Poster Code: PT48

Using a database analysis to determine alignment between physician-reported and objectively derived fibrosis scores for US patients with metabolic dysfunction-associated steatohepatitis (MASH)

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Background and Aims

- Metabolic dysfunction-associated steatotic liver disease (MASLD*):
  - Significantly prevalent and rapidly growing disease affecting over 80 million individuals in the United States (US).[1]
- Metabolic dysfunction-associated steatohepatitis (MASH**):
  - Severe manifestation of MASLD that can progress to cirrhosis, hepatocellular carcinoma, and liver-related mortality.[2]
  - Parallels the prevalence of obesity, metabolic syndrome, and type 2 diabetes (T2D) and projected to become leading indication for liver transplantation.[3]
  - Requires a high degree of clinical suspicion to accurately risk stratify individuals, which is critical for effective disease management.
- Non-invasive tests (NITs) and advanced confirmatory diagnostic modalities can serve as alternatives to liver biopsies, which are invasive, costly, and diagnostically imperfect.
- Clinical practice guidance in the US was recently updated.[4] Although a gap exists between current guidance in the European Union and methods used in clinical practice,[5] this is still to be assessed in the US.
- This study aimed to:
  - Determine whether US physicians' classifications of fibrosis scores using existing clinical data are aligned with objectively derived measures from NITs, such as vibration-controlled transient elastography (VCTE) and Fibrosis-4 (FIB-4) index, in patients with MASH (PwM).
  - Quantify the degree of alignment between physicians' classification of fibrosis score and objectively derived score.
  - Assess factors associated with fibrosis classification misalignment in PwM.

*Formerly nonalcoholic fatty liver disease [NAFLD]; **formerly nonalcoholic steatohepatitis [NASH]

Methods

- The Adelphi Real World MASH Disease Specific Programme™ (DSP) was applied for this analysis, a cross-sectional secondary database study of US physician and patient survey data obtained from January to June 2022.
  - The DSP criteria have been published and validated previously.[6-9]
- Physician inclusion criteria:
  - Endocrinologist, gastroenterologist, or hepatologist
  - Managing/treating ≥10 PwM per month
- PwM inclusion criteria:
  - Age ≥18 years
  - Had a physician-confirmed diagnosis of suspected MASH or confirmed MASH
  - Not involved in a clinical trial for MASH at the time of data collection
- Physicians provided PwM information for 10 consecutively qualifying PwM, which included:
  - Patient demographics (age, sex, body mass index [BMI], ethnicity)
  - Patient comorbidities and disease duration
  - Fibrosis scores and laboratory results
- All respondents provided informed consent; ethics exemption was obtained from Pearl Institutional Review Board.
- Physicians reported each PwM fibrosis scores as F0, F1, F2, F3, F4 according to interpretation of the available clinical data; PwM were then categorized as no/early fibrosis (F0-F2), advanced fibrosis (F3-F4), or undetermined/unknown.
- Objectively derived fibrosis scores were retrospectively determined by a hierarchical series of tests, as shown in **Figure 1**.
  - Low- and high-risk fibrosis categories were reclassified using the approach illustrated in **Figure 1** as no/early and advanced fibrosis, respectively.
- Alignment was defined based on the concordance between physician-reported and objectively derived fibrosis classification to create four subgroups:

Aligned no/early fibrosis:	**Aligned advanced fibrosis:**	**Physician underestimated:**	**Physician overestimated:**
Both physician-reported and objectively derived classifications aligned, indicating the absence of fibrosis or presence of early-stage fibrosis	Both physician-reported and objectively derived classifications aligned, indicating the presence of advanced fibrosis	Physician-reported fibrosis classification lower than objectively derived classification	Physician-reported fibrosis classification higher than objectively derived classification

- Descriptive statistics were used to summarize the data and assess the alignment in fibrosis scores.
- A logistic regression analysis was performed using predictive values and bivariate analyses to identify factors associated with misalignment in fibrosis scores.

Results

- A total of 85 physicians identified 832 PwM; among these, n=535 had both physician-reported and objectively derived fibrosis scores.
- Demographic and clinical characteristics of PwM are presented in **Table 1**.
- Physician-reported fibrosis score assessment was not assigned in 11% of PwM (**Figure 2A**). About one quarter (26%) of objectively derived fibrosis score classification could not be determined via the approach applied (**Figure 2B**).

Table 1. Demographics and clinical characteristics of patients with MASH

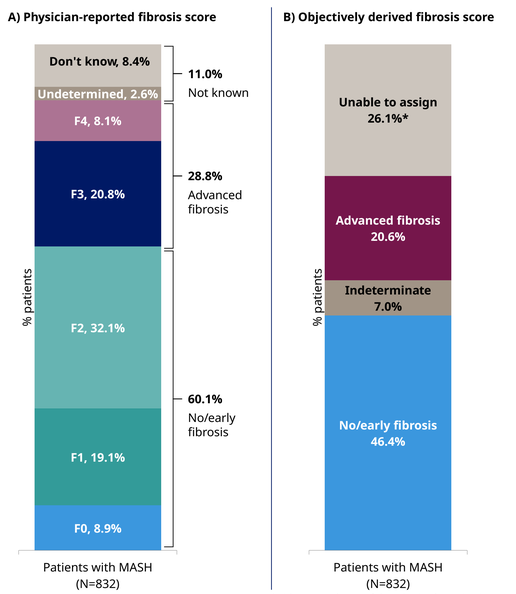
Characteristic		Total (N=832)	Patients with physician-reported and objectively derived scores (n=535)
Age	<50 years, n (%)	279 (33.5)	184 (34.4)
	50-64 years, n (%)	380 (45.7)	233 (43.6)
	≥65 years, n (%)	173 (20.8)	118 (22.1)
Sex	Male, n (%)	406 (48.8)	256 (47.9)
	Female, n (%)	425 (51.1)	278 (52.0)
	Intersex, n (%)	1 (0.1)	1 (0.2)
Race/ethnicity	White/Caucasian, n (%)	508 (61.1)	312 (58.3)
	Black/African American, n (%)	131 (15.7)	88 (16.4)
	Hispanic/Latino, n (%)	113 (13.6)	83 (15.5)
	Other, n (%)	80 (9.6)	52 (9.7)
BMI	<30 kg/m², n (%)	318 (38.2)	197 (36.8)
	≥30 kg/m², n (%)	514 (61.8)	338 (63.2)

Figure 1. Methods used to determine the objectively derived fibrosis score

*For PwM to be defined with the same nomenclature regardless of test applied, low risk was redefined as no/early fibrosis, intermediate risk as indeterminate fibrosis, and high risk as advanced fibrosis.
#Definitions determined using literature: VCTE[10,11]; ELF[12]; FIB-4[13,14]; secondary indicators and evidence of clinical parameters[15,16]; NAS.[17]

- Of the PwM who had both physician-reported and objectively derived fibrosis scores (n=535), 88.1% of scores were aligned; few scores were misaligned (**Figure 3**).
  - Alignment was slightly higher within the no/early fibrosis group and slightly lower in the advanced fibrosis group.
- Significant variables included in the bivariate analyses included in the logistic regression model were physician specialty, physician setting, physician level of difficulty in determining if a PwM needs a liver biopsy, PwM age, and PwM BMI.
- Significant factors associated with misalignment included PwM BMI ≥30 kg/m², PwM age ≥50 years, and physician difficulty in determining the need for liver biopsy (**Table 2**).

Figure 2. Classification of fibrosis scores as determined by physician-reported and objectively derived scores



*Did not match any of the criteria shown in Figure 1

Figure 3. Level of alignment between physician-reported and objectively derived fibrosis scores in patients with MASH

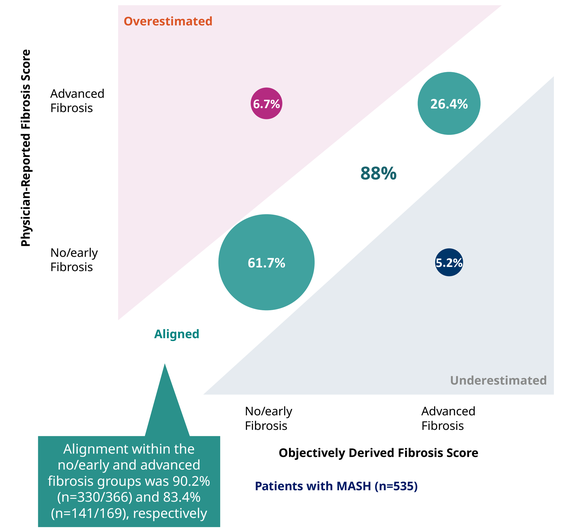


Table 2. Factors influencing misalignment of fibrosis scores

Variable	Odds Ratio	95% Confidence Interval	P-value
Physician specialty (hepatologist)	0.45	0.19-1.08	P=0.075
Physician setting (office and hospital)	1.48	0.74-2.96	P=0.264
Difficulty in determining if PwM need biopsy (slightly difficult to very difficult)	5.07	1.70-15.1	P=0.004
PwM age, ≥50 years	3.05	1.56-5.95	P=0.001
PwM BMI at data capture, ≥30 kg/m²	2.07	1.07-3.99	P=0.03

Summary and Conclusions

- While most physician-reported and objectively derived scores aligned, some US physicians faced challenges with fibrosis risk classification in 12% of PwM.
- Misalignment was more likely in older PwM, those with obesity, and PwM whose physicians reported difficulty in determining the need for liver biopsy.
- Highlighting these factors may help prevent misalignment when risk stratifying PwM, which may lead to earlier intervention and better disease management.
- Limitations included the following:
  - Identification of PwM was based on the physician's judgment, as no formal definitions or guidelines were provided to physicians; this is likely to be representative of physicians' real-world patient classification.
  - Although PwM were selected for this analysis based on availability of pre-specified test results, some physicians had access to additional testing information for their PwM on which fibrosis assessment could have been made.
  - We could not retrospectively assess liver biopsy results for further verification.

Abbreviations: ALT, alanine transaminase; BMI, body mass index; ELF, enhanced liver fibrosis; FIB-4, fibrosis-4 index; MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, metabolic dysfunction-associated steatohepatitis; NAS, NAFLD activity score; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; NITs, non-invasive tests; PwM, patients with MASH; T2D, type 2 diabetes; VCTE, vibration controlled transient elastography

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VH, AL, and GM are employees of Adelphi Real World.
SOG is an employee of Novo Nordisk Inc. and a shareholder of Novo Nordisk A/S. At the time of the study, BPS was an employee of Novo Nordisk Inc.
Data collection was undertaken by Adelphi Real World as part of an independent survey entitled the "Adelphi MASH DSP." Novo Nordisk Inc. did not influence the original survey through either contribution to the design of questionnaires or data collection. The analysis described here used data from the Adelphi MASH DSP. The DSP is a wholly owned Adelphi product. Novo Nordisk Inc. is one of multiple subscribers to the DSP.
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