Guidance Statement

9. AASLD suggests against the use of blood-based NILDA to detect steatosis in pateints with NAFLD (ungraded statement).

TECHNICAL REMARKS

- In adult patients with CLD, Controlled attenuated parameter (CAP) and MRI can reliably quantify the degree of steatosis. MRI-PDFF and MRS have excellent correlation with histology for detecting and grading steatosis and can be used as reference standards.[3]
- Steatosis, independent of fibrosis, is associated with increased systemic inflammation and has prognostic importance as a predictor of cardiovascular disease, DM, and, in severe cases, liver-related mortality.
- Patients with chronic liver disease associated with steatosis other than NASH, such as chronic HCV genotype 3, have not been well-studied.
- The available evidence is insufficient to make a recommendation as to which noninvasive test(s) or algorithm(s) should be used, compared with others, to assess steatosis.
- There is insufficient evidence to recommend blood tests as clinical endpoints to monitor changes in steatosis, independent of fibrosis over time.
- There is insufficient evidence to make a recommendation regarding a specific blood-based test or algorithm to use in combination with imaging-based testing for the assessment of steatosis.
- Because BMI is included in many of the indices, caution is necessary when using NILDA to assess steatosis in patients who have undergone bariatric surgery.

BACKGROUND

Although liver fibrosis assessment has been the focus of noninvasive tests in liver diseases, steatosis is also important in the assessment of disease severity in NAFLD. Histologically, steatosis (S) is graded 0 to 3 based on the proportion of hepatocytes that contain fat as follows: S0 (<5%), S1 (5%–33%), S2 (34%–66%), and S3 (>66%) steatosis (Table 3).[21,22] In addition to liver-related outcomes in NASH (decompensation, HCC),[198,199] steatosis is associated with systemic inflammatory markers,[200,201] DM,[202–204] the metabolic syndrome,[205] cardiovascular disease,[203,204,206–209] and atherosclerosis.[210] Several noninvasive algorithms have been developed to assess steatosis using biochemical and clinical variables.[211,212] Although many steatosis algorithms have been developed or validated based on ultrasound (US)[202,213–219] several have utilized histologic[182,217–221] or MR-based assessments[205,222,223] as the reference standard (Table 9). However, there are limited data to support longitudinal assessments of steatosis using these algorithms.[25]

EVIDENCE AND RATIONALE

Most algorithms include standard liver-related blood tests (AST, ALT, bilirubin, GGT), blood tests associated with hyperlipidemia (triglycerides [TG], cholesterol), and conditions associated with steatosis (DM, increased BMI, increased waist circumference [WC], and the metabolic syndrome) in some combination (Table 9). Of note, some algorithms differ by sex. Table 10 summarizes the performance and cutoffs for algorithms to assess steatosis.[202,205,217–223,225–227,229–232]

Fatty liver index (FLI)

This algorithm utilizes TG, BMI, WC, and GGT. Although initially developed in comparison to conventional B-mode US,[214,217] FLI has also been validated against liver histology and MRI.[205,218,219,221,230,233] Depending on the cutoff, studies have shown sensitivity ranges from 44% to 100%, whereas specificity ranged from 3% to 91% with AUROC 0.59 to 0.86. Furthermore, a FLI modified for North American patients (compared with non-North American patients) and including age, race and ethnicity, fasting insulin, and glucose seemed to perform better in a US population.[234]

Hepatic steatosis index (HSI)

This algorithm includes AST, ALT, BMI, and GGT. Although initially developed in a cohort compared with US,[213] HSI has also been validated against liver histology and MRI.[204,218,221,230] Depending on the cutoff, HSI had a sensitivity ranging from 7% to 88%, specificity ranging from 9% to 93%, and AUROC 0.49 to 0.81. One advantage of HSI is its simplicity because it uses routine tests and does not require additional factors such as WC or insulin resistance to be measured. However, one limitation is that those with increased BMI, especially if over age