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TOPICAL COLLECTION ON HEPATITIS B

Noninvasive Tests for Liver Fibrosis in Chronic Hepatitis B Virus

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Abstract

Purpose of Review Hepatitis B virus (HBV) can be a potentially life-threatening liver infection. Prior to starting therapy, the first step is to establish the diagnosis, then to assess disease severity and determine if treatment is indicated. Assessing the degree of liver fibrosis is imperative to guiding treatment options. While liver biopsy has been the primary method to establish the degree of fibrosis, noninvasive tests (NIT) have now replaced liver biopsy as the initial step.

Recent Findings Here, we present a recent review of literature on NIT to assess liver fibrosis in chronic HBV from 2019 to 2022.

Summary Being able to use NIT (blood- and/or imaging-based) to assess fibrosis and help guide treatment can help impact and lower disease burden as well as life-threatening complications of liver disease.

Keywords Chronic hepatitis B (CHB) · Noninvasive test (NIT) · AST to Platelet Ratio Index (APRI) · Fibrosis-4 Index (FIB-4) · Transient elastography (TE) · Magnetic resonance elastography (MRE)

Introduction

Hepatitis B virus (HBV) can be a potentially life-threatening liver infection [1]. Vaccination is available for HBV with rates upwards of 98% for protection. However, despite vaccination efforts, HBV remains a global health burden [1, 2]. The prevalence of HBV varies throughout the world with high prevalence regions defined as having HBsAg-positive persons of ≥ 8%, intermediate at 2 to 7%, and low as < 2% [3]. Given the varied distribution, the screening guidelines for HBV incorporate those with high or intermediate HBV endemicity amongst other parameters such as offspring of those from a high endemic region, IV drug users, men who have sex with men, immunocompromised hosts, inmates of correctional facilities, and patients with chronic liver disease.

HBV is most commonly spread via perinatal transmission or horizontal transmission through exposure to blood [1]. The development of chronic hepatitis B (CHB) is more common when infection occurs earlier in life when compared to HBV acquired in adulthood [1]. CHB infects over 257 million people worldwide and is the cause of 887,000 deaths each year [2]. Furthermore, without treatment, it can confer a mortality rate of 20–33% due to complications of cirrhosis, liver failure, or hepatocellular carcinoma [2, 4•].

Although HBV is not a completely curable disease, there are multiple treatment modalities in modern-day medicine that result in functional cure. The current mainstays of treatment are nucleoside/nucleotide analogues (NAs) and pegylated interferon (PEG-IFN) [2]. Prior to starting therapy, the first step is to establish the diagnosis, then to assess disease severity and determine if treatment is indicated. While liver biopsy has been the primary method to establish the degree of fibrosis, noninvasive tests (NIT) have now replaced liver biopsy as the initial step. Here, we present a recent review of the literature on NIT to assess liver fibrosis in chronic HBV from 2019 to 2022.

Establishing a Diagnosis of Chronic Hepatitis B

The American Association for the Study of Liver Diseases (AASLD) defines chronic hepatitis B as having HBsAg present for ≥ 6 months, serum HBV DNA that varies from undetectable to several billion IU/mL (requires serial monitoring). CHB is further phenotyped as immune tolerant (high HBV DNA,

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positive HBeAg, normal alanine aminotransferase (ALT), and little inflammation or fibrosis), immune active (moderate to high HBV DNA, presence or absence of HBeAg, increased ALT with varying degrees of inflammation and fibrosis), and inactive (low HBV DNA and normal ALT). AASLD identifies the upper limit of normal for ALT as 35 U/L for males and 25 U/L for females to guide treatment/management decisions with [3]. However, some with CHB fall in between these phenotypes, termed indeterminant CHB.

Liver fibrosis is the main predictor of long-term outcomes and thus is an important parameter to monitor serially. Despite these specific parameters for treatment guidance, complications of liver disease have been described in patients with lower HBV DNA levels, and as such, other patient factors such as age, duration of infection, ALT elevation, and stage of disease should be considered [3]. As such, predictors of liver fibrosis are imperative to patient's care and outcome. Early initiation of treatment has shown to arrest the progression of liver disease, and as such, it is recommended to initiate treatment in the presence of moderate inflammation and fibrosis to help prevent further complication/progression [4•]. Therefore, assessing the degree of liver fibrosis is imperative to guiding treatment options.

Assessing Disease Severity

Liver biopsy is the gold standard method for detecting the degree of tissue inflammation and fibrosis; however, liver biopsy has complications including but not limited to pain (0.05–84%), hemorrhagic complications (11%), bacterial translocation and transient bacteremia (9.6–14%), and incorrect sampling [4•, 5, 6]. Liver fibrosis can be staged using multiple systems. There are four stages of fibrosis (F): F0 representing a lack of fibrosis, F1 with portal fibrosis, F2 with periportal fibrosis, F3 with bridging fibrosis, and F4 which represents cirrhosis [7]. In patients with CHB who have developed cirrhosis, treatment can show regression of fibrosis and/or improvement in decompensated cirrhosis [2].

Literature on Noninvasive Testing for Liver Fibrosis in CHB

NIT can be obtained through biological methods (blood-based markers, algorithms, etc.) or physical methods (elastography for imaging assessment of liver stiffness). NIT for detection of advanced fibrosis has emerged and with improving accuracy has reduced the need for liver biopsy [6]. NIT also allows for more frequent follow-up [8] and has become the standard for the assessment of liver fibrosis.

Blood-Based NIT

One modality for noninvasive assessment of fibrosis is via algorithms using serologic markers. Blood-based NIT includes combinations of tests of "direct" markers, which are mostly derived from myofibroblasts and extracellular matrix remodeling, or "indirect" markers reflective of inflammation and/or portal hypertension [9]. Algorithms used are conceptually divided into simple, non-proprietary models that include routine blood tests, such as the aspartate to Platelet Ratio Index (APRI) and fibrosis 4 index (FIB-4) and more complex proprietary models that include direct measurements of collagen synthesis or degradation with or without clinical variables, such as FibroTest(FT)/Fibrosure (LabCorp, Burlington, NC) and Enhanced Liver Fibrosis (ELF) (Siemens Healthineers AG, Erlangen, Germany). Examples of the serologic markers include bilirubin, aspartate aminotransferase (AST), ALT, gamma-glutamyl transferase (GGT), and platelet count [10]. These algorithms are comprised of some overlapping blood-based markers as found in Table 1. Aspartate to Platelet Ratio Index (APRI) and the Fibrosis-4 Index (FIB-4) are the two most widely recognized serum models to identify liver fibrosis and cirrhosis. Because of similar performance, the simple, non-proprietary tests (APRI and FIB-4) are preferred in clinical practice. Furthermore, these tests are low-cost and easily accessible and can provide serial monitoring [11]. Using blood-based testing offers a more convenient and lower-risk modality to assess liver fibrosis with the ability for more longitudinal assessment as these markers can be obtained at regular intervals. This ability for more frequent assessment in a less invasive fashion is important especially as the degree of fibrosis in patients with CHB confers prognostication but also helps guide treatment.

Imaging-Based NIT

An additional modality for noninvasive assessment of liver fibrosis is by radiographic assessment. Ultrasound-based elastography (transient elastography [TE] and shear wave elastrography [SWE]) have been used to assess fibrosis by transmitting radio waves to assess the degree of liver stiffness. Similar to blood-based tests, radiographic modalities present a less invasive modality to assess fibrosis. However, several confounding factors can limit the diagnostic accuracy of ultrasound-based elastography including body habitus of patient and hepatic inflammation from other causes (acute hepatitis, cholestasis, food intake) [10]. In addition to ultrasound-based assessment, magnetic resonance (MR) elastrography (MRE) is also used as an alternative radiographic modality. Very few studies, if any, directly compare

Table 1 Blood-based algorithms to assess liver fibrosis

Name of algorithm	Blood-based markers	Limitations
APRI	AST, platelet count	Impacted by alcohol
FIB-4	Age, AST, ALT, platelet count	Impacted by alcohol and may be skewed by older age
GPR	GGT, platelet count	Impacted by alcohol
King's Score	Age, AST, INR, platelet count	Impacted by alcohol and may be skewed by older age

APRI, AST to Platelet Ratio Index; *FIB-4*, Fibrosis 4 Index for Liver Fibrosis; *GPR*, gamma-glutamyl transpeptidase to platelet ratio; *GGT*, gamma-glutamyl transferase

TE, 2D-SWE, and MRE. Because TE and 2D-SWE have similar performance, they are the preferred modalities and the choice of test will depend on availability and local expertise.

Review of Literature

A prior study by Xu et al. reviewed the effectiveness of NIT to predict hepatitis B-related significant fibrosis and cirrhosis [12]. They specifically evaluated the efficacy of APRI, FIB-4, and FibroTest and found that FibroTest performed the best at detecting not only cirrhosis but also significant fibrosis. FIB-4 and APRI had good diagnostic accuracy at predicting fibrosis and cirrhosis, though less accurate than FibroTest. A prior study by Kim et al. evaluated FIB-4 and APRI in relation to liver biopsy and identified that these NIT were not applicable especially in predicting improvement in fibrosis with treatment of hepatitis B [13]. Furthermore, Leroy et al. performed a prospective study evaluating the efficacy of FibroTest (FibroSure), FibroMeter, and HepaScore for staging liver fibrosis in hepatitis B when compared to hepatitis C. When comparing the accuracy between those mono-infected with hepatitis B vs. hepatitis C, they identified that the performance of these blood tests was similar amongst the two groups; however, there was a higher risk of underestimating significant fibrosis and cirrhosis in those with hepatitis B due to lower cutoffs needed than for hepatitis C [14].

There have been several more recent studies on NIT in CHB published since 2019 (Table 2). Hamidi et al. evaluated a single center cohort based out of Turkey of 202 patients with CHB who underwent liver biopsy [4•]. These patients were defined as having HBsAg positivity for at least 6 months with HBV-DNA > 2000 IU/mL; exclusion criteria included those with hepatitis D, hepatitis C virus (HCV), or human immunodeficiency infection (HIV) co-infection. This study identified that the aspartate APRI, FIB-4, FibroQ, Gotebort University Cirrhosis Index (GUCI), King score, age-platelet index (API), and GGT were successful in detecting liver fibrosis in those with CHB [4•]. Furthermore, they identified FIB-4 as having the most diagnostic accuracy. They also identified the strong negative predictive value or noninvasive scoring, though positive predictive value was not statistically significant.

Ding et al. evaluated a single-center cohort based out of China of 543 patients with CHB who underwent liver biopsy [8]. These patients were defined as having CHB if they had HBsAg positivity for at least 6 months; exclusion criteria included those with HCC, antiviral treatment, decompensated cirrhosis, inadequate biopsy samples, coinfection with other viral hepatitis, history of overt alcohol use, autoimmune liver disease, hereditary metabolic liver disease, and use of anticoagulant drugs. They formulated a novel test comparing international normalized ratio (INR) to platelets, called INR-to-platelet ratio (INPR) and which is defined as follows: INR/platelet counts ($\times 10^9$/L) $\times$ 100. INR and platelets were used as these are documented independent predictors of cirrhosis in patients with CHB. They identified INPR to significantly increase as the stage of liver fibrosis increased. Furthermore, they identified larger AUROCs for both F3 and F4 fibrosis as defined by liver biopsy when compared to APRI, FIB-4, and gamma-glutamyl transpeptidase to platelet ratio (GPR).

Huang et al. evaluated a single-center cohort based out of China of 91 patients with CHB who underwent liver biopsy [15]. These patients were defined as having CHB as per the Asian Pacific clinical practice guidelines; exclusion criteria included those patients with other types of hepatitis, patients with metabolic disease, patients with liver disease associated with drugs, patients with alcoholic liver disease, patients with HIV, and patients with cardiopulmonary disease. The aim was to evaluate the accuracy of liver fibrosis in patients with HBV by real-time ultrasound elastography (RTE), to determine the liver fibrosis index (LFI), and to compare the accuracy among LFI, the APRI, and the FIB-4 for grading stages of LF in comparison to liver biopsy. They identified

Table 2 Studies on NIT in CHB published since 2019

Article	Population	Tests	Liver biopsy as comparator	Outcome
Hamidi AA. et al., 2019. [4•]	Cohort: Single center, adult (> 18 years) who had undergone liver biopsy between 2011 and 2016 ($n=202$ with biopsy)	APRI FIB-4 GPR FibroQ [defined as: (10 × age × AST × INR)/(PLT/ALT)] GUCI King score API	Yes	In advanced fibrosis: GPR, FIbroQ, GUCI, FIB-4, APRI, API, and King scores were significantly higher when compared to those in the mild fibrosis group. Non-invasive scoring had a high negative predictive value but the positive predictive value was not significant. FIB-4 had the highest diagnostic accuracy rate
Ding R. et al., 2021. [8]	Cohort: Single center, $n=543$ anti-HBV naïve patients with CHB who had undergone liver biopsy within one week of the blood laboratory examinations from 2016 to 2019	INR-to-platelet ratio (INPR) [defined as: INR/platelet counts ($\times 10^9$/L) × 100] APRI FIB-4 GPR	Yes	INPR was significantly positively correlated with Metavir fibrosis stage with a higher correlation coefficient than GPR, APRI, and FIB-4
Huang, D. et al., 2019. [15]	Cohort: Single center, $n=91$ from 2014 to 2018. Lab work obtained within 24 h before liver biopsy	FIB-4 APRI LFI	Yes	APRI, FIB-4, and LFI were significantly higher in each chronologically escalating fibrosis group. LFI was identified to have significant power when differentiating between F0 and F1 and F3 and F4 and for identifying F4
Çelik D. et al., 2020. [16•]	Cohort: Single center retrospective study, $n=539$ from 2010 to 2017 all with liver biopsy	APRI FIB-4 NLR GPR AAR RPR API King's score FibroQ Mean platelet volume (MPV) for moderate liver fibrosis (≥F2), significant liver fibrosis (≥F3), advanced liver fibrosis (≥F4), and liver cirrhosis (≥F5)	Yes	APRI and FIB-4 were found to be successful in predicting significant fibrosis and cirrhosis (in alliance with meta-analysis performed by WHO. GPR had the highest diagnostic sensitivity for prediction of significant fibrosis amongst the NIT (Ren T. et al. found GPR to perform better at all levels of fibrosis an APRI, however, was comparable but not superior to FIB-4). RPR and API performed weak and moderately in this study in detecting fibrosis. King's score performed well with high diagnostic sensitivity. Fibro Q performed lower when compared to APRI and FIB-4. NLR and AAR was found to not be sufficient to predict fibrosis (specifically ≥F3 and F5 for AAR). MPV was statistically significant at identifying ≥F3; this study found it was not reliable at identifying advanced fibrosis. For detecting ≥F5, King's score, FIB-4, and GPR had the most powerful predictive values

Table 2 (continued)

Article	Population	Tests	Liver biopsy as comparator	Outcome
Lu W. et al., 2019. [17]	Cohort: Cross-sectional retrospective study in a single center, $n = 196$, from 2017 to 2018	FIB-4 APRI GPR NLR AAR RPR PLR	No. Compared serologic testing to liver stiffness as identified by transient elastography	Identified normal range for females as: ALT 9–50 IU/L, AST 15–40 IU/L, and GGT 7–45 IU/L. Identified normal range for men as: ALT 7–40 IU/L, AST 13–35 IU/L, and GGT 10–60 IU/L. Total bilirubin, FIB-4, and GPR are predictors of liver stiffness. In comparison, FIB-4 and APRI had similar diagnostic accuracy at detecting significant fibrosis, advanced fibrosis, and cirrhosis. GPR demonstrated better performance in comparison to FIB-4 and APRI in assessing significant fibrosis, advanced fibrosis, and cirrhosis. For patients who were HBeAg positive, GPR performed better than APRI in assessing advanced fibrosis and cirrhosis, however, was comparable to FIB-4 in assessing significant fibrosis, advanced fibrosis, and cirrhosis. However in patients who had a negative HBeAg, GPR, FIB-4, and APRI were similar in detecting significant fibrosis, advanced fibrosis, and cirrhosis. This study was unable to confirm the prognostic ability of AAR and NLR
Lefebvre T. et al., 2019. [18]	Cohort: Dual-center study, $n = 100$ from 2014 to 2018	Transient elastography (TE) Point shear-wave elastography (pSWE) Magnetic resonance elastography (MRE)	Yes	Imaging was performed within 6 weeks of liver biopsy. For TE, needed to obtain at least 10 valid measurements. Reliability defined per criteria by Boursier et al. based on ratio of interquartile range to the median (IQR/M). For pSWE, success was defined as having 10 valid measurements in 20 repetitions or less. Reliability defined by IQR/M
Ben Ayed H. et al., 2019. [18]	Cohort: Retrospective study evaluating 179 patients between 2008 and 2016	APRI FIB-4 GPR AAR Combined APRI and FIB-4 into a new combined score	Yes	APRI, FIB-4, and GPR performed well at predicting severe fibrosis. APRI and FIB-4 were the best scores in predicting significant fibrosis, severe fibrosis, and cirrhosis. Additionally, these two tests had high NPV to exclude severe fibrosis or cirrhosis. GPR had a good performance in predicting severe fibrosis. The combined score using APRI and FIB-4 performed better diagnostically in predicting fibrosis than the two scores independently. No significant correlation was identified using AAR in relation to fibrosis

AAR, AST-ALT ratio; *API*, age-platelet index; *APRI*, AST to Platelet Ratio Index; *FIB-4*, Fibrosis-4 Index for Liver Fibrosis; *FibroQ*, Fibrosis Quotient; GPR, gamma-glutamyltransferase/platelet ratio; *GUCI*, Gotebort University Cirrhosis Index; *INPR*, INR-to-platelet ratio; *LFI*, liver fibrosis index; *NLR*, neutrophil–lymphocyte ratio; *PLR*, platelet to lymphocyte ratio; *RPR*, red cell distribution width (RDW)-platelet ratio

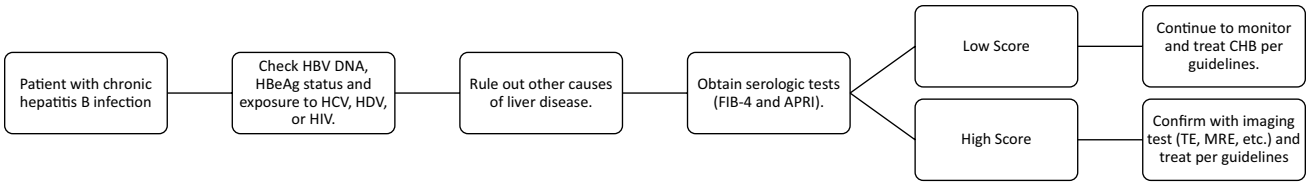

Fig. 1 Diagnostic approach for patients with chronic hepatitis B. FIB-4, Fibrosis-4 Index; APRI, AST to Platelet Ratio Index; TE, transient elastography; MRE, magnetic resonance elastography

that APRI, FIB-4, and LFI were significantly higher in each chronologically escalating fibrosis group; however, amongst the NIT, LFI was identified to have significant power when differentiating between F0 and F1 and F3 and F4 and for identifying F4.

Çelik et al. evaluated a large Turkish cohort comprised of 539 patients and performed a retrospective analysis to assess the accuracy of multiple NIT in detecting liver fibrosis in patients with CHB when compared to liver biopsy [16•]. This study excluded several cohorts of patients including but not limited to those with alcohol use or alcohol-related liver disease, thrombocytopenia or thrombocytosis, and other viral infections such as HIV, hepatitis C, and hepatitis D. This study identified that the APRI, King's, and GPR had the best diagnostic accuracy of identifying significant fibrosis, however weaker for those with moderate fibrosis. They also identified the diagnostic accuracy of FIB-4 in identifying significant fibrosis and cirrhosis, in alignment with the meta-analysis from WHO. Limitations of this study included a single-center population and using NIT that was initially developed to evaluate liver fibrosis in patients with hepatitis C. However, given the diagnostic accuracy identified in this study, it is promising for future use in the detection of fibrosis rather than liver biopsy.

Lu et al. evaluated and compared the performance of blood tests in predicting liver fibrosis in CHB as compared to transient elastography [17]. Though the WHO recommends using serum biomarkers and transient elastography as NIT for patients with CHB, this study aimed to focus on serologic evaluation as imaging modalities are costly and require expertise to perform, which may be limited in resource-limited regions. This study evaluated one-hundred and ninety-six patients from a single-center retrospective study from China who had CHB and assessed the prognostic ability of the following serologic tests at detecting liver fibrosis in comparison with TE: FIB-4, APRI, GPR, neutrophil to lymphocyte ratio (NLR), aspartate aminotransferase to alanine aminotransferase ratio (AAR), red cell distribution width-to-platelet ratio (RPR), and platelet to lymphocyte ratio (PLR). This study identified GPR was superior to FIB-4 and APRI in detecting advanced fibrosis and cirrhosis in patients who were HBeAg positive. However, in patients that were HBeAg negative, FIB-4, APRI, and GPR performed comparably. Overall, they identified GPR had the best diagnostic performance, and FIB-4, APRI, and RPR were similar in predicting fibrosis and cirrhosis.

Lefebvre et al. assessed the efficacy of elastography via transient elastography, point shear-wave elastography (p-SWE), and magnetic resonance elastography to assess fibrosis in those with chronic liver disease from hepatitis B virus, hepatitis C virus, nonalcoholic fatty liver disease, or autoimmune hepatitis [18]. This study assessed the efficacy of the aforementioned tests in a head-to-head evaluation within 6 weeks of the patients undergoing liver biopsy. The technical failure rate was 0% for TE, 1% for pSWE, and 6% for MRE (not statistically significant) with unreliable exam rates at 8% for TE, 19% for pSWE, and 3% for MRE. This study identified that MRE was superior to TE and pSWE in diagnostic accuracy for detecting early states of fibrosis. pSWE was identified to have higher rates of unreliable exams when compared to TE and MRE. All elastography techniques performed better at detecting/differentiating higher stages of fibrosis than lower stages. This reinforces the findings from an earlier study by Salkic et al. as they performed a meta-analysis of sixteen studies (largely all prospective studies with two being retrospective and one being mixed) to review the accuracy of using FibroTest (FT) to evaluate liver fibrosis in patients with chronic hepatitis B [19]. They identified that FT performed well in identifying

Table 3 Suggested parameters for NITs for advanced fibrosis

Advanced fibrosis, F3–F4			
Noninvasive test	Cutoff	Sensitivity	Specificity
APRI	1.5	0.45	0.87
FIB-4	3.25	0.67	0.97
ELF	9.8	0.53	0.66
FT	0.52	0.86	0.90
TE	9 kPa	0.82	0.83
2D-SWE	8.3 kPa	0.90	0.77
MRE	5.45 kPa	1.0	1.0

APRI, AST to Platelet Ratio Index; *FIB-4*, Fibrosis-4 Index; *ELF*, Enhanced Liver Fibrosis; *FT*, FibroTest; *TE*, transient elastography; *2D-SWE*, 2D shear-wave elastography; *MRE*, magnetic resonance elastography

cirrhosis, however, was less accurate at differentiating significant fibrosis and cirrhosis.

Lastly, Ben Ayed et al. performed a retrospective study assessing the efficacy of a new combined model using APRI and FIB-4 together to predict liver fibrosis in patients with CHB in comparison with those serological tests independently, GPR, and AAR in comparison with liver biopsy [20]. This study evaluated one-hundred and seventy-nine patients with CHB to evaluate the efficacy of a new combined test. This study identified that a combined test using FIB-4 and APRI outperformed the aforementioned independently in predicting fibrosis. As others have identified, APRI and FIB-4 were otherwise the best scores at independently identifying degrees of fibrosis.

Conclusions

CHB impacts a large percentage of our population worldwide and the World Health Organization recognized CHB as a major global health problem [20]. Though there is no cure for CHB, treatment modalities do exist and require serologic testing as well as fibrosis staging to help guide treatment. While liver biopsy remains the gold standard in assessing and staging liver fibrosis in those with chronic liver disease, liver biopsies are not available in all clinical settings, and furthermore, there are several risks that are associated with liver biopsy. As such, NIT to accurately and reliably assess liver fibrosis has emerged as a lower-risk and more universally available alternative to liver biopsy. Several studies have evaluated both serologic and imaging modalities to assess liver fibrosis and FIB-4, APRI, GPR, and King's score were most commonly identified to have better accuracy in detecting fibrosis. Amongst imaging modalities, MRE was superior to TE and SWE in detecting stages of fibrosis and between two stages of fibrosis when compared in a head-to-head trial [6–15, 16•, 17–20].

The fibrosis staging can start at either blood- or imaging-based NIT and does not imply the use of sequential testing. However, sequential testing has been found to be more informative than single testing. Zhang et al. aimed to create algorithms to assess significant fibrosis and cirrhosis in those with CHB. They used APRI and FIB-4 as initial tests followed by FS or combined a blood-based and imaging test. When comparing using an individual test to using a blood- and imaging-based test at the same time, they identified that the combined algorithm reduced the need for biopsy [21]. However, combination testing has limitations such as cost and accessibility; as such, we first recommend FIB-4 (Fig. 1). In those with FIB-4 values > 1.45, we recommend transient elastography. In rare instances where uncertainty remains, liver biopsy may still be needed. Table 3 shows the performance and cutoff values for both blood- and imaging-based NIT. Advanced fibrosis, F3-F4, was chosen specifically as it identifies those with CHB who are at higher risk of hepatocellular carcinoma.

Figure 1 shows our approach to those with CHB. After HBV replicative status is assessed (HBV DNA and HBeAg/Ab) and coinfections established (HCV, HDV, and HIV), simple blood-based NIT (APRI and/or FIB-4) are calculated. Patients can then be stratified as low or significant fibrosis with treatment per guidelines. Those with high blood-based scores should then undergo imaging-based NIT for confirmation. Being able to use NIT (blood- and/or imaging-based) to assess fibrosis and help guide treatment can help impact and lower disease burden as well as life-threatening complications of liver disease. Further direction should include longitudinal assessment of accuracy of NIT in predicting the degree of fibrosis as it changes with treatment.

Declarations

Conflict of Interest The authors do not have existing conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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