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Supplementary material: Methods

UCSD-NAFLD Cohort's Exclusion Criteria

i. Clinical or histological evidence of alcoholic liver disease.
    1. Regular and excessive use of alcohol within the 2 years prior to interview defined as alcohol intake greater than 14 drinks per week in a man or greater than 7 drinks per week in a woman. Approximately 10 g of alcohol equals one 'drink' unit. One unit equals 1 ounce of distilled spirits, one 12-oz beer, or one 4-oz glass of wine
ii. Total parenteral nutrition for more than 1 month within a 6 month period before baseline liver biopsy
iii. Short bowel syndrome
iv. History of gastric or jejunoileal bypass preceding the diagnosis of NAFLD. Bariatric surgery performed following enrollment is not exclusionary. Liver biopsies obtained during bariatric surgery cannot be used for enrollment because of the associated surgical or anesthetic acute changes and the weight loss efforts that precede bariatric surgery
v. History of biliopancreatic diversion
vi. Evidence of advanced liver disease defined as a Child-Pugh-Turcotte score equal to or greater than 10
vii. Evidence of chronic hepatitis B as marked by the presence of HBsAg in serum (subjects with isolated antibody to hepatitis B core antigen, anti-HBc total, are not excluded)
viii. Evidence of chronic hepatitis C as marked by the presence of anti-HCV or HCV RNA in serum
ix. Low alpha-1-antitrypsin level and ZZ phenotype (both determined at the discretion of the investigator)
x. Wilson's disease
xi. Known glycogen storage disease
xii. Known dysbetalipoproteinemia
xiii. Known phenotypic hemochromatosis (HII greater than 1.9 or removal of more than 4 g of iron by phlebotomy)
xiv. Prominent bile duct injury (florid duct lesions or periductal sclerosis) or bile duct paucity
xv. Chronic cholestasis
xvi. Vascular lesions (vasculitis, cardiac sclerosis, acute or chronic Budd-Chiari, hepatoportal sclerosis, peliosis)
xvii. Iron overload greater than 3+
xviii. Zones of confluent necrosis, infarction, massive or sub-massive, pan-acinar necrosis
xix. Multiple epithelioid granulomas
xx. Congenital hepatic fibrosis
xxi. Polycystic liver disease
xxii. Other metabolic or congenital liver disease
xxiii. Evidence of systemic infectious disease
xxiv. Known HIV positive
xxv. Disseminated or advanced malignancy
xxvi. Concomitant severe underlying systemic illness that in the opinion of the investigator would interfere with completion of potential follow-ups
xxvii. Active drug use or dependence that, in the opinion of the study investigator, would interfere with adherence to study requirements

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xxviii. Any other condition, which in the opinion of the investigator would impede compliance or hinder completion of study
xxix. Inability to provide informed consent

Supplementary material: Results

Table 1. Cross-tabulation of the number of patients in UCSD-NAFLD Cohort and Japan-NAFLD Cohort comparing the MEFIB Index, MRE≥3.3kPa and FIB-4≥1.6, with liver biopsy.

		≥ stage 2 fibrosis*		
		Positive	Negative	Total
UCSD-NAFLD Cohort	Positive†	34	1	35
	Negative	34	169	203
	Total	68	170	238
Japan-NAFLD Cohort	Positive†	81	8	89
	Negative	54	79	133
	Total	135	87	222

***** NASH CRN histology scoring system was used.

†determined by categorizing a positive response as MRE ≥ 3.3kPa and FIB-4 ≥ 1.6 vs any other combination

Table 2. Diagnostic test characteristic of MRE, FIB-4, and MRE+FIB-4 in detecting ≥ stage 2 fibrosis in the Japan-NAFLD Cohort

	Japan-NAFLD Cohort			
Model:	AUROC (95% CI)	p-value*	PPV‡	NPV
MRE ≥ 3.0 kPa†	0.81 (0.75-0.86)	ref	82.6	83.2
FIB-4 ≥ 1.6†	0.73 (0.68-0.79)	**0.0324**	84.6	60.2
MRE ≥ 3.0 kPa + FIB-4 ≥ 1.6	0.85 (0.80-0.90)	**0.0042**	89.5	60.6

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; MRE, magnetic resonance elastography, FIB-4, fibrosis – 4

*p-value for comparison to MRE alone

†cut-points have been recalculated using the Youden's Index from the Japan-NAFLD Cohort

‡ determined by categorizing a positive response as MRE ≥ 3.0kPa and FIB-4 ≥ 1.6 vs any other combination