CHANGES IN THE FIBROSIS-4 (FIB-4) SCORE ACCURATELY REFLECTS THE DISEASE TRAJECTORY OF METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE

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Introduction

- A FIB-4 score of 1.3-2.6 reflects **an intermediate risk stratum** of MASLD where secondary tests with VCTE or repeat testing is recommended.
- VCTE is not however universally available and the utility of repeat FIB-4 testing to assess changes in clinical status in MASLD is not known.
- This is particularly relevant since MASLD can both progress and regress without specific intervention.
- We hypothesized that changes in FIB-4 will coordinately track the risk of clinical outcomes in MASLD.

Aim

The aim of this study was to define the performance of changes in **FIB-4 as a disease-monitoring test** in MASLD.

Methods

- A retrospective analysis of a US cohort with MASLD followed prospectively in a non-interventional longitudinal registry (**TARGET-NASH**) was performed.
- MASLD was diagnosed by metabolic risk factors, histology or NITs, and AUDIT score < 7[1]. Adults with FIB-4 between 1.3-2.6 who had 2 FIB-4 measurements > 6 months apart within 3 years from baseline and a total of 5 years of follow up were included.
- Changes in FIB-4 from baseline to year 3 were associated with clinical outcomes occurring between years 3 and 5.
- Key outcomes included **all-cause mortal**ity and major adverse liver outcomes (**MALO**), defined as ascites, overt hepatic encephalopathy, or variceal hemorrhage.
- Time-to-event analysis were conducted to evaluate the association between FIB-4 changes and the risk of clinical outcomes, adjusting for age, type 2 diabetes, and other potential confounders.
- Bootstrap validation confirmed the robustness of the model results.

Results

Table 1. Patient Characteristics at Index Date for Participants with FIB-4 1.3- 2.6

Patient Characteristics	Values (N =687)
Demographics	
Age at Index Date (years)	
Mean (SD)	60 (9.6)
Range (Min-Max)	21.0 - 86.0
Sex, n (%)	
Female	387 (56.3%)
Male	300 (43.7%)
Race- Ethnicity, n (%)	
Non-Hispanic White	439 (63.9%)
Lifestyle	
BMI (kg/m^2) at enrollment	
Mean (SD)	32.4 (7.2)
Min-Max	16.9 - 58.2
BMI(kg/m2) categories, n (%)	687
< 25 (Healthy Weight)	102 (15.0%)
25 - < 30 (Overweight)	187 (27.5%)
30 - < 35 (Obese)	174 (25.6%)
35 - < 40 (Severe Obesity)	110 (16.2%)
>=40 (Morbid Obesity)	106 (15.6%)
Alcohol use at enrollment, n (%)	687
Former	44 (6.4%)
Current	209 (30.4%)
Never	299 (43.5%)
Not reported	135 (19.7%)
AUDIT at enrollment	
Mean (SD)	1.1 (2.04)
Min - Max	0.0 - 18.0
FIB-4 at enrollment	
Mean (SD)	1.8 (0.35)
Min - Max	1.3 - 2.6
Comorbidities	
Type 2 Diabetes	282 (41.0%)
Hypertension	543 (79.0)
Obesity	390 (57.4%)

Index date is the first date within the 3-year retrospective period where the first FIB-4 > 1.3 and ≤ 2.6.

- A total of 687 individuals were included in the study **(Table 1).**
- Between baseline and Year 3, **171 MALO** outcomes were recorded, with an additional **94** events occurring between Years 3 and 5. From baseline to Year 3, FIB-4 scores declined by more than 10% in 489 patients (71%) and increased by more than 10% in 198 patients (29%).
- **An increase in FIB-4 was strongly associated with elevated MALO risk and incidence,** HR 5.6 (95% CI: 3.0–10.2) **(Fig. 1,2)**
- Age and hypertension did not significantly influence MALO risk, whereas **T2DM** was associated with increased risk (OR 1.6, 95% CI: 1.1–2.4) (Fig. 2).

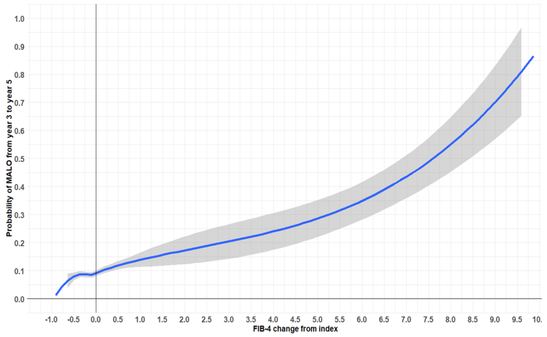

Figure 1. Probability of MALO Incidence compared to Change in FIB-4 from Index Date

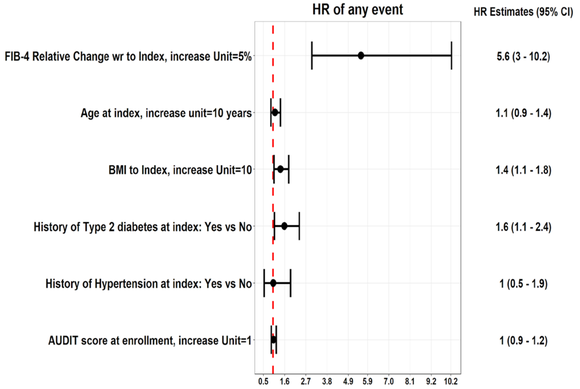

Figure 2. Hazard Ratio for Any Outcome (MALO Events or Death)

Conclusion

Changes in FIB-4 over time are predictive of future adverse health outcomes, independent of baseline age.
An increase in FIB-4 was strongly associated with elevated MALO risk and incidence.
Tracking changes in FIB-4 can support risk stratification and clinical decision-making.

References

1. **Barritt A.S. et al.** High Concordance Between Nonalcoholic Fatty Liver Disease and Metabolic Dysfunction-Associated Steatotic Liver Disease in the TARGET-NASH Real-World Cohort. *Am J Gastroenterol 2024; 119(8):1624-1627*

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Full Abstract