS DUE TO NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) VS. OTHER ETIOLOGIES

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Introduction and Objectives: Non-alcoholic fatty liver disease (NAFLD) is the fastest growing cause of hepatocarcinoma (HCC) in the USA and parts of Europe and is expected to increase exponentially in parallel with the global obesity epidemic. This study aimed to determine the differences in the characteristics of HCC in patients with NASH vs. other etiologies.

Materials and Methods: Observational, descriptive study of patients with a diagnosis of HCC presented to the HCC Committee and included in the local Research Registry between March and December 2022. Demographic, clinical and tumor variables at HCC diagnosis were collected. Survival was assessed based on death certificates. Chi2 was calculated considering $p<0.05$ significant.

Results: During the study period, 143 patients were presented to the HCC Committee; 109 of them fulfilled the criteria for this study, 66 with NAFLD etiology (61%) and 43 with cirrhosis due to other etiologies (39%). When comparing sociodemographic and clinical variables in relation to cirrhosis etiology, higher average age (67 vs. 63; p=0.027), lower frequency of men (51% vs. 73%, p=0.026), lower Child-Pugh (Child-Pugh A 55% vs. 40%, p=0.033) and lower average Meld-Na (10.5 vs. 12, p=0.075) were observed in the NAFLD groups vs. other etiologies. No differences were observed in laboratory analysis at HCC diagnosis. There were also no differences in tumor characteristics or recommended therapies. Survival was higher in the NAFLD group, although it was not significant (76% vs. 65%, p=0.228).

Conclusions: HCC in patients with NAFLD cirrhosis occurs more frequently in women, older patients and with better overall probably related to the severity of the chronic liver disease. No differences were observed in tumor characteristics or suggested treatment options, with loco-regional therapy being the most indicated (45% of all patients).

	Total N = 109 (%)	NAFLD N = 66 (%)	Other etiologies N = 43 (%)	P value
HCC characteristics				
N° of lesions Single Multiple	 53 (49) 56 (51)	 32 (48) 34 (52)	 21 (49) 22 (51)	 0.971
Size of the largest lesion (mm)	37 (11 – 170)	36 (11 – 140)	45 (11 – 170)	0.267
Sum of lesions size (mm)	51 (11 – 190)	51 (12 – 190)	50 (11 – 175)	0.857
Portal vein involvement	16 (15)	6 (9)	10 (23)	0.053
Extrahepatic disease	5 (5)	4 (6)	2 (5)	1
HCC treatment suggestion				
Loco-regional therapy Surgery Liver transplant Systemic chemotherapy Palliative care Image and clinical follow-up	49 (45) 16 (15) 19 (17) 14 (13) 5 (5) 6 (6)	32 (48) 9 (14) 11 (17) 7 (11) 3 (5) 4 (6)	17 (40) 7 (16) 8 (19) 7 (16) 2 (5) 2 (5)	0.432 0.784 0.801 0.397 1 1
Survival				
Mortality	31 (28)	16 (24)	15 (35)	0.228

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O-17 NUTRICIONAL AND PHYSICAL THERAPHY IMPROVES LIVER FRAILTY INDEX IN LISTED PATIENTS WITH CIRRHOSIS: RANDOMIZED CONTROLLED TRIAL. INTERIM ANALYSIS

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Introduction and Objectives: Frailty is independently associated with a lower survival in cirrhotic patients. Liver Frailty Index (LFI) determine frailty in listed patients predicting survival. This study aimed to evaluate the effect of a physical and nutritional therapy (intervention group) over LFI compared with a physical and nutritional counseling (control group).

Materials and Methods: Patients were recruited and randomized to an intervention group or a control group. Patients were followed for 12 weeks with evaluations every 4 weeks. We compared LFI and LFI at different time points between both groups during the follow-up.

Results: 46 patients were recruited, 27 of them in control group and 19 of them in the intervention group. 50% were women and the most common etiologies were metabolic associated fatty liver disease (37%) and alcoholic liver disease (19.6%), primary biliary cholangitis (6.52%), autoimmune hepatitis (6.52%) and hepatitis C virus (2.17%).

The median (IQR) age was 60 years (53-63 years), MELD-Na 17 (15-21), creatinine 0.75 mg/dl (0.6-0.8) albumin 3.1 g/dl (2.9-3.1), INR 1.54 (1.4-1.75) and bilirubin 2.6 mg/dl (1.4-1.7). Child-Pugh scores were A/B/C 13%/58.7%/28.3% respectively. No differences in baseline characteristics were found between the groups. Notably, there was a significant improvement in LFI (median; IQR) in the intervention group (Figure 1) after 8 weeks LFI 3.74 (3.37-3.97) with LFI -0.86 vs. control group LFI 4.15 (3.94-4.23) with LFI -0.02, p=0.007) and after 12 weeks (intervention group 3.73 (3.31-4.11) with LFI -0.87 vs. control group LFI 4.14 (4.06-4.50) with LFI -0.03, p=0.023).

Conclusions: In this interim analysis nutritional and physical therapy improves LFI. This is the first randomized controlled trial with positive results in listed patients with cirrhosis.

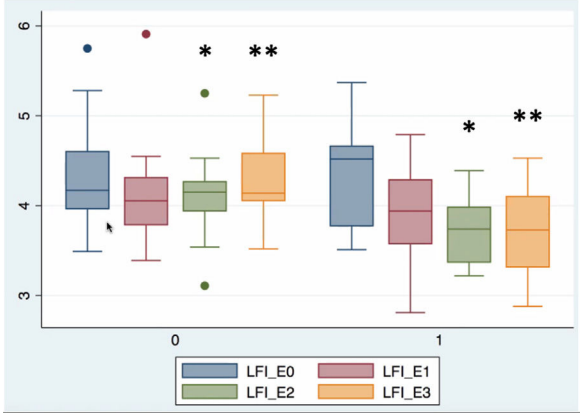

Figure 1. LFI of control group (0) and intervention group (1). LFI_E0: Baseline LFI; LFI_E1: LFI after 4 weeks; LFI_E2: LFI after 8 weeks. LFI_E3: LFI after 12 weeks.

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O-18 DIFFERENCES IN BODY COMPOSITION OF MAFLD PATIENTS ACCORDING TO BODY MASS INDEX AND METABOLIC PROFILE

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Introduction and Objectives: Body composition (BC) has been linked to liver steatosis. The aim of this study is to describe differences in BC in MAFLD patients.

Materials and Methods: Liver steatosis was evaluated by controlled attenuation parameter, patients were classified according to body mass index (BMI) and definitions of MAFLD in five groups: G1: <25kg/m2-non-MAFLD; G2: <25kg/m2-MAFLD; G3: 25-30kg/m2-MAFLD; G4:>30kg/m2-MAFLD and metabolically healthy (<3 metabolic abnormalities) (MH) and G5: >30kg/m2-MAFLD and metabolically unhealthy (MU). BC was assessed by bioelectrical impedance obtaining measurements of resistance; reactance; phase angle; percentages of fat; total body water (TBW%); intracellular and extracellular water (ICW%, ECW%) and skeletal muscle mass (SMM%). Differences in BC was analyzed by Kruskall-Wallis test. Continuous data showed as median and IQR.

Results: 140 patients were included (G1 n=30; G2 n=24; G3 n=30; G4 n=26; G5 n=30). 56.4% (n=79) were male with median of age of 49 [41- 55] years. Overweight/obese MAFLD patients showed significant lower resistance and reactance levels (p0.05). According to vectorial analysis, chaquexia was observed in 18.4% (n=7) of patients in G4 and 15.8% (n=6) in G5 patients. Fat% was higher in patients of G5 (MU) than G2 (34.3[29.8-40.4], p=0.02) and G3 (35[31.1-38.3], p=0.01). Obese MAFLD patients showed lower TBW%, ICW% and ECW% (p0.001). (Figure). SMM% was lower in MU obese patients (29.1[26.3-31.1]) compared to healthy controls (33.4[29.3-36.8], p=0.006) and overweight patients (32[29.7-34.4], p=0.02). Phase angle did not show significant differences.

Conclusions: Overweight/obese MAFLD patients shows BC abnormalities in comparison with healthy controls and lean MAFLD patients. Resistance, reactance, body water and skeletal muscle mass are significant lower in both metabolically healthy/unhealthy obese patients. Changes could be explained for the sarcopenia and fat-muscle interchange and no necessary for the presence of metabolic abnormalities.

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O-19 IMPLICATIONS OF GLYPHOSATE ON NON-ALCOHOLIC FATTY LIVER DISEASE IN MICE

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Introduction and Objectives: Non-alcoholic fatty liver disease (NAFLD) affects ~25% of the world's population, presenting a multi-axis pathogenesis closely related to westernized dietary (WD) patterns, and to metabolic comorbidities. In addition to WD, individuals are frequently exposed to crops and dairy products presenting glyphosate (Glypho) residues, the most used broad-spectrum herbicide worldwide. This study aimed to evaluate whether chronic Glypho exposure promotes WD-induced NAFLD.

Materials and Methods: Male C57BL/6J mice were fed WD (chow containing 20% lard, 0.2% cholesterol, 20% sucrose, and high sugar solution with 23.1/18.9 g/L of D-fructose/D-glucose), and received glyphosate (0.05, 5 or 50 mg/kg/day) by gavage (5 × /week) for six months. Doses were below/within the regulatory limits (Acceptable Daily Intake or No Observed Adverse Effect Level).

Results: Glypho did not promote WD-induced obesity, hypercholesterolemia, and glucose intolerance, as this herbicide did not exert major effects on WD-induced hepatic macro/micro vesicular steatosis and perivascular fibrosis. Nonetheless, Glypho at the higher dose (50 mg) exerted the most pronounced effects on enhancing CD68+ macrophage density, p65 (NF-B), TNF-, and IL-6 protein levels in the liver. Furthermore, this dose also decreased hepatic Nrf2 levels, while enhanced lipid peroxidation in the liver and adipose tissue. The hepatic RNASeq analysis revealed that Glypho at 50 mg upregulated 212 genes, while downregulated 731 compared to WD counterpart. Glypho upregulated genes associated to "xenobiotic metabolic process" (Cyp2c37, Cyp2c23, Cyp2c54, Cyp2b10, Cyp2c50, and Cyp2e1), directly involved in oxidative stress, as well as "positive regulation of immune response"-related mRNAs (Egfr, Ccl7, Cfd, C6, C8a, and C8b).