dose-range finding. In Cohort 4, 78 patients were randomized to aldafermin 1mg (n=53) or placebo (n=25) for 24 weeks. Key inclusion criteria included biopsy-proven NASH with NAS ≥4 (at least 1 point in each component), Stage 1-3 fibrosis and absolute liver fat content (LFC) by MRI-PDFF ≥8%. APRI, FIB-4, fatty liver index (FLI) and ratio of triglyceride and HDL (TG/HDL) were evaluated at baseline (BL) and week 12 (W12) or W24. **Results:** At BL, mean APRI, FIB-4, FLI and TG/HDL values were similar across all groups. At the end of treatment at W12 or W24, aldafermin-treated patients showed reductions in NITs of fibrosis (APRI and FIB-4) and fatty liver (FLI). In contrast, no improvement was seen with placebo-treated patients. Improvements were observed as early as 2 weeks on aldafermin and were maintained throughout treatment duration. TG/HDL ratio, a simple measure of cardiovascular risk, decreased significantly with aldafermin treatment. In Cohort 4, among at-risk patients classified by the primary care referral pathway, fibrosis improvement with no worsening of NASH was achieved in 29% of patients in the aldafermin group and 9% in the placebo group. 21% and 0% of patients treated with aldafermin and placebo, respectively, achieved NASH resolution with no worsening of fibrosis. **Conclusion:** Aldafermin therapy produced improvements in several simple and inexpensive NITs of liver fibrosis, steatosis and cardiovascular risk. Among at-risk patients identified by NITs, a greater proportion of patients in the aldafermin group achieved fibrosis improvement and NASH resolution than placebo.

Table 1. Change from baseline to end of treatment in non-invasive tests

	APRI	FIB-4	FLI	TG/HDL
Cohort 1: Double-Blind, Placebo-Controlled (12-week)				
Placebo	0.03	0.08	0.3	−0.7
Aldafermin 3mg	−0.24***	−0.14	−1.2	−0.9
Aldafermin 6mg	−0.17***	−0.01	−2.2	−1.3**
Cohorts 2-3: Open-Label (12-week)				
Aldafermin 0.3mg	−0.14*	−0.04	−2.2	−0.9
Aldafermin 1mg	−0.38***	−0.22**	−3.1***	−1.4***

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Aldafermin 3mg	−0.44***	−0.35**	−2.7	−1.7***
Cohort 4: Double-Blind, Placebo-Controlled (24-week)				
Placebo	0	0.09	−1.3	−1.6
Aldafermin 1mg	−0.24***	−0.05	−2.3***	−3.9***

***p<0.001, **p<0.01, *p<0.05 vs baseline

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AN UNSUSPECTED LINK BETWEEN MYOSTEATOSIS AND NAFLD GRADING IN A PROSPECTIVE NUTRITIONAL INTERVENTION STUDY IN OBESE PATIENTS

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Background: Retrospective cross-sectional studies link sarcopenia and myosteatosis with non-alcoholic fatty liver disease (NAFLD) stages. In the present prospective study, we aimed at clarifying the dynamic relationship between sarcopenia, myosteatosis and NAFLD severity. **Methods:** A cohort of 48 obese patients were stratified according to NAFLD severity, evaluated with transient elastography (TE) derived steatosis and stiffness measurements. Skeletal muscle mass index (SMI) and fat index (SMFI; a surrogate of myosteatosis) were evaluated in whole muscle at the third lumbar vertebrae (L3) using the gold standard computed tomography (CT) scan. After baseline assessment (M0),

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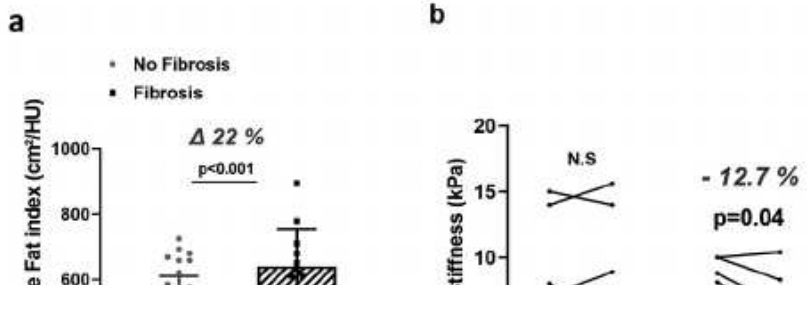
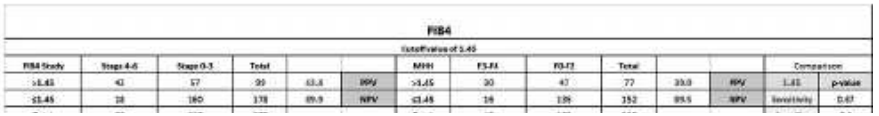
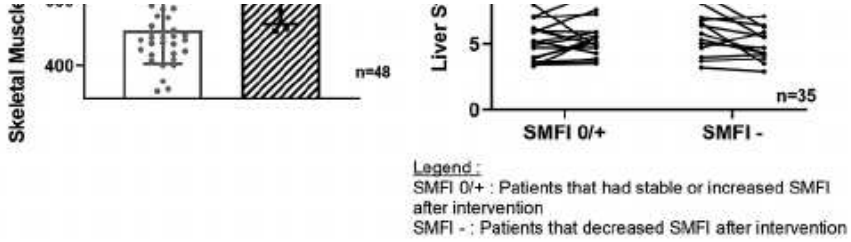
patients were assigned to a dietary regimen supplemented with inulin or maltodextrin (16g/day) and muscles and liver were re-evaluated after 3 months (M3). **Results:** All patients had NAFLD evaluated by TE. Sarcopenia was uncommon in those patients (4/48, 8.3%). SMFI was higher in patients with high liver stiffness (compatible with liver fibrosis) than in the others (640.6±114.3 cm²/HU vs 507.9±103.0 cm²/HU, p<0.001) (Fig. 1a). In multivariate analysis, SMFI, but not SMI, was robustly associated with fibrosis even when adjusted for multiple confounders (all p<0.05). After dietary regimen (n=35), there was no liver stiffness improvement when patients were stratified according to weight loss, treatment group allocation, liver steatosis decrease or muscle mass increase. Interestingly, only patients that decreased SMFI (regardless of intervention) had decreased liver stiffness (M0 = 6.36 kPa ± 2.15 vs M3= 5.55 kPa ± 1.97, -12.7 %, p=0.04) (Fig. 1b). **Conclusion:** High SMFI (indicative of myosteatosis), but not sarcopenia, is strongly and independently associated with high liver stiffness in obese NAFLD patients. A significant decrease in liver stiffness is observed only in patients with reduced myosteatosis, following a 3-month intervention. The potential role of myosteatosis as an independent contributor to liver disease progression and perhaps as a novel therapeutic target in NAFLD should be investigated.

Figure 1



with biopsy proven NASH. **Methods:** This was a retrospective study in patients with biopsy proven NASH between 2015-2018. Data was compiled from the electronic medical record to calculate FIB4, APRI, and NAFLD fibrosis scores. Using their liver biopsy results as the gold standard, the sensitivity, specificity, PPV, and NPV were calculated for each scoring system using the published cutoff values. We then compared our data to the published data using the chi-square test and the Fisher's Exact Test to evaluate for statistical significance. **Results:** A total of 229 patients were included in the study. The mean age of the population was 46 years old and 51.2% were Caucasian. The population was obese with a mean BMI of 36.6. Mean laboratory values were as follows: ALT 96.48, AST 77.07, Albumin 3.96, total bilirubin 0.85, platelets 241, and glucose 119. 54.1% had hypertension, 38.4% had diabetes mellitus. Biopsies revealed 27.5% F0, 33.6% F1, 18.8% F2, 12.2% F3, and 7.9% F4. Statistical analysis was performed in order to evaluate the correlation of the noninvasive scores and the liver biopsies; furthermore, this was compared to the data published for the respective studies (Table 1). **Conclusion:** FIB4 correlated well with the biopsies and performed as expected when compared to the validation group. However, the APRI and NAFLD fibrosis scores did not correlate when compared to the published data. In both groups, we saw a statistically significant discrepancy in both positive and negative predictive values. Our population was predominantly female, higher average BMI, and tended to have more severe liver disease when compared to the populations used to create the FIB4 and NAFLD fibrosis score. This would suggest that these non-invasive screening tools cannot be universally applied to all populations; moreover, they should to be tailored to individual patient populations.





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ARE INDIRECT MARKERS OF LIVER FIBROSIS UNIVERSALLY APPLICABLE?

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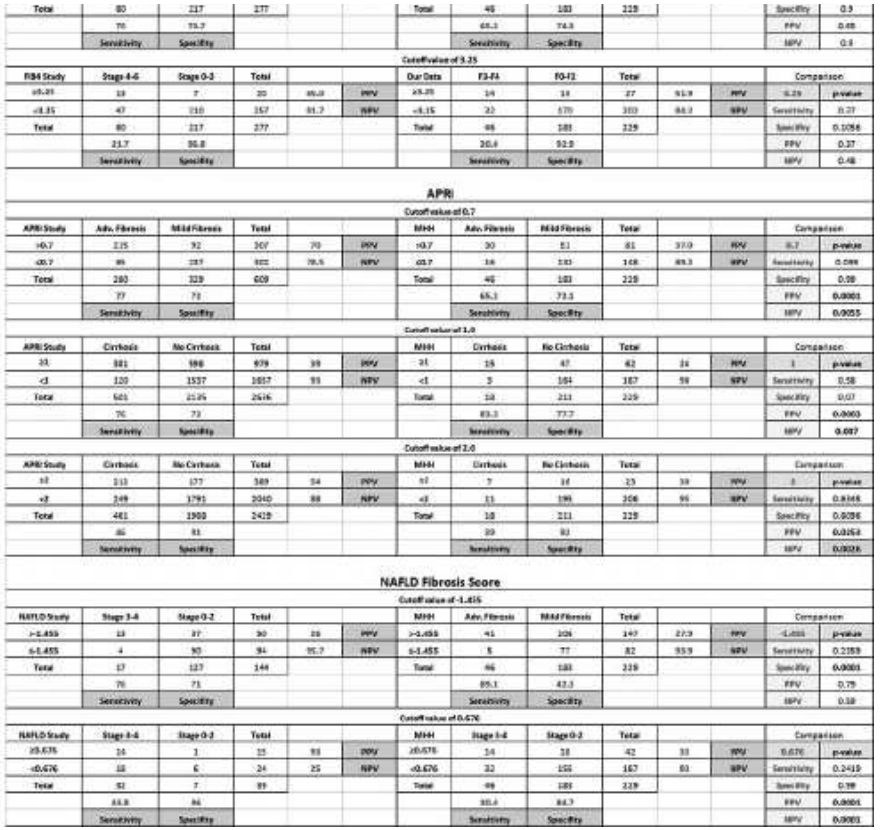
Background: Liver fibrosis develops in response to chronic liver injury. Studies have shown that 34% of patients in the US have some degree of NAFLD, fibrosis assessment in these patients aids in risk stratification. While the liver biopsy is the gold standard in this assessment, it is highly invasive. Noninvasive tests have been developed to aid in the diagnosis of liver disease such as the Fib4, APRI, and NAFLD fibrosis scores. We aim to assess the efficacy and reliability of these scoring systems in a single center patient population



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