Fast™

Scores by echosens
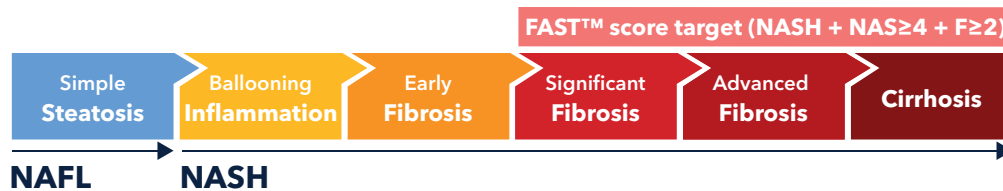
Identification of at-risk NASH patients

The burden of non-alcoholic fatty liver disease (NAFLD) is increasing globally. One of the major priority is to identify patients with non-alcoholic steatohepatitis (NASH) who are at greater risk of progression to cirrhosis and who will be candidates for clinical trials and emerging new pharmacotherapies.

Target

FAST™ score target (NASH + NAS≥4 + F≥2)

Simple **Steatosis**	Ballooning **Inflammation**	Early **Fibrosis**	Significant **Fibrosis**	Advanced **Fibrosis**	**Cirrhosis**

NAFL   **NASH**

Construction

FibroScan® by echosens

LSM by VCTE™

FIBROSIS

AST

STEATOSIS

INFLAMMATION

CAP™

Performance

- Good to excellent performance in derivation cohort as well as in external validation cohorts from different clinical settings (NAFLD tertiary care unit, screening, bariatric surgery) and geographical origins (USA, Europe, Asia)

Fast™

CAP [dB/m]	E [kPa]	AST [U/L]
238	15.1	35

Fast = 0.36
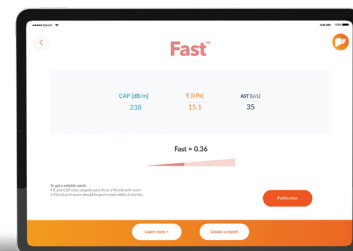
Formula is public with a free calculator available on myFibroScan app

myFibroScan

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Free app

📖 **References:**

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LSM: Liver Stiffness Measurement /AST: Aspartate Aminotransferase

CE

Publication (Lancet Gastroenterol Hepatol 2020)

FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study

P.N. Newsome, M. Sasso, J.J. Deeks, A. Paredes, J. Boursier, W.K. Chan, Y. Yilmaz, S. Czernichow, M.H. Zheng, V.W. Wong, M. Allison, E. Tsochatzis, Q.M. Anstee, D.A. Sheridan, P.J. Eddowes, I.N. Guha, J.F. Cobbold, V. Paradis, P. Bedossa, V . Miette, C. Fournier-Poizat, L. Sandrin, S.A. Harrison

	Derivation cohort (UK NAFLD)	French bariatric surgery cohort	USA screening cohort	China Hong-Kong NAFLD cohort	China Wenzhou NAFLD cohort	French NAFLD cohort	Malaysian NAFLD cohort	Turkish NAFLD cohort	Pooled external cohort
N Patients	**350**	**110**	**242**	**83**	**104**	**182**	**176**	**129**	**1026**
AUROC [95% CI]	0.80	0.95	0.86	0.85	0.84	0.80	0.85	0.74	0.85
Rule out cut-off	≤0.35								
% patients	32%	63%	80%	34%	53%	37%	44%	20%	51%
Se/Sp	0.90/0.53	1/0.73	0.64/0.86	0.94/0.55	0.89/0.56	0.88/0.56	0.94/0.54	0.91/0.35	0.89/0.64
NPV	0.85	1	0.95	0.93	0.98	0.87	0.97	0.73	0.94
Indeterminate	0.35 – 0.67								
% patients	39%	20%	16%	35%	36%	38%	34%	44%	30%
Rule in cut-off	≥0.67								
% patients	29%	17%	4%	31%	11%	24%	22%	36%	19%
Se/Sp	0.90/0.48	0.93/0.75	0.99/0.25	0.89/0.58	0.92/0.44	0.89/0.45	0.87/0.58	0.82/0.49	0.92/0.49
PPV	0.83	0.63	0.78	0.81	0.33	0.76	0.54	0.78	0.69

Se Sensitivity/Sp Specificity/NPV Negative Predictive Value/PPV Positive Predictive Value

ILC 2019

A FibroScan-based score : FAST™, combining liver stiffness, controlled attenuation parameter and AST can efficiently screen for presence of at risk fibrotic NASH

S.Harrison, J. Whitehead, V. Paradis, P. Bedossa , A. Paredes

BACKGROUND & AIMS: Given the increased need to identify NASH patients with fibrosis in drug development, Echosens has developed a score to identify patients with NASH+NAS≥4+F≥2. The score combined the FibroScan liver stiffness measurement (LSM), controlled attenuation parameter (CAP) and AST. The objective was to assess its performance in a cohort of patients screened for NAFLD.

METHODS: Patients were screened for NAFLD in one American center. Patients with MRI-PDFF≥5% or liver inflammation and fibrosis score (LIF)≥2 or FibroScan LSM≥7kPa or MRE LSM≥3kPa were advised to undergo a liver biopsy (LB). The performance of the score was assessed using area under the receiver operating characteristics (AUC).

RESULTS: 510 patients were included in the analysis: 240 with LB and 270 with no LB (all 4 liver imaging modalities "normal" (below the predefined cutoffs)). 50% of were female, median age was 56 [IQR=10] years and BMI was 30.3 [7.3] kg/m2. At LB, 37 (15%) patients had at F≥2, 91 (38%) had NASH and 27 (11%) had a NASH+NAS≥4+F≥2. Of note, 7 (3%) had F≥2 but no NASH and 3 (1%) had NASH, F≥2 and NAS≥4. Cutoffs value for a sensitivity (Se) and specificity (Sp) ≥0.90 and associated diagnostic metrics are provided in Table 1. AUC for the score to detect NASH+NAS≥4+F≥2 was 0.88 (0.81-0.94) and significantly outperforming FibroScan LSM (0.77 (0.68-0.86), p=0.006), CAP (0.71 (0.63-0.80), p<10-3) and AST (0.76 (0.66-0.86), p=0.004) alone. Using the lower cutoff, 97 patients (19% of the population) would have been sent for referral. Among those patients, 26% were NASH+NAS≥4+F≥2, 69% weren't and 5% had normal imaging modalities. Using the higher cutoff, 38 patients (7% of the population) would have been sent for referral. Among those patients 42% were NASH+NAS≥4+F≥2, 55% weren't and 3% had normal imaging modalities. With the hypothesis that patients with normal imaging were not NASH+NAS≥4+F≥2, prevalence of NASH+NAS≥4+F≥2would drop to 5%. Corresponding positive and negative value (PPV/NPV) of the score would be 0.26/99.5 for the lower cutoff and 0.42/97.7 for the higher cutoff.

CONCLUSION: A simple score based on FibroScan LSM, CAP and AST can be used to efficiently identify patients eligible for potential pharmacologic therapy.
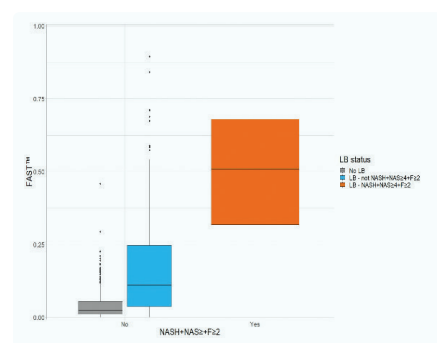
ILC 2020

Validation of FibroScan®-asparate aminotransferase based score to detect at risk non-alcoholic steatohepatitis in a large North American non-alcoholic fatty liver disease cohort.

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BACKGROUND & AIMS: An unmet need for management of patients with nonalcoholic fatty liver disease (NAFLD) is an accurate non-invasive tool to identify the NAFLD patients who have "at risk" nonalcoholic steatohepatitis (NASH) – the type of NASH puts patients at risk for progression to cirrhosis. The FAST (FibroScan®-aspartate aminotransferase [AST]) score was recently developed and validated in 7 external cohorts (n=1026) and showed moderate diagnostic accuracy for "at risk" NASH (AUROC=0.85). Our aims were to: (1) evaluate the diagnostic accuracy of the FAST score in a large North American NAFLD cohort, the NIH/NIDDK's NASH Clinical Research Network (NASH CRN) and (2) to determine whether the FAST diagnostic accuracy differs by patient subgroups or FibroScan® exam features.

METHODS: We conducted a cross-sectional study in 585 adults with biopsy-confirmed NAFLD. We defined "at risk NASH", as patients with NASH who had a NAFLD Activity Score (NAS) ≥4 and a fibrosis stage ≥2, as determined using the NASH CRN's centrally-graded histology panel. We calculated FAST score using liver stiffness (E kPa), steatosis (controlled attenuation parameter [CAP] dB/m), and AST (U/L) in the formula provided by Echosens; we also used the provided FAST-based "Rule-Out" (sensitivity = 90%) and "Rule-In" (specificity =90%) zones defined by FAST cut-points = 0.35 and 0.67 respectively. The primary measure of accuracy was

area-under-the-Receiver-Operating-Characteristic (AUROC). We also calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the cut-points above in the NASH CRN cohort. We repeated the above for subgroups of patients defined by gender, age, race, obesity, diabetes and dyslipidemia status, FibroScan® exam probe, and quality criteria.

RESULTS: Our sample of 585 adults was 38% male, 79% white, 14% Hispanic, and had mean (range) age = 51 (18-77) yrs, ALT = 66 (13-351) U/L, and AST = 50 (11-368) U/L, 73% with obesity). A total of 214 (37%) had "at risk" NASH. The AUROC for the FAST score for "at risk" NASH was 0.81 (95% CI: 0.77, 0.84). Using the "rule out at-risk NASH" cut-off, the sensitivity, specificity, PPV and NPV were 0.91, 0.50, 0.51 and 0.90, respectively. Using the "rule in at-risk NASH" cut-off, the sensitivity, specificity, PPV and NPV were 0.51, 0.87, 0.69 and 0.76, respectively. The performance of the FAST score was higher in non-whites vs. whites (AUROC: 0.91 vs 0.78; p=0.0002) and inversely related to obesity status (AUROC: 0.94 in normal, 0.84 in overweight, and 0.78 in both obese and morbid obese; p=0.04). No differences were observed by other patient demographics, co-morbidities, size of probe or unreliability of measurement.

CONCLUSION: We validated moderate accuracy of Fibroscan®-based FAST score for diagnosing "at risk" NASH, in a large, multi-racial population from North America. Future studies are needed to further examine the usefulness of the FAST score or its variants to track changes in histological outcomes over time.