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

Simple Steatosis  Ballooning Inflammation  Early Fibrosis  Significant Fibrosis  Advanced Fibrosis  Cirrhosis

NAFL  NASH

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

Construction

LSM by VCTE™  AST  FIBROSIS

STEATOSIS  INFLAMMATION

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)

References:
• Newsome P.N. et al., 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. Lancet Gastroenterology & Hepatology 2020
• Anand et al., FibroScan-AST score in an Asian cohort of NAFLD and its utility in predicting histological resolution with bariatric surgery. J Gastroenterol Hepatol 2020
• Blank et al., Current NAFLD guidelines for risk stratification in diabetic patients have poor diagnostic discrimination. Sci Rep 2020
• Eslam et al., The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease, Hepatology International, 2020
• Puri et al., Use of FibroScan-AST Score to Stratify High-Risk Nonalcoholic Steatohepatitis in US Veterans. Clinical gastroenterology and Hepatology 2020
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• Oeda, S. et al., Diagnostic accuracy of FibroScan-AST score to identify non-alcoholic steatohepatitis with significant activity and fibrosis in Japanese patients with non-alcoholic fatty liver disease: Comparison between M and XL probes. Hepatol Res, 2020
• Oh et al., Weight-loss-independent benefits of exercise on liver steatosis and stiffness in Japanese men with NAFLD. JHEP Reports, 2021

LSM: Liver Stiffness Measurement / AST: Aspartate Aminotransferase
A FibroScan-based score: FastTM, combining liver stiffness, controlled attenuation parameter and AST can efficiently screen for presence of at risk fibrotic NASH

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 females, median age was 56 (IQR=10) years and BMI was 30.3 (7.3) kg/m2. At LB, 37 (15%) patients had at F2, 91 (38%) had F37 and 27 (11%) had a NASH+NAS=4+F2. 60% of note, 7 (3%) had F2 but no NASH and 3 (1%) had NASH, F2 and NAS4. 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+NAS4+F2 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<0.05) and AST (0.76 (0.66-0.86), p<0.004) alone. Using the lower cutoff, 97 patients (11% of the population) would have been sent for referral. Among those patients, 20% were NASH+NAS4+F2, 7% were NAS4+NAS2+F2, 7% were NAS4+F4, and 5% had normal imaging modalities. With the higher cutoff, 38 patients (% of the population) would have been sent for referral. Among those patients, 2% were NASH+NAS4+F2, 5% were NAS4+NAS2+F2, 5% were NAS4+F4, and 5% had normal imaging modalities. With the hypothesis that patients with normal imaging were not NASH+NAS4+F2, prevalence of NASH+NAS4+F2would 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®-aspartate aminotransferase based score to detect at risk non-alcoholic steatohepatitis in a large North American cohort of non-alcoholic fatty liver disease cohort.

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 out 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: 0.94 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.