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Fibrometer-VCTE-Light provides h i g h e s t discrimination over other Fibrometerderived biomarkers and outperforms FIB-4 for stratification of fibrosis across a spectrum of fibrosis stages.

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Performance of fibrometerderived biomarker panels for assessment of fibrosis stage in NAFLD: NIMBLE stage 1 and the NASH CRN **collaborative Study**

Introduction

The intent of the current collaborative study between Non-invasive Biomarkers of Metabolic Liver Disease (NIMBLE) and the Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) was to further evaluate the performance of Fibrometer-based biomarker panels, including those developed for non-alcoholic fatty liver disease (NAFLD) or other liver diseases, with and without vibrationcontrolled transient elastography (VCTE) for identification of fibrosis strata in those with NAFLD.

Aim

• To evaluate the diagnostic-test performance characteristics of four Fibrometerbased biomarker panels for assessing fibrosis in a well-characterized cohort of patients with biopsy-confirmed NAFLD with description of sensitivity and specificity at Youden's cutoff for their intended diagnostic use in a large, multicenter US cohort of patients with NAFLD/NASH.

Methods

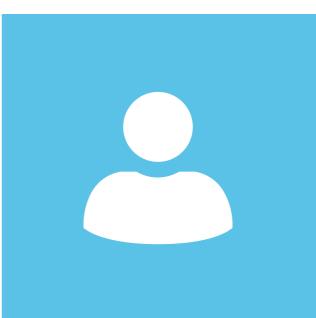
- The performance of Fibrometer Virus (FM-VIRUS), Cirrhometer Virus (CM-VIRUS), Fibrometer NAFLD (FM-NAFLD) and Fibrometer VCTE-Light (FM-VCTE-Light) was evaluated for the assessment of fibrosis.
- Blood-based parameters were tested from aliquots of the same blood sample from each patient obtained within 90 days of a liver biopsy demonstrating NAFLD of varying activity and stages (Stages 0-4). VCTE measurements were performed in a subgroup of trial participants within this time window.
- In order to minimize spectrum bias, the cohort was selected a priori to have a similar distribution of fibrosis stages across its entire range.
- The primary hypothesis was that the AUROC for each panel for its intended use was numerically > 0.7 and significantly superior to 0.5. The secondary hypothesis was that the AUROC for each panel for fibrosis was significantly greater than that for FIB-4 (as the common reference).

	FIB-4	FM-VIRUS	CM-VIRUS	FM-NAFLD	FM-VCTE-Light
Parameters	Age, ALT, AST, PLT		Age, sex, A2M, AST, BUN, GGT, INR, PLT		Age, sex, A2M, AST, GGT, LSM, PLT

alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; FER: ferritin; GGT: gamma-glutamyl transferase; GLU: fasting glucose; INR: international normalized ratio; LSM: liver stiffness by VCTE; PLT: platelet count.

Results

- 1073 patients with biopsy-proven NAFLD including NAFL (n = 220) and NASH (n = 853) were evaluated.
- The number of patients with fibrosis stages 0, 1, 2, 3 and 4 were 222, 114, 262, 277 and 198, respectively.
- The dataset for Fibrometer VCTE-Light was smaller as VCTE data were available in only 393 patients.
- The AUROCs, Youden's cutoff with its sensitivity/specificity are provided below: All 4 panels met criteria for intended use for diagnosis of fibrosis stage ≥2, advanced fibrosis, and cirrhosis.
- Compared to FIB-4, FM-VIRUS and FM-NAFLD met criteria for diagnosis of advanced fibrosis but not for fibrosis stage ≥2 or cirrhosis, while CM-VIRUS was not superior to FIB-4 for any of the intended uses.
- In contrast, FM-VCTE-Light was significantly superior to FIB-4 for all three intended uses.



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Table. Diagnostic test characteristics of various ribrometer-derived parters for detection of hbrosis in NALD								
	FIB-4	FM-VIRUS	CM-VIRUS	FM-NAFLD	FM-VCTE-Light			
Diagnostic test	AUROC							
characteristics	(Youden cut-off value) [Sensitivity, Specificity]							
F stage \geq 2	0.80	0.80	0.72	0.81	0.84**			
	(1.4)	(0.4)	(0.0)	(0.4)	(0.4)			
	[65.4 <i>,</i> 80.8]	[69.2 <i>,</i> 77.4]	[65.2 <i>,</i> 69.9]	[67.7 <i>,</i> 80.0]	[71.6, 81.1]			
F stage \geq 3	0.79	0.81*	0.76	0.80*	0.85			
	(1.4)	(0.4)	(0.0)	(0.4)	(0.4)			
	[75.1, 68.6]	[76.4, 69.9]	[76.2, 63.0]	[77.9 <i>,</i> 67.0]	[89.9 <i>,</i> 65.3]			
F stage 4	0.81	0.83	0.82	0.80	0.90*			
	(1.5)	(0.6)	(0.1)	(0.5)	(0.7)			
	[85, 63.4]	[75.0, 73.2]	[65.6, 81.5]	[76.7, 68.0]	[94.2, 74.7]			

Table: Diagnostic test characteristics of various Fibrometer-derived panels for detection of fibrosis in NAFLD

comparison with FIB-4 for their intended us All AUROCs are statistically significant and superior to AUROC=0.5 (p<0.001)



Conclusions

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FM-VCTE-Light consistently outperformed FIB-4 for stratification of fibrosis across a spectrum of fibrosis stages. FM-VIRUS and FM-NAFLD appear to be better than FIB-4 for detecting advanced fibrosis but not for other fibrosis stages.

These data will be helpful in informing trial design for future studies using these Fibrometer-based non-invasive tools across various intended use populations.

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