

A prospective assessment of disease progression impact on patient-reported outcomes in metabolic dysfunction-associated steatotic liver disease

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Background and Aims

- Metabolic dysfunction associated-steatotic liver disease and steatohepatitis (MASLD and MASH respectively) are major causes of liver-related morbidity and mortality
- While studies have reported clinical event rates in patients with MASLD, there is a paucity of data on the impact of progression to cirrhosis on patient reported outcomes (PRO)
- AIM:** To perform a prospective, cross-sectional analysis of a MASLD-specific PRO in patients with MASLD in a real-world setting

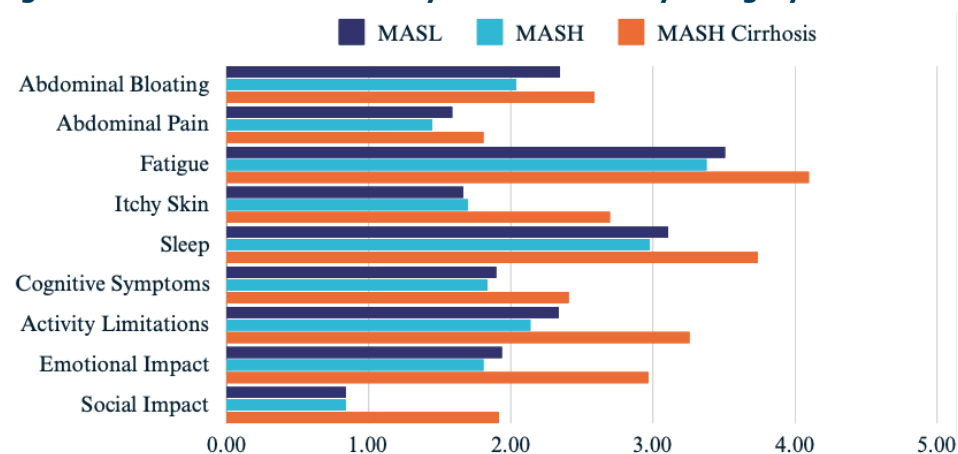
Methods

- This was a cross-sectional analysis of the NASH-CHECK PRO measure completed by a subset of patients enrolled in the real-world TARGET-NASH observational longitudinal ongoing study, which has >6,000 patients enrolled at academic and community sites in the United States with more than 6 years of median follow up
- The NASH-CHECK instrument (version 1.0)¹ was completed between 2021 and 2023; NASH-CHECK was developed and validated previously
- MASLD was defined per the TARGET-NASH definitions using available biopsy, imaging, and clinical criteria as described previously²
- Three categories of patients were compared using previously published and validated case-definitions: (1) MASL, (2) MASH, (3) MASH cirrhosis³
- NASH-CHECK has 6 symptom scale scores and three additional HRQOL scores; each has a score of 0-10 with higher scores indicating greater impairment¹
- Scores across classes were compared using linear regression examining the relationship between PRO scores and disease progression controlling for covariates: age, sex, race/ethnicity, presence or absence of Type 2 Diabetes, and number of cardiometabolic risk factors (out of 5)

Table 1. TARGET-NASH Cohort Characteristics

	MASL (n=287)	MASH (n=320)	MASH Cirrhosis (n=281)	Overall (n=888)
Age at first NASH-CHECK				
Median	63.0	60.0	64.0	62.0
Female, n(%)	177 (62%)	194 (61%)	176 (63%)	547 (62%)
Hispanic/Latino, n(%)	31 (11%)	19 (6%)	15 (5%)	65 (7%)
Private Insurance	131 (46%)	184 (58%)	140 (50%)	455 (51%)
Site Type				
Academic	144 (50%)	210 (66%)	233 (83%)	587 (66%)
Community	143 (50%)	110 (34%)	48 (17%)	301 (34%)
Number of cardiometabolic criteria met at first NASH-CHECK				
1	38 (13%)	21 (7%)	18 (6%)	77 (9%)
2	24 (8%)	33 (10%)	18 (6%)	75 (8%)
3	75 (26%)	77 (24%)	54 (19%)	206 (23%)
4	36 (13%)	32 (10%)	26 (9%)	94 (11%)
5	114 (40%)	157 (49%)	165 (59%)	436 (49%)

Figure 1. NASH-CHECK Scores by Disease Severity Category



Results

- 888 adult participants with a completed NASH-CHECK PRO and MASLD were obtained (n=287, 320, 281 for MASL, MASH, and MASH cirrhosis respectively)
- Median age was 62, 62% female, 80% Non-Hispanic White, 7% Non-Hispanic Black, 7% Hispanic/Latino, 68% BMI ≥ 25, 72% type 2 diabetes, 89% blood pressure ≥ 130/85 (or specific antihypertensive drug treatment), 77% plasma triglycerides ≥ 1.70 mmol/L (or lipid lowering treatment), 78% plasma HDL-cholesterol ≤ 1.0 mmol/L if male or ≤ 1.3 mmol/L if female (or lipid lower treatment)
- Significant differences were noted between MASL, MASH, and cirrhosis: p < 0.001 for itchy skin, emotional impact, social impact; p=0.003 for activity limitation, p=0.036 for cognitive symptoms; p=0.025 for fatigue; p=0.009 for sleep (Figure 1)
- NASH-CHECK scores for those with cirrhosis were higher than MASL and MASH for all domains

Conclusions

- In a real-world clinical setting, the recently validated MASLD-specific PRO measure NASH-CHECK showed significant differences between disease groups in 7 of 9 domains both in a univariate comparison and when controlling for clinically-meaningful covariates; Scores for cirrhosis were higher than those for MASL and MASH across all domains
- This analysis provides support that the spectrum of MASLD is indeed burdensome for patients; PRO burden appears higher among those with more advanced liver disease
- Further investigations into the mechanisms of patient symptoms and the impact of treatment are needed

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¹Doward, Lynda C., et al. (2021). Development of a patient-reported outcome measure for non-alcoholic steatohepatitis (NASH-CHECK): results of a qualitative study. *The Patient-Patient-Centered Outcomes Research*, 14, 533-543.
²Barritt IV, A. Sidney, et al. (2022). High concordance between nonalcoholic fatty liver disease and metabolic dysfunction associated steatotic liver disease in the TARGET-NASH real world cohort. *Official Journal of the American College of Gastroenterology | ACG*: 10-14309.
³Kim, Hannah et al. (2021). Liver Biopsy in the Real World—Reporting, Expert Concordance and Correlation with a Pragmatic Clinical Diagnosis. *Alimentary Pharmacology and Therapeutics*. *Alimentary Pharmacology and Therapeutics*, 54 (11-12), 1472-1480.