A Clinical Review of Noninvasive Tests for Hepatic Fibrosis

Nikita Chadha, DO, and Richard K. Sterling, MD, MSc

Department of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University Health System, Richmond, Virginia

Corresponding author:
Dr Richard K. Sterling
1200 E. Broad Street
West Hospital, Room 1478
Richmond, VA 23298-0341
Tel: (804) 828-9034
Fax: (804) 828-5348
E-mail: Richard.sterling@vcuhealth.org

Abstract: Identifying hepatic fibrosis is paramount in managing patients with chronic liver disease. The etiology of liver disease can be owing to many factors, including chronic viral hepatitis, steatotic liver diseases such as alcohol-associated liver disease or metabolic dysfunction-associated steatotic liver disease, autoimmune hepatitis, and cholestatic liver diseases. Currently, invasive liver biopsy with histopathologic evaluation is the gold standard; however, noninvasive tests are becoming more prevalent, especially because they do not carry the risks of invasive procedures such as biopsy. This article reviews noninvasive tests for fibrosis, separating them into blood-based and imaging-based tests.

Keywords
Chronic liver disease, elastography, hepatic fibrosis, metabolic dysfunction-associated steatotic liver disease, noninvasive tests

Hepatic fibrosis develops as a mechanism of healing in response to an injury in chronic liver disease.[1] The etiology of liver disease can be attributed to many factors, including chronic viral hepatitis owing to hepatitis B virus (HBV) or hepatitis C virus (HCV), steatotic liver diseases such as alcohol-associated liver disease or metabolic dysfunction-associated steatotic liver disease (MASLD; formerly known as nonalcoholic fatty liver disease [NAFLD]) and metabolic dysfunction-associated steatohepatitis (MASH; formerly known as nonalcoholic steatohepatitis [NASH]), autoimmune hepatitis, and cholestatic liver diseases.[2] An ongoing injury resulting in a sustained wound-healing response can lead to advanced stages of fibrosis and even cirrhosis with sequela of portal hypertension.[3] Fibrosis can be reversible unless the insult is persistent and the progressive inflammation leads to cirrhosis.[2] Diagnosis of fibrosis is important not only for identification of its presence but also to stratify its degree into 1 of 3 categories: significant fibrosis (SF; F2-F4), advanced fibrosis (AF; F3-F4), and cirrhosis (F4). Assessment of liver fibrosis can be performed via invasive or noninvasive testing. Currently, invasive liver biopsy with histopathologic evaluation is the gold standard; however, noninvasive tests (NITs) are integral to clinical practice and do not carry the risks of invasive procedures such as biopsy.[4] This article reviews both blood-based and imaging-based NITs for fibrosis.

Blood-Based Tests

Blood-based tests are one of the mainstays of NITs for liver fibrosis. In comparison with liver biopsy, the advantages of blood-based tests include safety, cost, and availability.[5] Blood-based tests use serum laboratory values as surrogates when assessing patients for fibrosis and can be separated into indirect and direct markers. This article focuses on indirect markers, which include both blood- and imaging-based tests as surrogates for sequela of portal hypertension. Serologic markers for blood-based tests include, but are not limited to, aminotransferases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]), prothrombin time, platelet count, gamma-glutamyl transpeptidase (GGT), and albumin. Many algorithms have been created and validated for certain etiologies of underlying liver disease.[5] The most commonly used and validated blood-based tests for fibrosis include the Fibrosis-4 (FIB-4) index, AST to Platelet Ratio Index (APRI), NAFLD Fibrosis Score (NFS), FibroSure, and Enhanced Liver Fibrosis (ELF) test. Because most studies in steatotic liver disease were done prior to the recent nomenclature change to MASLD and MASH, the terms NAFLD and NASH are used when referring to the existing literature.

Fibrosis-4 Index

The FIB-4 algorithm includes age, AST, ALT, and platelet count. The FIB-4 index was originally created to assess the degree of fibrosis in a cohort of patients with HCV and HIV.[6] However, it has been well validated among other etiologies of fibrosis or cirrhosis, including HCV monoinfection, HBV, and NAFLD.[7-10]

de Oliveira and colleagues assessed the utility and limitations of the FIB-4 index in a population with HCV using the cutoffs of no more than 1.45 and at least 3.27.[10] They stratified the diagnostic accuracy of APRI and FIB-4 stage of fibrosis as follows: SF (≥F2), AF (F3-F4), and cirrhosis (F4). The area under the receiver operating curve (AUROC) with 95% CI by degree of fibrosis was 0.803 (95% CI, 0.771-0.836) for SF, 0.836 (0.805-0.866) for AF, and 0.852 (0.821-0.883) for cirrhosis.[10] The FIB-4 index has also been evaluated in patients with HBV. Kim and colleagues identified that the FIB-4 index was statistically significant (P<.001) in distinguishing between F0 to F1 vs F2 to F4, F0 to F2 vs F3 to F4, and F0 to F3 vs F4.[7] Furthermore, the AUROC for predicting fibrosis in patients with chronic HBV was 0.865 (95% CI, 0.835-0.895) for SF (≥F2), 0.910 (95% CI, 0.888-0.933) for AF (≥F3), and 0.926 (95% CI, 0.907-0.945) for cirrhosis (F4).[7] The FIB-4 index has also been studied for predicting outcomes and management in patients with NAFLD, with increasing FIB-4 cutoffs correlating with higher risk.[11,12] The index has been recommended as a screening tool to identify NAFLD in the primary care population as well as for excluding advanced degrees of fibrosis and evaluating prognosis.[9,13] For patients with NAFLD, a FIB-4 score greater than 1.3 was found to be superior in comparison with 7 other noninvasive markers of fibrosis with an AUROC of 0.802 (95% CI, 0.758-0.847) for detection of AF.[14] The FIB-4 index has also been assessed for identifying fibrosis in alcohol-associated liver disease. Chrostek and Panasiuk found that the FIB-4 index has an AUROC of 0.70 (95% CI, 0.62-0.76) when diagnosing F2 to F4 in comparison with F0 to F1 and an AUROC of 0.80 (95% CI, 0.72-0.86) for diagnosing F4 in comparison with F0 to F3.[15] In reviewing the accuracy of the FIB-4 index, it is important to keep in mind that studies may use different cutoffs, which may make comparison challenging.

As with any age-based index, the FIB-4 index does not perform as well in young patients (aged <30 years) compared with older patients (aged >65 years). Li and colleagues evaluated the impact of age on the accuracy of APRI and the FIB-4 index and observed that they have better diagnostic performance in patients older than 30 years compared with patients younger than 30 years.[16] The authors recommend using different cutoffs for these age groups; however, the best cutoff for these populations is not defined.[16]

Aspartate Aminotransferase to Platelet Ratio Index

The APRI algorithm includes AST, the upper limit of normal of AST, and platelet count. APRI was originally created with the intention of being a low-cost method of assessing fibrosis in patients with chronic HCV using routine laboratory work.[17]

de Oliveira and colleagues assessed the accuracy of APRI (in addition to the FIB-4 index, as previously discussed) in identifying the degree of fibrosis in patients with HCV and used the cutoffs of no more than 0.5 and at least 1.50.[10] The AUROC by degree of fibrosis for APRI was 0.809 (95% CI, 0.776-0.841; P<.001) for SF, 0.819 (95% CI, 0.788-0.851; P<.001) for AF, and 0.815 (95% CI, 0.781-0.849; P<.01) for cirrhosis.[10] A meta-analysis from 2012 identified 9 studies with a total of 1798 patients that described the utility of APRI in patients with HBV-associated fibrosis. The authors found that the AUROC was 0.79 for SF (F2-F4) and 0.75 for cirrhosis (F4).[18] Given that the average AUROC for detection of both SF and cirrhosis in a population with HBV was less than 0.8, this meta-analysis concluded that APRI may not be a useful tool to detect the degree of fibrosis in patients with HBV. Rigor and colleagues evaluated the utility of multiple NITs in NAFLD to detect AF (≥F3) in a Portuguese population with a total of 121 patients across 2

Table 1. Noninvasive Blood-Based Tests Stratified by Underlying Etiology of Liver Disease

		Fibrosis-4 index	AST to Platelet Ratio Index	NAFLD Fibrosis Score	FibroSure	Enhanced Liver Fibrosis test
	Test components	Age, ALT, AST, platelet count	AST, upper limit of normal of AST, platelet count	Age, BMI, diabetes, AST/ALT ratio, platelet count, albumin	Total bilirubin, gamma-glutamyl transferase, α2-macroglobulin, apolipoprotein A1, haptoglobin, ALT	Tissue inhibitor of metalloproteinase 1, amino-terminal propeptide of type III procollagen, hyaluronic acid
HCV (AUROC with 95% CI)	**Study**	de Oliveira et al[10] (2016)	de Oliveira et al[10] (2016)	N/A	Poynard et al[25] (2004)	Crespo et al[28] (2012)
	Significant fibrosis	0.803 (0.771-0.836)	0.809 (0.776-0.841)	N/A	0.73-0.87	N/A
	Advanced fibrosis	0.836 (0.805-0.866)	0.819 (0.788-0.851)	N/A	N/A	0.764
	Cirrhosis	0.852 (0.821-0.883)	0.815 (0.781-0.849)	N/A	N/A	0.841
HBV (AUROC with 95% CI)	**Study**	Kim et al[7] (2010)	Jin et al[18] (2012)	N/A	Salkic et al[4] (2014)	Trembling et al[29] (2014)
	Significant fibrosis	0.865 (0.835-0.895)	0.79 (95% CI not provided)	N/A	N/A	0.77
	Advanced fibrosis	0.910 (0.888-0.933)	N/A	N/A	0.84	≥F2=0.82 ≥F3=0.80
	Cirrhosis	0.926 (0.907-0.945)	0.75	N/A	0.87	0.83
NAFLD (AUROC with 95% CI)	**Study**	Shah et al[14] (2009)	Rigor et al[8] (2022)	Adams and Chan[20] (2020), Xiao et al[21] (2017)	Ratziu et al[24] (2006)	Vali et al[30] (2020)
	Significant fibrosis	N/A	N/A	0.72 (0.65-0.79)	N/A	N/A
	Advanced fibrosis	0.802 (0.758-0.847)	0.80	0.78 (0.75-0.81)	0.81 (0.74-0.86)	0.83 (0.71-0.90)
	Cirrhosis	N/A	N/A	0.83 (0.76-0.89)	0.88 (0.82-0.92)	N/A
ALD (AUROC with 95% CI)	**Study**	Chrostek and Panasiuk[15] (2014)	N/A	N/A	Naveau et al[26] (2005)	N/A
	Significant fibrosis	N/A	N/A	N/A	N/A	N/A
	Advanced fibrosis	0.70 (0.62-0.76)	N/A	N/A	0.84 (0.81-0.87)	N/A
	Cirrhosis	0.80 (0.72-0.86)	N/A	N/A	0.95 (0.94-0.96)	N/A

ALD, alcohol-associated liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AUROC, area under the receiver operating curve; BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease; N/A, not applicable.

centers.[8] They found that APRI had an AUROC of 0.8 and performed well at detecting AF.[8]

Nonalcoholic Fatty Liver Disease Fibrosis Score

Angulo and colleagues identified age, hyperglycemia, body mass index, platelet count, albumin, and AST/ALT ratio as independent indicators for AF, hence giving rise to NFS.[19] NFS is a validated scoring system that uses routine objective data to distinguish between patients with and without AF in a population with underlying NAFLD.[19]

In a meta-analysis, NFS was found to have an AUROC of 0.84 for the diagnosis of AF in patients with underlying NAFLD. Broken down by the degree of fibrosis, the AUROC for NFS was 0.72 (95% CI, 0.65-0.79) for SF, 0.78 (95% CI, 0.75-0.81) for AF, and 0.83 (95% CI, 0.76-0.89) for cirrhosis. The cutoffs used were less than -1.455 and greater than 0.676.[20,21] Although NAFLD is commonly associated with metabolic syndrome, it is important to note that there are 2 types of NAFLD: lean and nonlean. A large prospective study identified that lean individuals had a higher rate of AF and poor outcomes related to underlying liver disease compared with nonlean patients with NAFLD (patients who are overweight or obese). This distinction further drives the importance of accurate detection of fibrosis.[22]

FibroSure

FibroSure is a proprietary blood-based algorithm comprised of 6 biochemical markers, including total bilirubin, GGT, α2-macroglobulin, apolipoprotein A1, and haptoglobin, which are corrected for age and sex. FibroSure was created with wide applicability; however, it is noted to have limitations with comorbidities, including Gilbert syndrome, hemolysis, acute inflammation, and extrahepatic cholestasis.[4,23,24]

FibroSure had an AUROC ranging from 0.73 to 0.87 for detecting SF in patients who have HCV.[25] A 2014 meta-analysis of 16 studies including 2494 patients reviewed the accuracy of FibroSure for predicting fibrosis in patients with HBV. Across all studies that were reviewed, the AUROC was 0.84 for AF and 0.87 for cirrhosis.[4] FibroSure was also evaluated for validity in patients with NAFLD and had an AUROC of 0.81 (95% CI, 0.74-0.86) for AF (≥F2) and an AUROC of 0.88 (95% CI, 0.82-0.92) for bridging fibrosis or cirrhosis (F3-F4).[24] FibroSure demonstrated more accuracy evaluating for cirrhosis than advanced cirrhosis in patients with NAFLD. Finally, FibroSure has been evaluated in patients who have alcohol-associated liver disease. Naveau and colleagues found that FibroSure had an AUROC of 0.84 (95% CI, 0.81-0.87) for detecting AF (F2-F4) and an AUROC of 0.95 (95% CI, 0.94-0.96) for detecting cirrhosis (F4).[26]

Enhanced Liver Fibrosis Test

The proprietary ELF score was created to assess the degree of hepatic fibrosis in patients with liver disease. The ELF test is comprised of the following extracellular matrix markers: tissue inhibitor of metalloproteinase 1, amino-terminal propeptide of type III procollagen, and hyaluronic acid. Age and sex were identified as factors that influenced the score and need to be taken into consideration.[27]

Crespo and colleagues assessed the accuracy of the ELF test in detecting at least F2 fibrosis or cirrhosis and found AUROCs of 0.764 and 0.841, respectively.[28] The ELF test was also evaluated for accuracy in detecting fibrosis in patients with chronic HBV, with AUROCs by degree of fibrosis of 0.77 (≥F1), 0.82 (≥F2), 0.80 (≥F3), and 0.83 (≥F4).[29] This study compared the ELF test with transient elastography (TE) and found that TE outperformed the ELF test with AUROCs of 0.77 for the ELF test and 0.86 for TE to diagnose any degree of fibrosis. To some degree, it seems that the accuracy of the ELF test to assess the degree of fibrosis correlates with the severity of fibrosis for HBV. The ELF test performed similarly in patients with NAFLD. A systematic review found that the ELF test had an AUROC of 0.83 (95% CI, 0.71-0.90) for diagnosing AF (F3/F4).[30] A recent meta-analysis of 63 studies including 19,285 patients found considerable variability in the ELF test to stage fibrosis across disease etiologies with AUROCs (95% CI) of 0.811 (0.736-0.870), 0.812 (0.758-0.856), and 0.810 (0.694-0.888) to detect SF, AF, and cirrhosis, respectively.[31] The ELF test also has a role in assessing prognosis in patients with NASH and was the first NIT approved by the US Food and Drug Administration to do so for this patient population.[32,33]

Table 1 summarizes performances of the previously discussed blood-based tests for assessing degree of fibrosis by AUROC stratified by underlying etiology of liver disease, with a better performance being closer to 1.[34]

Imaging-Based Tests

Noninvasive imaging-based tests have similar advantages over liver biopsy as blood-based tests. However, imaging-based tests require facilities to be equipped with the appropriate technology as well as skilled professionals to perform the tests. Imaging-based tests also have limitations, including body habitus and acute hepatic inflammation. The most commonly used imaging-based tests include liver stiffness measurement (LSM) by vibration-controlled TE, shear wave elastography (SWE), and magnetic resonance elastography (MRE).[35] The following sections discuss the accuracy of the aforementioned tests stratified by underlying diagnosis.

Transient Elastography

TE is an imaging modality in which low-frequency shear waves are created by a probe that is adjacent to the skin, with different-sized probes available depending on body habitus. The velocity of the propagated wave correlates to the stiffness or elasticity of the liver, resulting in an LSM, which is a marker of hepatic fibrosis. With increasing degrees of fibrosis, the waves propagated by ultrasound have increased velocity. The resulting velocity of the wave is measured in kilopascals (kPa), and the validity of this measurement is assessed by the interquartile range (IQR) and number of successful measurements.[34] In addition to being a surrogate for measuring fibrosis, vibration-controlled TE (FibroScan) can measure hepatic steatosis by calculating the attenuation of the ultrasound signal in what is known as the controlled attenuation parameter.[36]

Siddiqui and colleagues reviewed the diagnostic accuracy of LSM in assessing the stage of fibrosis in a cohort of patients with NAFLD.[36] The authors identified the following median cutoffs: 7.4 kPa for differentiating F0 from F1 to F4, 10.5 kPa for differentiating F0 to F1 from F2 to F4, 10.5 kPa for differentiating F0 to F2 from F3 to F4, and 20.9 for differentiating F0 to F3 from F4. The IQR helps delineate the validity of the test as does the number of valid measurements obtained. It is recommended to have an IQR of less than 30% and at least 10 valid measurements for an accurate LSM.[37]

A study including 1270 patients from Egypt found that the AUROC for TE detecting fibrosis in patients with HCV was 0.906 (95% CI, 0.889-0.921) for F1, 0.829 (95% CI, 0.808-0.850) for F2, 0.925 (95% CI, 0.909-0.938) for F3, and 0.918 (95% CI, 0.902-0.932) for F4.[38] A study from 2010 by Sporea and colleagues compared LSM in patients with HBV with patients with HCV and found that TE was more statistically significant in identifying fibrosis in those with HCV compared with HBV.[39] The authors found that TE had an AUROC of 0.658 for identifying F2, 0.753 for F3, and 0.974 for F4.[39] Zhang and colleagues reviewed the performance of TE in patients with NAFLD and found that the AUROC was 0.82 for F1, 0.85 for F2, 0.94 for F3, and 0.96 for F4.[40] Nahon and colleagues evaluated 147 patients with alcohol-associated liver disease with fibrosis and cirrhosis.[41] The authors focused on patients with cirrhosis and found that patients with AF (F3-F4) had an AUROC of 0.94 (95% CI, 0.90-0.97) compared with patients with F1 to F2, and there was an AUROC of 0.87 (95% CI, 0.81-0.93) when comparing patients with cirrhosis (F4) with patients with all other stages of fibrosis.[41]

Shear Wave Elastography

SWE is another imaging-based noninvasive method to assess LSM as a surrogate for liver fibrosis. SWE is an ultrasound-based technique that generates shear waves with real-time imaging, and the elasticity or stiffness of the liver is measured indirectly by calculating the velocity of the propagated waves. Similar to TE, SWE can be impacted by food intake, edema, inflammation, extrahepatic cholestasis, and congestion, which must be considered when interpreting results.[42] Ferraioli and colleagues studied the accuracy of SWE to assess fibrosis in 121 patients with chronic HCV compared with TE and liver biopsy.[43] The authors found an AUROC of 0.92 (95% CI, 0.85-0.96) for F0 to F1 vs F2 to F4, 0.98 (95% CI, 0.94-1.00) for F0 to F2 vs F3 to F4, and 0.98 (95% CI, 0.93-1.00) for F0 to F3 vs F4. When comparing SWE with TE, this study demonstrated that real-time SWE was more accurate than TE in assessing SF.[43] SWE has also been studied in patients with chronic HBV. Gao and colleagues performed a large prospective study assessing the diagnostic performance of 2-dimensional SWE (2D SWE) using histology as a reference and compared it with TE and serum markers.[44] In comparison with serum markers, the authors found that 2D SWE had an AUROC of 0.87 (95% CI, 0.83-0.90) when evaluating for cirrhosis and an AUROC of 0.75 (95% CI, 0.70-0.79) for AF (≥F3). It was identified that 2D SWE performed better in evaluating for cirrhosis than advanced cirrhosis in patients with HBV.[44] For NAFLD, SWE performed well in assessing patients for AF and cirrhosis. In a meta-analysis, Jiang and colleagues found an AUROC of 0.86 (95% CI, 0.83-0.89) for SF (F2-F4), 0.94 (95% CI, 0.91-0.95) for AF (F3-F4), and 0.95 (95% CI, 0.93-0.97) for cirrhosis (F4).[45]

Magnetic Resonance Elastography

MRE is similar to the other imaging-based tests in that shear waves are produced by a probe abutted to the abdominal wall, which is followed by magnetic resonance imaging to capture the propagated waves. In a study evaluating 114 patients, Ichikawa and colleagues found that MRE was reliable in assessing the degree of fibrosis in patients with HCV.[46] The AUROC for degree of fibrosis was 0.984 (95% CI, 0.933-0.996) for at least F1, 0.986 (95% CI, 0.956-0.996) for at least F2, 0.973 (95% CI, 0.935-0.989) for at least F3, and 0.976 (95% CI, 0.945-0.990) for at least F4.[46] Dong and colleagues compared 2D SWE, MRE, and serum markers to assess the degree of fibrosis in patients with chronic HBV.[47] For MRE, the AUROC was 0.97 for SF, 0.94 for AF, and 0.97 for cirrhosis.[47] Additionally, Xiao and colleagues performed a meta-analysis of 64 articles and 13,046 patients reviewing the performance of blood-based and imaging-based tests for the diagnosis of fibrosis in patients with NAFLD.[21] The authors found an AUROC of 0.92 for MRE to detect SF, 0.96 to detect AF, and 0.97 to detect cirrhosis.[21]

Table 2. Noninvasive Imaging-Based Tests Stratified by Underlying Etiology of Liver Disease

		Vibration-controlled transient elastography	Shear wave elastography	Magnetic resonance elastography
HCV (AUROC with 95% CI)	**Study**	Abdelsameea et al[38] (2020)	Ferraioli et al[43] (2012)	Ichikawa et al[46] (2012)
	Significant fibrosis	F1=0.906 (0.889-0.921)	0.92 (0.85-0.96)	≥F1=0.984 (0.933-0.996)
	Advanced fibrosis	F2=0.829 (0.808-0.850) F3=0.925 (0.909-0.938)	0.98 (0.94-1.00)	≥F2=0.986 (0.956-0.996) ≥F3=0.973 (0.935-0.989)
	Cirrhosis	F4=0.918 (0.902-0.932)	0.98 (0.93-1.00)	≥F4=0.976 (0.945-0.990)
HBV (AUROC with 95% CI)	**Study**	Sporea et al[39] (2010)	Gao et al[44] (2018)	Dong et al[47] (2021)
	Significant fibrosis	N/A	N/A	0.97
	Advanced fibrosis	F2=0.658 F3=0.753	0.75 (0.70-0.79)	0.94
	Cirrhosis	F4=0.974	0.87 (0.83-0.90)	0.97
NAFLD (AUROC with 95% CI)	**Study**	Zhang et al[40] (2020)	Jiang et al[45] (2018)	Xiao et al[21] (2017)
	Significant fibrosis	F1=0.82	0.86 (0.83-0.89)	0.92
	Advanced fibrosis	F2=0.85 F3=0.94	0.94 (0.91-0.95)	0.96
	Cirrhosis	F4=0.96	0.95 (0.93-0.97)	0.97
ALD (AUROC with 95% CI)	**Study**	Nahon et al[41] (2008)	N/A	N/A
	Significant fibrosis	N/A	N/A	N/A
	Advanced fibrosis	0.94 (0.90-0.97)	N/A	N/A
	Cirrhosis	0.87 (0.81-0.93)	N/A	N/A

ALD, alcohol-associated liver disease; AUROC, area under the receiver operating curve; HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease; N/A, not applicable.

Table 2 summarizes the accuracy of imaging-based tests in assessing the degree of fibrosis by AUROC stratified by underlying etiology of liver disease.

Combining Blood-Based and Imaging-Based Noninvasive Tests

Although there are many individual NITs to assess the degree of fibrosis in patients with chronic liver disease, the accuracy of these tests varies when compared with each other and for underlying etiology of disease. To help improve accuracy, several combined test algorithms have been proposed.

A prospective study of 390 patients with chronic liver disease of different etiologies evaluated the combining of blood-based tests (APRI, the FIB-4 index, Hepascore, FibroTest [the name for FibroSure outside the United States], and FibroMeter) with LSM. The authors found that this combination improved accuracy of fibrosis and significantly decreased the need for biopsy.[48] Specifically for patients with NAFLD who had severe fibrosis, Petta and colleagues found that combining the FIB-4 index or NFS with LSM had good diagnostic accuracy and improved diagnostic performance to 69.8% to 70.1%.[49] Similarly, Pennisi and colleagues evaluated the accuracy of NITs in patients with NAFLD and type 2 diabetes mellitus.[50] The authors concluded that combination testing with the FIB-4 index or NFS followed by LSM had good accuracy for AF.[50] In patients with chronic HCV, Castéra and colleagues identified that combining TE and FibroTest/FibroSure yielded a confirmed diagnosis of 84% in patients with at least F2, 95% in those with at least F3, and 94% for F4 when compared with biopsy.[51]

Conclusion

Chronic liver disease can develop in response to multiple underlying conditions. Despite the underlying etiology of chronic liver disease, identifying and assessing the degree of hepatic steatosis or fibrosis is paramount to determine treatment options and prognostication. Although liver biopsy remains the gold standard, NITs offer an alternative route of evaluation for fibrosis that is noninvasive, has less risks, is cheaper, and generally is more accessible.[52,53] Limitations of NITs include, but are not limited to, varying cutoffs, age, fasting status, acute inflammation of the liver, availability, and (for some) operator dependence. Furthermore, although NITs offer an opportunity to identify fibrosis, they are unable to provide information regarding patterns of inflammation, cytologic ballooning, ductal involvement/inflammation, location of fibrosis, or other histopathologic information. This article evaluated the accuracy of NITs stratified by underlying etiology of disease. Generally, NITs were found to perform better with higher degrees of underlying fibrosis. Furthermore, combining blood-based and imaging-based tests was found to have higher accuracy in identifying the degree of fibrosis.

Disclosures

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