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Liver Fibrosis Assessment in Chronic Liver Diseases Using Elastography: A Comprehensive Review of Vibration-Controlled Transient Elastography and Shear Wave Elastography

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Chronic liver diseases (CLD) are a major global health issue, with liver fibrosis progression and cirrhosis as critical determinants of prognosis and treatment strategy. Historically, liver biopsy has been the gold standard for assessing fibrosis, but limitations such as invasiveness, variability in results, and cost have spurred the development of non-invasive tests. Elastography techniques measure liver stiffness, providing important insights into fibrosis severity across various CLDs, including hepatitis B and C and metabolic dysfunction-associated steatotic liver disease (MASLD). Ultrasound-based elastography techniques include vibration-controlled transient elastography (VCTE), point shear wave elastography, and 2D shear wave elastography. Most studies report high accuracy for diagnosing significant fibrosis and cirrhosis. While VCTE is the most widely used elastography method, each technique has strengths and limitations in different patient populations, affected by factors like alanine aminotransaminase levels, obesity, and presence of hepatic inflammation. Elastography proves valuable informations in treatment decisions for hepatitis B patients in the "gray zone" and helps identify high-risk groups requiring post-hepatitis C eradication surveillance. Recent studies emphasize the potential of elastography-based scores, such as the FibroScan-AST and AGILE scores, in improving diagnostic accuracy for patients with MASLD. However, diagnostic performance may vary by setting, requiring validation in primary care. Emerging precision medicine approaches, integrating genomics and novel biomarkers, promise to further enhance risk stratification in CLD management. Despite substantial advances, broader clinical application of elastography and related biomarkers necessitates further validation, particularly in diverse care settings, to ensure their optimal utility in routine clinical practice.

Keywords: Elastography; Chronic liver disease; Liver fibrosis; Non-invasive test

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INTRODUCTION

Chronic liver diseases (CLD) are a significant public health concern, contributing substantially to global morbidity and mortality [1]. The prognosis and treatment strategies for these conditions largely depend on the degree and progression of liver fibrosis, as well as the risk of advancing to cirrhosis. Advanced fibrosis is the most clinically significant marker, while cirrhosis in CLD patients triggers surveillance for hepatocellular carcinoma (HCC) and gastroesophageal varices and serves as a key prognostic factor [2,3].

Since the late 1950s, liver biopsy has been regarded as the gold standard for assessing liver fibrosis severity, however, liver biopsy has several notable limitations [4]. Its accuracy in assessing fibrosis is often questioned due to issues like sampling errors and variability between and within observers, which can result in over- or under-staging [5,6]. Additionally, liver biopsy is a costly procedure that requires medical expertise and a facility equipped with periprocedural monitoring [7]. Importantly, it is an invasive procedure with associated risks, ranging from common, mild complications (such as transient pain in 30% to 50% of cases) to rare but potentially life-threatening ones (including serious hemorrhage in 0.6% of cases and a mortality rate of up to 0.1%) [8]. These limitations, along with the availability of effective antiviral therapies and the global increase in metabolic dysfunction-associated steatotic liver disease (MASLD) cases, have driven the development of non-invasive methods to improve diagnosis and prognosis in CLD.

Non-invasive strategies utilize two distinct but complementary approaches of serum biomarkers and elastography techniques based on ultrasound or magnetic resonance imaging [9]. The introduction of vibration-controlled transient elastography (VCTE) in 2003, using the FibroScan device (Echosens, Paris, France), marked the start of a new era in liver stiffness measurement [10]. Since then, numerous other elastography techniques have emerged, including ultrasound-based methods integrated into ultrasound devices, such as point-shear wave elastography (pSWE) and 2D-shear wave elastography (2D-SWE), as well as more recently, magnetic resonance elastography (MRE) [11].

In this review, we explore the role of ultrasound-based

elastography in CLD, evaluating its accuracy and clinical implication in assessing the severity of liver fibrosis.

TYPES OF ELASTOGRAPHY

Elastography techniques assess liver stiffness by measuring the speed of an induced shear wave as an indicator of hepatic fibrosis [12]. These methods include ultrasound-based VCTE (FibroScan), pSWE (also called acoustic radiation force impulse), 2D-SWE, and MRI-based MRE.

Vibration-Controlled Transient Elastography

The most commonly used and well-validated technique, VCTE, uses pulse-echo ultrasound to measure the velocity of low-frequency vibrations transmitted into the liver [10,13]. The speed at which these ultrasound waves propagate and return through the transducer is recorded. This speed is then converted into LS values based on Hooke's law, expressed in kilopascals (kPa). Since tissue stiffness is directly related to the square of the shear wave's propagation speed, faster wave speeds indicate a stiffer liver, which correlates with more advanced liver fibrosis. LS values on VCTE range from 1.5 to 75 kPa, with a normal upper limit of approximately 5 to 5.5 kPa [14].

The liver stiffness measurement (LSM) obtained through VCTE correlates with the stage of hepatic fibrosis and has been validated across various liver diseases, including hepatitis B virus (HBV), hepatitis C virus (HCV), primary biliary cholangitis, metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease (ALD) [9]. However, the effectiveness of VCTE can depend on the operator and may be affected by factors that elevate liver stiffness or complicate accurate measurement, such as congestive heart failure, cholestasis, acute hepatitis, recent alcohol or food intake, and obesity [15]. To aid in interpreting results, reliability criteria for VCTE have been established (IQR/M < 0.30, or IQR/M > 0.30 if the median reading is below 7.1 kPa) [15].

The advantages of VCTE include being painless and noninvasive, allowing for quick and simple assessments in an outpatient setting, and providing immediate results. The method

also has high reproducibility, directly measures LS, and assesses a liver parenchyma volume over 100 times greater than that in a traditional liver biopsy [16]. Additionally, VCTE is user-friendly, requiring minimal training for clinicians, and offers excellent diagnostic accuracy for detecting liver fibrosis in chronic liver diseases of various etiologies [17,18].

On the downside, obtaining VCTE results may be challenging in patients with ascites or a narrow intercostal space [10]. Ascites can obstruct the elastic waves from reaching the liver parenchyma, and a narrow intercostal space complicates proper probe positioning. Results may also be less reliable in individuals with a high body mass index (BMI) ($>28 \text{ kg/m}^2$), though studies report a lower risk of unreliable readings in Asian populations (1.1–3.5%) than in Western populations (4.3–7.0%), possibly due to lower BMI levels among Asians [19].

Shear Wave Elastography

SWE evaluates liver fibrosis severity by measuring the speed of shear waves and capturing imaging data during an abdominal ultrasound exam [20]. This technique includes both pSWE and 2D-SWE. pSWE calculates the speed of shear waves created by focal tissue displacement through acoustic radiation force impulse (ARFI) technology [14,20]. A shear wave is produced from the probe by emitting a longitudinal wave at a frequency of 2.67 MHz within the region of interest (ROI). Ultrasound detection pulses from multiple channels then measure the shear wave speed at a specific location, providing an elasticity measurement in meters per second (m/s) within a range of 0.5–4.4 m/s [14]. The test is repeated approximately 10 times, and the median elastic modulus value, expressed in m/s or kPa, is recorded [21,22].

2D-SWE uses ARFI and produces a focused wave through a B-mode ultrasound transducer. Unlike pSWE, which focuses on a single area and generates shear waves at one frequency, 2D-SWE continuously sends sound waves aimed at multiple focal zones in the direction of the ultrasound beam. This process produces a high-frequency (60–600 Hz) shear wave that is concentrated into a cone shape. Because of these differences, 2D-SWE has demonstrated greater diagnostic accuracy than pSWE [22–24]. The progress of the shear wave is

captured in real time via ultrafast imaging, which can achieve frame rates of up to 20,000 per second. The quantitative elasticity value is displayed in m/s or kPa on the ultrasound monitor. Additionally, 2D-SWE allows for a larger SWETM box range than pSWE and can assess elasticity using one or more adjustable circular ROIs [14,20]. Results are acquired after repeating the measurement 5 to 10 times, with the median of all valid readings being recorded [22].

SWE is an objective and reproducible test, offering the advantage of obtaining quantitative measurements without applying manual pressure and directly assessing tissue elasticity. It allows for real-time elastography with quantified values indicating liver fibrosis severity, and unlike VCTE, it can be conducted while visualizing the liver's anatomical structure. However, SWE values differ by disease across various studies, and optimal cutoff values for staging liver fibrosis have yet to be established [25]. Additionally, the range of shear wave elasticity values for each fibrosis stage is relatively broad, and the difference between cutoff values for successive stages is minimal [26]. For SWE to be a reliable criterion for staging, the interquartile range to median ratio (IQR/M) should be less than 30% for values reported in kPa and less than 15% for those in m/s [27]. As with VCTE, results may be overestimated in cases of intrahepatic inflammation, cholestasis, liver congestion due to right heart failure, amyloidosis, or after food intake, so careful interpretation is necessary [27,28].

Etiology-Specific Fibrosis Cutoffs in Elastography

In liver diseases, the cutoff values for fibrosis stages determined by elastography vary depending on the etiology. Chronic hepatitis B (CHB) generally has the lowest cutoff values, followed by chronic hepatitis C (CHC), MASLD, and alcohol-related liver disease [29]. Results in meta-analyses of ultrasound-based elastography for the assessment of liver fibrosis by each etiology are recorded in Table 1. The reason for this difference lies in the pathophysiological characteristics of each liver disease. HBV-induced fibrosis often presents with minimal structural stiffness in the early stages, resulting in lower elastography values for significant fibrosis. HCV tends to cause more inflammation and fibrotic progression, requiring

Table 1. Meta-analyses of ultrasound-based elastography for assessment of liver fibrosis

Noninvasive test	Significant fibrosis (≥F2)				Advanced fibrosis (≥F3)				Cirrhosis (F4)			
	No. of studies (patients)	AUC (95% CI)	Cutoff value	Sensitivity/specificity%	No. of studies (patients)	AUC (95% CI)	Cutoff value	Sensitivity/specificity%	No. of studies (patients)	AUC (95% CI)	Cutoff value	Sensitivity/specificity%
Chronic hepatitis B												
VCTE	10 (1,625)	0.859 (0.857–0.860)	79 kPa	74.3/78.3	4 (960)	0.887 (0.886–0.887)	8.8	74.0/63.8	13 (2,051)	0.929 (0.928–0.929)	11.7	84.6/81.5
	19	0.88 (0.85–0.81)	7.2 kPa	81.0/82.0	19	0.91 (0.88–0.93)	9.1	82.0/87.0	24	0.93 (0.91–0.95)	12.2	86.0/88.0
pSWE	35 (6,202)	0.86 (0.83–0.89)	73 kPa	78.0/81.0	-	-	-	-	41 (7,205)	0.92 (0.90–0.94)	12.4	84.0/87.0
	23 (3,879)	0.84 (0.81–0.87)	6.0–8.8 kPa	76.0/79.0	-	-	-	-	26 (4,441)	0.90 (0.88–0.93)	8.0–14.1	84.0/84.0
2D-SWE	8 (518)	0.79 (0.63–0.96)	1.34	79.0/85.0	8 (518)	0.83 (0.70–0.96)	1.55	86.0/86.0	8 (518)	0.90 (0.79–1.00)	1.80	92.0/86.0
	4 (400)	0.91	7.1	87.6/73.6	4 (400)	0.93	8.1	94.9/73.1	4 (400)	0.96	11.5	79.9/93.3
Chronic hepatitis C	-	0.92 (0.89–0.94)	7.9	88.0/83.0	-	-	-	-	-	-	-	-
	13 (1,716)	0.89 (0.86–0.92)	7.6	80.9/79.3	8 (1,020)	0.95 (0.91–0.95)	9.1	89.1/84.7	12 (782)	0.94 (0.92–0.96)	10.9	87.3/86.1
VCTE	37	-	5.2–10.1 kPa	79.0/83.0	19	-	8.6–15.4 kPa	88.0/90.0	36	-	9.2–17.3 kPa	89.0/91.0
pSWE	3	-	1.21–1.34 m/s	79.0/89.0	4	-	1.49–2.11 m/s	85.0/89.0	4	-	1.6–2.3 m/s	84.0/77.0
Metabolic dysfunction-associated steatotic liver disease												
VCTE	37 (2,763)	0.83 (0.80–0.87)	3.8–10.2 kPa	80.0/73.0	44 (4,219)	0.85 (0.83–0.87)	6.8–12.9 kPa	80.0/77.0	22 (337)	0.89 (0.84–0.93)	6.9–19.4 kPa	76.0/88.0
pSWE	9 (805)	0.86 (0.78–0.90)	1.18–1.81 m/s	69.0/85.0	11 (1,209)	0.89 (0.83–0.95)	1.34–4.21 m/s	80.0/86.0	8 (759)	0.90 (0.82–0.95)	1.36–2.54 m/s	76.0/88.0
2D-SWE	4 (488)	0.75 (0.58–0.87)	8.3–11.6 kPa	71.0/67.0	4 (488)	0.72 (0.60–0.84)	9.3–13.1 kPa	72.0/72.0	3 (372)	0.88 (0.81–0.91)	14.4–15.7 kPa	78.0/84.0

VCTE, vibration-controlled transient elastography; pSWE, point shear wave elastography; 2D-SWE, two-dimensional shear wave elastography; AUC, area under the curve; CI, confidence interval; kPa, kilopascal.

Assessment of liver fibrosis using elastography

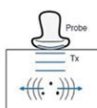
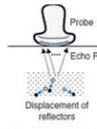
	HBV	HCV	MASLD
 Transient elastography	- Widely validated for fibrosis and cirrhosis - ALT levels may affect readings - Useful in the assessment for treatment decision	- Widely validated for fibrosis and cirrhosis - ALT impacts results - Post-SVR monitoring can aid in HCC risk	- High diagnostic accuracy for advanced fibrosis and cirrhosis - Limited accuracy in obesity; XL probe recommended
 Point-SWE	- Comparable to VCTE - ALT may elevate cutoff	- Reliable for fibrosis and cirrhosis - Similar performance with VCTE	- Comparable to VCTE in performance - Accuracy affected by steatosis severity
 2D-SWE	- High diagnostic accuracy - ALT-based cutoffs improve performance - Larger ROI provides flexibility	- Comparable to VCTE - Has not been as extensively validated as other non-invasive tests	- Effective for fibrosis staging, especially in real-time adjustments - Diagnostic performance slightly lower than pSWE and VCTE

Figure 1. Characteristics and applications of ultrasound-based elastography for assessment of liver fibrosis in various chronic liver diseases. HBV, hepatitis B virus; HCV, hepatitis C virus; MASLD, metabolic dysfunction-associated steatotic liver disease; ALT, alanine aminotransaminase; HCC, hepatocellular carcinoma; SVR, sustained virologic response; VCTE, vibration-controlled transient elastography; ROI, region of interest; pSWE, point-shear wave elastography; 2D-SWE, two-dimensional shear wave elastography.

slightly higher cutoffs. MASLD and ALD, on the other hand, are associated with a combination of fibrosis and fatty infiltration, leading to even higher baseline stiffness values, which increase the thresholds for identifying fibrosis stages through elastography. The advantages and disadvantages of elastography for each etiology are summarized in Figure 1.

CHRONIC HEPATITIS B

Assessing liver fibrosis in patients with CHB is essential for determining the appropriate timing of treatment and predicting prognosis. Liver biopsy provides insight into the degree of inflammation and fibrosis, which can guide treatment decisions, however, because liver biopsy is invasive, alternative non-invasive tests are used as substitutes [30].

Vibration-Controlled Transient Elastography

The effectiveness of VCTE in evaluating liver fibrosis in CHB patients has been extensively validated through liver histology. For significant fibrosis diagnosis, VCTE’s area under the curve (AUC), cutoff values, sensitivity, and specificity range between 0.66–0.97, 5.2–8.8 kPa, 59–93%, and 38–92%, respectively,

while for cirrhosis, these parameters are 0.85–0.98, 9.4–14.1 kPa, 52–100%, and 83–99% [18,31–34]. Diagnostic accuracy for cirrhosis is generally higher than for significant fibrosis in CHB patients.

One meta-analysis, including 4,540 CHB patients, showed an AUC of 0.84, with cutoff values between 6.0–8.8 kPa for significant fibrosis and 8.0–14.1 kPa for cirrhosis [34]. Another meta-analysis, including eight studies (2,003 patients) showed that sensitivity and specificity for diagnosis of significant liver fibrosis were 0.78 and 0.72 respectively [35]. The HSROC for the diagnosis of significant liver fibrosis was 0.81. However, it remains unclear whether patients with conditions like acute liver disease, congestive hepatopathy, infiltrative liver disease, or obstructive cholestasis were excluded from these meta-analyses. Additionally, the reliability of the VCTE results (fasting status and IQR/M ≤0.3) and the probe type used for liver stiffness (LS) measurement were not consistently reported.

A meta-analysis comparing VCTE performance for significant fibrosis and cirrhosis in European and Asian CHB patients found notable ethnic differences [36]. For diagnosing significant fibrosis, AUC, sensitivity, and specificity were 0.80, 73%, and 66% in Europe, compared to 0.87, 73%, and 82% in Asia, showing higher

diagnostic accuracy in Asia. For cirrhosis, studies in Europe reported an AUC of 0.91 with 67% sensitivity and 92% specificity, while Asian studies showed a sensitivity of 81% and specificity of 86% with the same AUC. These differences may stem from regional variations or disparities in BMI and obesity rates, suggesting a need for further investigation.

Diagnostic performance across studies varies with patient characteristics and cutoff values, though most studies report a high AUC (>0.80). An algorithm in Europe using cutoffs of 9.4 and 13.1 kPa for cirrhosis diagnosis improved sensitivity and specificity to over 90% [33]. A meta-analysis showed the optimal cutoff value of VCTE for diagnosis of significant liver fibrosis was 7.7 kPa with a sensitivity of 0.64 and specificity of 0.83 [35]. Another meta-analysis of 27 studies involving 4,386 patients found that for diagnosing significant fibrosis, the AUC was 0.81, with a cutoff value of 7.2 kPa, sensitivity of 81%, and specificity of 82%. For diagnosing cirrhosis, the AUC was 0.93, with a cutoff value of 12.2 kPa, sensitivity of 86%, and specificity of 88% [37].

VCTE results may be influenced by intrahepatic inflammation in CHB patients, leading to potential overestimation of fibrosis [38]. Elevated ALT levels can independently raise LS values, so results should be carefully interpreted [9]. Additionally, antiviral therapy (AVT) may lower LS values due to reduced intrahepatic inflammation, meaning cutoff values established in untreated patients may not be applicable for those on AVT. VCTE can be difficult to perform in patients with right hepatectomy, ascites, severe obesity, or during pregnancy, and results may be affected by recent food intake, liver masses, congestion, cholestasis, or infiltrative liver disease [31].

Point Shear Wave Elastography

For diagnosing significant fibrosis, pSWE's AUC, cutoff values, sensitivity, and specificity ranged from 0.76 to 0.86, 1.23–1.59 m/s, 59–90%, and 63–88%, respectively. For cirrhosis diagnosis, the AUC, cutoff values, sensitivity, and specificity were 0.72–0.97, 1.75–1.98 m/s, 67–85%, and 73–92%, respectively [39–44]. A meta-analysis of eight studies involving 518 CHB patients found AUCs of 0.79 for significant fibrosis and 0.90 for cirrhosis, with cutoff values of 1.34 and 1.80 m/s, respectively [40]. Among 126

CHB patients who underwent liver resection, pSWE yielded AUCs of 0.86 for significant fibrosis and 0.95 for cirrhosis, surpassing AST to platelet ratio index (APRI) and fibrosis-4 index (FIB-4), which had AUCs of 0.75–0.77 and 0.75–0.78, respectively [44].

In a study with 180 CHB patients, pSWE and VCTE showed comparable diagnostic accuracy, with AUCs of 0.76 and 0.83 for pSWE, and 0.81 and 0.80 for VCTE in diagnosing significant fibrosis and cirrhosis, respectively. Like VCTE, pSWE's cutoff values for fibrosis and cirrhosis were higher in patients with elevated ALT levels [41]. In a Chinese study of 81 CHB patients undergoing liver biopsy, pSWE and VCTE had AUCs of 0.76 and 0.72 for significant fibrosis and 0.75 and 0.87 for cirrhosis, indicating similar diagnostic capabilities between the two methods [44].

2D-Shear Wave Elastography

Numerous studies have demonstrated the high diagnostic accuracy of 2D-SWE in evaluating liver fibrosis in CHB patients [45–54]. Using 2D-SWE, the AUC, cutoff values, sensitivity, and specificity for diagnosing significant fibrosis ranged from 0.88 to 0.97, 6.9–8.2 kPa, 77–94%, and 74–92%, respectively. For diagnosing cirrhosis, these values were 0.83–0.98, 8.0–21.4 kPa, 80–97%, and 73–95%, respectively.

A meta-analysis of 13 studies involving 400 CHB patients found that the AUC, cutoff, sensitivity, and specificity were 0.91, 7.1 kPa, 88%, and 74% for significant fibrosis, and 0.91, 11.5 kPa, 80%, and 93% for cirrhosis [55]. Another meta-analysis of 11 studies including 2,623 patients reported an AUC of 0.92 with a 7.9 kPa cutoff for significant fibrosis [56]. Studies excluding patients on AVT showed a lower average cutoff of 7.2 kPa for significant fibrosis compared to 8.9 kPa in studies with patients receiving AVT, indicating the need for AVT-specific cutoffs [53].

Another meta-analysis found that 2D-SWE outperformed VCTE by 11.2% for significant fibrosis and 6.5% for cirrhosis [55]. However, a Greek study involving 106 CHB patients showed that VCTE had a slightly higher success rate in measurements for obese patients compared to 2D-SWE (92% vs. 86%) [57]. ALT levels also influence SWE results. In a study of 515 CHB patients, using two ALT-based cutoffs enhanced

2D-SWE's diagnostic performance [58]. Cutoffs of 5.4 and 9.0 kPa were applied for ALT levels ≤ 2 times the upper limit of normal (ULN), while 7.1 and 11.2 kPa were used for ALT levels > 2 times the ULN for diagnosing significant fibrosis. For cirrhosis, cutoff values were 8.1 and 12.3 kPa for ALT levels ≤ 2 times the ULN, and 11.9 and 24.7 kPa for ALT levels > 2 times the ULN [56].

Treatment Decisions Using Elastography in CHB

CHB patients with ALT levels consistently one to two times the ULN are typically classified in the gray zone. Approximately 30% of CHB patients fall into a "gray zone," where serum HBV DNA and ALT levels do not clearly correspond to any specific phase in the virus's natural progression [59,60]. Studies have shown that CHB patients in the gray zone have a higher HCC risk compared to those in the immune-tolerant and immune-inactive phases. However, AVT is often withheld in these cases because ALT levels, a marker of liver injury, are not significantly elevated [61].

A recent multinational study indicates that AVT in gray zone CHB patients may reduce HCC risk by up to 70% compared to untreated patients, with a notable reduction in cumulative HCC incidence within five years after AVT initiation [62]. Consequently, strategies are being developed to identify high-risk gray zone patients who may benefit from AVT. AVT can be started if moderate or greater inflammation or significant fibrosis is confirmed [30]. Patients aged 30–40 years or older with ALT at the ULN, or those with normal ALT but persistently high HBV DNA levels, also face elevated HCC risk and should be evaluated for liver fibrosis, with AVT considered as needed [30]. Liver fibrosis can be assessed using non-invasive tests like VCTE and MRE, and AVT may be initiated if significant fibrosis is detected [63]. Considering the results of previously reported two meta-analyses, if VCTE results are above 7.2–7.7 kPa, there is a possibility of significant fibrosis, and antiviral therapy could be actively considered [35,37].

CHRONIC HEPATITIS C

Assessing fibrotic burden in CHC patients is essential, as it significantly impacts prognosis, including risks of HCC, liver-

related complications, and mortality [64]. Imaging techniques such as VCTE and SWE have been used to diagnose liver fibrosis in CHC patients.

Vibration-Controlled Transient Elastography

The effectiveness of VCTE for assessing liver fibrosis in CHC patients has been supported by numerous studies. Sensitivity for diagnosing significant fibrosis ranges from 48% to 96%, with specificity between 32% and 93%, depending on study-specific characteristics and cutoff values. For cirrhosis diagnosis, sensitivity varies from 65% to 100%, while specificity is between 85% and 96% [32,38,65–70].

The largest study to date, involving 1,289 CHC patients across three cohorts, reported an AUC of 0.76 for significant fibrosis with an 8.8 kPa cutoff, 48% sensitivity, and 93% specificity. For cirrhosis, the AUC was 0.90, with a 14.5 kPa cutoff, 65% sensitivity, and 95% specificity, showing comparable results [66]. However, in a multicenter study conducted in Korea with 349 CHC patients, the AUC for diagnosing significant fibrosis using VCTE was 0.82, with a cutoff of 6.8 kPa, sensitivity of 67.0%, and specificity of 86.4% [70]. The cutoff values for significant or advanced fibrosis in this study were slightly lower than in previous research, as it only included patients with ALT levels below five times the upper limit of normal to adjust for the higher LS values seen with elevated ALT. The AUC for cirrhosis diagnosis was 0.91, with a cutoff of 14.5 kPa, sensitivity of 81.8%, and specificity of 89.0%, aligning with results from studies in Western populations.

A meta-analysis of 37 studies on CHC patients found that VCTE cutoff values for significant fibrosis ranged from 5.2 to 10.1 kPa, with a sensitivity of 79% and specificity of 83%, while for cirrhosis, cutoffs ranged from 9.2 to 17.3 kPa, with 89% sensitivity and 91% specificity [71]. Another meta-analysis, presented by the American Gastroenterological Association and including 17 studies with 5,812 CHC patients, reported a VCTE cutoff of 12.5 kPa, with a sensitivity of 86% and specificity of 90% [72]. For groups with a cirrhosis prevalence below 5%, a cutoff of 12.5 kPa yielded a 0.7% false-negative rate and an 8.6% false-positive rate. In high-risk groups with a 30% cirrhosis prevalence, the false-negative rate was 4.2% and the

false-positive rate was 6.3%.

Research on VCTE's diagnostic accuracy for liver fibrosis in CHC patients after antiviral therapy and achieving sustained virologic response (SVR) is limited. In a study involving patients with an initial LS value of 10 kPa or higher who achieved SVR after AVT, LS values decreased post-SVR, yet over half showed histological evidence of cirrhosis three years later [73]. The AUC of VCTE for diagnosing cirrhosis post-SVR was 0.75, with pre-treatment LS values being the strongest predictor of cirrhosis. Serum markers, such as APRI and FIB-4, provided similar findings.

While VCTE generally shows high diagnostic accuracy with AUC values above 0.8 for fibrosis in CHC studies, limitations remain. Previous studies often lacked clear exclusion criteria for coexisting conditions that could affect VCTE results and included patients with substantial intrahepatic inflammation, potentially leading to overestimation of test values [38,74].

Point Shear Wave Elastography

Several studies have evaluated pSWE for diagnosing liver fibrosis in CHC patients. In a study of 61 CHC patients, the AUC of pSWE for significant fibrosis was 0.79 with a cutoff of 1.33 m/s. For advanced fibrosis, the AUC was 0.83 with a 1.43 m/s cutoff, and for cirrhosis, the AUC was 0.84 with a 1.55 m/s cutoff [75]. In another study involving 101 CHC patients in Korea, pSWE showed an AUC of 0.85 for significant fibrosis with a 1.335 m/s cutoff, yielding 84% sensitivity and 76% specificity. For advanced fibrosis, the AUC was 0.84 with a 1.645 m/s cutoff, providing 80% sensitivity and 76% specificity. For cirrhosis, the AUC was 0.83 with a 1.665 m/s cutoff, along with 85% sensitivity and 69% specificity [76]. A meta-analysis of three studies identified pSWE cutoff values of 1.21–1.34 m/s for significant fibrosis, with 79% sensitivity and 89% specificity. For cirrhosis, based on four studies, the cutoff ranged from 1.6 to 2.3 m/s, with sensitivity of 84% and specificity of 77% [71].

A multicenter prospective study in Europe with 241 CHC patients compared the diagnostic accuracy of pSWE and VCTE [77]. The AUCs for pSWE and VCTE were 0.81 and 0.85 for diagnosing significant fibrosis, 0.88 and 0.92 for advanced fibrosis, and 0.89 and 0.94 for cirrhosis, demonstrating similar

diagnostic effectiveness. However, VCTE had a higher measurement failure rate at 10%, compared to 5.3% for pSWE.

2D-Shear Wave Elastography

In a study of 211 CHC patients, 2D-SWE showed an AUC of 0.83 for diagnosing significant fibrosis with a cutoff of 6.16 kPa [78]. For advanced fibrosis, the AUC was 0.95 with a cutoff of 6.8 kPa, providing 97% sensitivity and 90% specificity. Diagnostic accuracy decreased in patients with a BMI over 30 kg/m². For another group, the AUC for significant fibrosis was 0.92 with a cutoff of 1.56 m/s, yielding 85% sensitivity and 86% specificity. For advanced fibrosis, the AUC was 0.94 with a cutoff of 1.72 m/s, achieving 89% sensitivity and 84% specificity. For cirrhosis, the AUC was 0.949 with a cutoff of 1.93 m/s, with 91.4% sensitivity and 90.8% specificity [78].

In a study assessing non-invasive tests among 79 CHC patients, the AUCs for diagnosing significant fibrosis were: 2D-SWE at 0.75, VCTE at 0.95, FIB-4 at 0.81, and APRI at 0.77, with 2D-SWE having the lowest AUC [76]. For cirrhosis diagnosis, the AUCs were 0.83 for 2D-SWE, 0.99 for VCTE, 0.81 for FIB-4, and 0.77 for APRI, with 2D-SWE showing lower diagnostic performance than VCTE.

The diagnostic accuracy of SWE in CHC patients has not been as extensively validated as other non-invasive tests, and caution is advised when interpreting results due to the variety of equipment used. Although SWE may achieve a higher measurement success rate, including in obese patients, there is a risk of overestimation in cases of severe intrahepatic inflammation. Comparative studies with other non-invasive tests (NITs) are limited, and findings have sometimes been inconsistent. Nonetheless, most studies report high diagnostic accuracy for SWE, comparable to VCTE, indicating its potential usefulness in assessing liver fibrosis in CHC patients.

Identifying High-Risk Groups Requiring Post-HCV Eradication Surveillance Using Elastography

Recommendations for HCC surveillance differ across guidelines for HCV patients in the post-SVR period who have advanced fibrosis (METAVIR F3) or cirrhosis (METAVIR F4) [79,80]. In addition to the limited research on the accuracy of

VCTE for diagnosing liver fibrosis in CHC patients post-SVR with antiviral therapy, the potential for antiviral therapy to improve liver health and reduce the risk of HCV-related HCC highlights the importance of tracking changes in non-invasive measurements during the post-SVR period as a crucial component of HCC risk assessment [81,82].

A large meta-analysis of 24 studies with 2,934 HCV patients reported a significant decrease in LSM using VCTE after SVR [83]. Without paired liver biopsies, it is unclear whether this LSM reduction reflects hepatic inflammation resolution or actual fibrosis regression. A recent meta-analysis including 27 studies (169,911 patients) showed that pre-treatment VCTE values of >9.2 – 13 kPa showed pooled AUCs of 0.79 for predicting HCC development after SVR [84]. While post-SVR VCTE values of >8.4 – 11 kPa retained strong predictive performance, though slightly lower, with pooled AUCs of 0.77. The optimal cut-off for HCC development after SVR was identified as 12.6 kPa for pre-treatment VCTE and 11.2 kPa for VCTE measured post-SVR.

METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

The prognosis of MASLD depends significantly on histological features, particularly liver fibrosis, which is the primary predictor of long-term outcomes, including risks of HCC and liver-related mortality [85]. In clinical practice, NITs such as VCTE, SWE, and MRE are commonly used to assess liver steatosis and fibrosis; however, in MASLD patients with obesity or elevated ALT, increased liver steatosis can decrease the diagnostic accuracy of VCTE, requiring cautious interpretation of results [86–88].

Vibration-Controlled Transient Elastography

Many studies have evaluated the diagnostic utility of VCTE in MASLD patients, showing high sensitivity and specificity in meta-analyses [88–93]. VCTE demonstrates an AUC of 0.65–0.98 for advanced fibrosis with cutoff values between 6.6–10.4 kPa, and an AUC of 0.94–0.97 for cirrhosis with cutoffs from 10.3–17 kPa, indicating strong diagnostic value in both cases. This meta-

analysis included data from 63 studies with 19,199 patients. However, accuracy decreases in patients with abdominal obesity, and around 5–20% cannot complete the test with a standard M probe [94,95]. Using an XL probe in these cases significantly reduces failure rates [96].

In a study of severely obese individuals undergoing bariatric surgery (mean BMI 42.3 kg/m²), VCTE showed an AUC of 0.85 and a cutoff of 7.6 kPa for advanced fibrosis, with the XL probe used in 96% of patients due to a skin-to-liver capsule distance of ≥ 2.5 cm [97]. A multicenter study in Hong Kong and France demonstrated similar median LS values and diagnostic performance with both M and XL probes for patients with BMI above or below 30 kg/m² [98]. Conversely, a study in Japan suggested different cutoffs for advanced fibrosis when using XL versus M probes (8.2 kPa for XL and 10.8 kPa for M), indicating further validation is needed [99].

In obese patients (BMI ≥ 30 kg/m²) or those with ALT ≥ 100 IU/L, VCTE accuracy decreased, with higher controlled attenuation parameter (CAP) scores linked to an increased false positive rate [88,100,101]. Researchers recommend combining NAFLD fibrosis score or liver biopsy for fibrosis assessment in patients with CAP scores over 300 dB/m and VCTE values between 10.1–12.5 kPa. VCTE results require cautious interpretation as they can be influenced by fasting status, abdominal obesity, cholestasis, elevated aspartate aminotransaminase (AST) and alanine aminotransaminase (ALT) levels, and liver steatosis [102].

A recent international, multicenter cohort study introduced the FibroScan-AST (FAST) score, integrating VCTE results, CAP score, and AST to assess patients with metabolic dysfunction-associated steatohepatitis and significant fibrosis [103]. With a cutoff of 0.35, the FAST score achieved a PPV of 83% and an NPV of 85%, and demonstrated a c-index of 0.85 in external validation, confirming high diagnostic accuracy.

Another international study across seven centers proposed the AGILE score, which leverages VCTE and outperformed FIB-4 and VCTE alone in diagnosing advanced fibrosis and cirrhosis [104]. AGILE 3+, which incorporates age, sex, AST/ALT ratio, platelet count, type 2 diabetes mellitus status, and VCTE, had a lower cutoff of 0.451 and upper cutoff of 0.679, achieving an AUC of 0.76 and a PPV of 0.72 for advanced fibrosis. For

cirrhosis, AGILE 4, with cutoffs of 0.251 and 0.565, showed an AUC of 0.93 and a PPV of 0.73.

Point Shear Wave Elastography

When used to detect significant fibrosis in MASLD patients, pSWE achieves an AUC of ≥ 0.8 [105,106]. pSWE is particularly effective for diagnosing advanced fibrosis, with reported sensitivity and specificity of 100% and 91%, respectively [107]. In a single-center study in Korea, pSWE demonstrated an AUC of 0.861 and a cutoff of 1.395 for advanced fibrosis; however, in patients with liver steatosis, diagnostic accuracy decreased as steatosis severity increased, with AUCs of 0.911, 0.847, and 0.686 for mild, moderate, and severe steatosis, respectively [26]. Several meta-analyses have shown pSWE's diagnostic performance to be comparable to that of VCTE [108,109].

2D-Shear Wave Elastography

In a prospective study, 2D-SWE achieved an AUC of 0.920 for diagnosing advanced fibrosis, comparable to VCTE (AUC 0.915) [110]. However, a recent meta-analysis of 82 studies involving 47,609 MASLD patients reported an AUC of 0.72 for 2D-SWE in diagnosing advanced fibrosis, slightly lower than pSWE (AUC 0.89) and VCTE (AUC 0.92), indicating the need for further investigation [109]. Interpretation of SWE results should be approached with caution, as they can be influenced by factors such as fasting, abdominal obesity, cholestasis, AST, ALT, and liver steatosis. Notably, 2D-SWE may be more user-friendly for obese patients, as its measurement location can be adjusted in real-time [111].

Referral Pathways and Strategies for Managing MASLD

Despite MASLD's high prevalence in primary care, it is largely unrecognized outside of Hepatology and Gastroenterology, with many physicians overlooking it [112]. Consequently, fewer than 10% of NAFLD patients are referred to specialists, missing opportunities for early intervention [113].

There is extensive evidence on the diagnostic accuracy of non-invasive tests for detecting advanced fibrosis in MASLD patients. However, these methods are limited in general population

application [114]. Test performance is heavily influenced by the prevalence of the condition being assessed, meaning that tests developed and validated in referral centers should only be applied in primary care if specifically validated for that context. Evaluations for MASLD and advanced fibrosis are recommended for individuals with (A) T2D, (B) abdominal obesity plus one or more additional metabolic risk factors, or (C) persistently elevated liver enzymes.

A multi-step process is recommended to identify individuals at risk for advanced fibrosis. First, the FIB-4 test should be administered. If the FIB-4 score is above 1.3 (or above 2.0 for individuals over 65), the likelihood of advanced fibrosis increases. However, due to a high false positive rate, this may lead to excessive additional testing. Therefore, in individuals with FIB-4 scores between 1.3 and 2.67, liver elastography could be performed as a second step to confirm fibrosis stage [114].

If VCTE fails or further assessment of liver fibrosis is required, MRE and liver biopsy are possible options [9,115]. Patients at moderate or high risk should be referred to a hepatologist for precise evaluation and appropriate management of liver fibrosis. The hepatologist will perform a thorough review of the patient's history and liver fibrosis risk, with additional non-invasive tests such as MRE, ELF, and the AGILE score, available for further fibrosis assessment. In cases where cirrhosis is diagnosed, careful monitoring and follow-up are essential due to the significantly elevated risk of liver-related complications and HCC. A liver biopsy may be conducted in patients with inconclusive NIT results or when the level of fibrosis is challenging to determine, with follow-up and treatment tailored according to fibrosis progression.

CONCLUSION

Over the past two decades, significant progress has been made in the non-invasive assessment and risk stratification of CLDs. These advances have largely been driven by high-throughput analytic platforms and data science, leading to a precision medicine approach, which tailors treatment to individual genetic and physiological profiles, potentially improving outcomes in CLDs. Although MRE demonstrates the highest diagnostic performance, particularly excelling in distinguishing fibrosis stage

2, US-based elastography offers notable advantages, including shorter examination time, lower cost, and greater accessibility. Considering the strengths and limitations of each method, the selection of an appropriate diagnostic tool or a sequential testing strategy may provide a more accurate assessment of fibrosis stages and prognosis in patients with chronic liver disease. Further validation and integration of elastography-based methods, along with novel biomarkers, are needed before these tools can be widely implemented in clinical practice.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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