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Stability of the NASH-CHECK patient-reported outcome measure over time in patients with metabolic dysfunction-associated steatotic liver disease and stable clinical status

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INTRODUCTION

- Metabolic dysfunction associated-steatotic liver disease and steatohepatitis (MASLD and MASH respectively) are major causes of liver-related morbidity and mortality.
- A key aspect of a valid patient-reported outcome (PRO) measure (PROM) is stability of scores over time in those whose clinical status remains stable.
- While several PROMs have been used for patients with metabolic dysfunction-associated steatotic liver disease and steatohepatitis (MASLD and MASH), none has been fully validated in the regulatory space. The NASH-CHECK® PROM was developed in accordance with regulatory standards, but its stability over time has not been established.

AIM

To define the stability of NASH-CHECK® scores over time in patients with varying severity of disease at baseline who have unchanged overall clinical status.

METHODS

- This was a longitudinal analysis of the NASH-CHECK PROM 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 previously.[2]
- The analysis population included patients without a change in MASLD disease severity (MASL, MASH, compensated cirrhosis, decompensated cirrhosis) between completion of the first and second NASH-CHECK.
- NASH-CHECK has 6 symptom scale scores and three additional HRQOL scores; each has a score of 0-10 with higher scores indicating greater impairment.[1]
- The null hypothesis was that the second score was significantly different from the first score. Significance was set at p<0.05.

Table 1. TARGET-NASH Cohort Characteristics

- at 1st NASH-CHECK	MASL (n=75)	MASH (n=92)	Compensated Cirrhosis (n=64)	Decompensated Cirrhosis (n=39)
Age (Median)	64.0	63.0	64.5	64.0
Female, n(%)	51 (68.0%)	58 (63.0%)	37 (57.8%)	25 (64.1%)
Medicaid or uninsured, n(%)	2 (2.7%)	6 (6.5%)	3 (4.7%)	4 (10.3%)
Site Type, n(%) Academic Community	 33 (44.0%) 42 (56.0%)	 57 (62.0%) 35 (38.0%)	 48 (75.0%) 16 (25.0%)	 36 (92.3%) 3 (7.7%)
BMI, Mean (SD)	32.90 (6.566)	34.84 (8.177)	33.25 (7.405)	35.00 (8.687)
A1c, Mean (SD)	6.43 (1.094)	6.20 (1.094)	6.94 (1.723)	6.60 (1.578)
AST, Mean (SD)	33.60 (23.57)	36.18 (21.69)	33.87 (20.31)	60.67 (112.4)
ALT, Mean (SD)	32.36 (26.84)	50.28 (44.55)	37.98 (29.02)	44.26 (89.02)
ALP, Mean (SD)	86.09 (35.33)	87.61 (40.64)	86.26 (31.89)	115.6 (46.55)
Bilirubin, Mean (SD)	0.64 (0.393)	0.61 (0.276)	0.79 (0.392)	1.57 (1.215)
Albumin, Mean (SD)	4.11 (0.639)	4.24 (0.456)	4.12 (0.378)	3.80 (0.512)
Creatinine, Mean (SD)	0.92 (0.285)	0.85 (0.202)	0.91 (0.232)	0.88 (0.356)
INR, Mean (SD)	1.11 (0.149)	1.05 (0.204)	1.11 (0.239)	1.38 (0.458)
MELD 3.0, Mean (SD)	8.00 (2.544)	7.16 (2.132)	7.91 (2.281)	11.57 (4.213)

Table 2. NASH-CHECK Scores, 1st and 2nd in those with unchanged severity

NASH-CHECK domains	MASL (n=75)		MASH (n=92)		Compensated Cirrhosis (n=64)		Decompensated Cirrhosis (n=39)	
	1st versus 2nd NC		1st versus 2nd NC		1st versus 2nd NC		1st versus 2nd NC	
Abdominal pain	1.72 (2.618)	1.68 (2.406)	1.46 (2.662)	1.43 (2.477)	1.81 (2.606)	1.63 (2.617)	1.85 (2.691)	1.63 (2.775)
Abdominal bloating	2.32 (2.652)	2.53 (2.713)	2.15 (2.840)	1.82 (2.573)	2.58 (3.186)	2.21 (2.824)	2.67 (3.239)	2.55 (3.055)
Fatigue	3.64 (2.917)	3.71 (2.865)	3.12 (2.953)	3.36 (2.769)	3.91 (3.069)	3.67 (2.845)	3.87 (3.139)	4.00 (3.361)
Itchy skin	1.97 (2.564)	2.07 (2.965)	1.85 (2.676)	1.91 (2.763)	2.16 (2.749)	1.97 (2.890)	1.82 (2.535)	2.22 (2.554)
Sleep	3.21 (3.068)	3.46 (3.126)	3.10 (3.006)	3.08 (3.061)	3.97 (3.008)	3.50 (3.303)	2.95 (3.385)	2.61 (3.009)
Cognitive symptoms	2.34 (2.436)	2.21 (2.220)	1.66 (2.426)	1.61 (2.056)	2.37 (2.521)	1.97 (2.291)	2.22 (2.585)	1.85 (1.985)
Activity limitations	2.49 (2.726)	2.48 (2.512)	2.29 (2.722)	2.36 (2.682)	2.82 (2.823)	2.83 (2.798)	3.31 (2.728)	3.39 (2.764)
Emotional impact	2.13 (2.263)	1.99 (2.096)	1.84 (2.008)	1.68 (1.876)	*2.46 (2.405)	*1.81 (1.845)	2.35 (2.528)	2.01 (1.904)
Social impact	0.92 (1.765)	1.07 (2.043)	0.63 (1.547)	0.54 (1.317)	1.21 (2.294)	0.88 (1.694)	1.88 (2.635)	2.20 (2.648)

Note: All domains of NASH-CHECK PROM scores (mean (SD)) stable across time in patients with unchanged severity of disease across time, with exception of improvement in emotional impact score for those with compensated cirrhosis.
**p<0.05*
Abbreviations Include: BMI – Body Mass Index; A1c – Hemoglobin A1c; AST-Aspartate aminotransferase; ALT-Alanine transaminase; ALP-Alkaline phosphatase; INR-International normalized ratio; MELD-Model for End-Stage Liver Disease

RESULTS

- 272 adult participants with two completed NASH-CHECK PROMs and whose MASLD disease severity was the same at each.
- The mean (±S.D.) duration between tests was 10.1 (5.7) months.
- Scores were not statistically different between the first and second NASH-CHECK within the disease severity subgroups except for emotional impact among compensated cirrhosis patients where an improvement was observed at the second NASH-CHECK (p<0.001).

CONCLUSIONS

- The NASH-CHECK PROM scores were stable over an extended period of time (mean [±S.D.] 10.1 [5.7] months) in patients with varying severity of MASLD whose clinical status remained unchanged during this time.
- Future investigations should further define stability of the NASH-CHECK PROM and begin defining other aspects such as sensitivity to change.

REFERENCES

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