Contemporary Assessment of Hepatic Fibrosis

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KEYWORDS

• Liver biopsy • Cirrhosis • Hepatitis • Non-alcoholic fatty liver disease

KEY POINTS

- Noninvasive tests now enable the clinician to successfully stage and monitor a wide variety of liver diseases and have significantly reduced the need for liver biopsy.
- The evaluation of liver fibrosis is of major importance for the management of chronic liver disease and the prediction of prognosis, as complications occur in patients with advanced fibrosis stages.
- Progression to cirrhosis is associated with a risk of liver-related complications, hepatocellular carcinoma, and mortality.

INTRODUCTION

The evaluation of liver fibrosis is of major importance for the management of chronic liver disease and the prediction of prognosis, as complications occur in patients with advanced fibrosis stages. Progression to cirrhosis is associated with a risk of liver-related complications, hepatocellular carcinoma (HCC), and mortality.

Liver biopsy is currently the gold standard in assessing liver histology. Although percutaneous liver biopsy is in general a safe procedure, it is costly and does carry a small risk for complication. In addition, there could be sampling error, because only 1/50,000 of the organ is sampled.[1] Furthermore, inter- and intraobserver discrepancies are around 10% to 20% in assessing hepatic fibrosis, which may lead to understaging of cirrhosis.[2] Noninvasive approaches to assess histology in patients with chronic liver diseases include clinical symptoms and signs, routine laboratory tests, serum markers of fibrosis and inflammation, quantitative assays of liver function, and radiologic imaging studies. However, at present, none of these tests or markers alone is accurate or reliable in predicting histology, in particular, liver fibrosis. An ideal noninvasive diagnostic test for hepatic fibrosis should be simple, readily available,

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inexpensive, and accurate. Herein, are reviewed the serologic tests such as AST (aspartate aminotransferase)-to-Platelet Ratio Index (APRI), Fibrometer, FibroTest, HepaScore, FIB-4 and the radiologic tests inclusive of vibration-controlled transient elastography (VCTE) and magnetic resonance elastography.

NONINVASIVE TESTS FOR HEPATIC FIBROSIS

Aspartate Aminotransferase-to-Platelet Ratio Index

The APRI is clinically best applied for the diagnosis or exclusion of cirrhosis alone. It does not give a linearity of scale allowing for intermediate disease staging. APRI is derived from the following formula: (AST/[AST upper limit of normal])/platelet count (10^9/L) $\times$ 100. Patients with APRI of 0.50 or less are unlikely to have significant cirrhosis, while in those with an APRI greater than 1.50, significant fibrosis is much more likely.[3] The area under the receiver operating curve (AUROC) of APRI for predicting significant fibrosis and cirrhosis is 0.80 and 0.89, respectively.

FIB-4

FIB-4 is a freely available test that utilizes the following formula: age (years) x AST [U/L]/platelets [10^9/L] x ALT (alanine aminotransferase) [U/L $^1/_2$].[4] FIB-4 correctly identifies patients with severe fibrosis (F3-F4) and cirrhosis with an AUROC of 0.85 (95% confidence interval [CI] 0.82–0.89) and 0.91 (95% CI 0.86–0.93). A threshold value of less than 1.45 has a negative predictive value for the exclusion of extended fibrosis (F4-F6 in the Ishak classification) of 90%. Similar issues of lack of linearity with FIB-4 as compared to APRI are applicable.

Nonalcoholic Fatty Liver Disease Fibrosis Score

The NAFLD (nonalcoholic fatty liver disease) Fibrosis Score is a freely available algorithm derived from an international validation study of 733 patients with NAFLD.[5] This score is based on a formula that incorporates age, hyperglycemia, body mass index (BMI), platelet count, albumin, and AST/ALT ratio. Using an online calculator, clinicians may input these variables to generate a continuous score. By applying a cutoff of -1.455, advanced fibrosis may be excluded, with a negative predictive value (NPV) of 88%. Conversely, by applying a cutoff of 0.676, the presence of advanced fibrosis may be predicted, with a positive predictive value (PPV) of 82%.

Fibrometer

The Fibrometer is a patented test that incorporates into an algorithm the following parameters: alpha-2-macroglobulin, ALT, AST, gamma glutamyl transpeptidase (GGT), prothrombin index, and urea.[6] The AUROC discerning fibrosis stage (F2-F4) is 0.892. It is reported as a value between 0 and 1 corresponding to the probability of advanced fibrosis and demonstrates a linearity of score across fibrosis stages.

FibroTest/Fibrosure

Developed by Poynard and colleagues,[7] FibroTest/Fibrosure (Biopredictive, Paris, France) is a patented algorithm using the combination of 5 serum biochemical parameters (α-2-macroglobulin, apolipoprotein A1, haptoglobin, L-glutamyltranspeptidase, and bilirubin). This test is reported as a linear score. As a result, it can risk stratify patients for mild disease F0-1 and for cirrhosis. Additionally, the probability of having any stage of disease is also given with the test result, so it may be used for making treatment decisions for direct-acting antiviral (DAA) therapy. Clear advantages of FibroTest/Fibrosure include widespread availability, interlaboratory reproducibility, and limited contraindications (<5%). The AUROC ranges from 0.73 to 0.87 for stages