Determination of Optimal Thresholds for Significant Fibrosis in NAFLD Using Non-Invasive Tests from TARGET-NASH Study

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Introduction

- Liver biopsy is considered the reference standard for fibrosis staging; however, its use is limited in clinical practice due to cost, variable interpretations, and risks associated with an invasive procedure.
- Once pharmacotherapy is available for nonalcoholic fatty liver disease, treatment might be initiated at varying stages of disease. Liver biopsy may be impractical for treatment decisions.
- While some non-invasive tests have been studied to identify *advanced* fibrosis (NASH CRN ≥F3), there is limited evidence on the ability of non-invasive tests (NITs) to discriminate *significant* liver fibrosis (NASH CRN ≥F2) in real-world cohorts.

Objective

- The aim of this study was to assess the performance of NITs to determine optimal thresholds for significant fibrosis using data from a real-world registry.

Methods

- TARGET-NASH is a longitudinal cohort of patients receiving care in usual clinical practice in the US and Europe.
- Liver biopsy results from TARGET-NASH participants were used as a reference for presence (NASH CRN ≥F2) or absence (NASH CRN F0 - F1) of significant fibrosis.
- Lab data for calculation of Fibrosis-4 (FIB-4: AST, ALT, platelet count) and AST to Platelet Ratio Index (APRI) were collected within +/-6 months of liver biopsy.

Methods (Continued)

- Values used to compute NITs were those closest to the biopsy date within this window using those measurements after the biopsy in case of a tie between pre- and post-biopsy measurements
- Area under receiver operating characteristic (AUROC) curves were used to determine optimal NIT thresholds.
- The predictive accuracy of each NIT was evaluated using logistic regression.
- Two thresholds were selected to maximize classification accuracy:
- A high threshold above which patients were likely to have significant fibrosis (optimized for specificity >=90%)
- A low threshold below which patients were unlikely to have significant fibrosis (optimized for sensitivity >=90%).

Results

- Liver biopsies from 952 adult study subjects with contemporaneous blood work were included in the analysis.
- Median age was 57 years (range: 18-79).
- 24% of the cohort was over age 65.
- The cohort was 61% female and 86% Caucasian.
- 72% of the cohort was obese (BMI >30 kg/m2), 48% had diabetes.
- Optimal thresholds and test characteristics for including and excluding significant fibrosis are shown in Table 1.
- AUROCs were 0.79 and 0.72 for FIB-4 and APRI, respectively, to discriminate significant fibrosis.

Conclusion

FIB-4 at a threshold ≥2.43 and APRI ≥1.07 of can be used to potentially identify significant fibrosis among real-world NASH patients with an acceptable level of accuracy.

Table 1: Thresholds and Test Characteristics for Non-Invasive Tests for Determining Significant Fibrosis

NIT	Fibrosis	Threshold	Sensitivity	Specificity	PPV	NPV	AUROC
FIB-4	Stage ≥ F2	≥ 2.43	49%	90%	87%	56%	0.79
	F0 - F1	≤ 0.95	90%	41%	68%	75%	
APRI	Stage ≥ F2	≥ 1.07	36%	90%	83%	51%	0.72
	F0 - F1	≤ 0.32	90%	36%	66%	72%	

Acknowledgements and Disclosures: TARGET-NASH is a study sponsored by Target RWE. Target RWE is a health evidence solutions company headquartered in Durham, NC. The authors would like to thank all the investigators, participants, and research staff associated with TARGET-NASH. ClinicalTrials.gov Identifier: NCT02815891.