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Transient Elastography and Fibroscan: Stethoscope of a Hepatologist in Today's World

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Abstract

Purpose of Review: Vibration-controlled transient elastography (VCTE) has become a cornerstone in the noninvasive assessment of liver disease across etiologies. This review highlights its role in risk stratification and longitudinal monitoring, emphasizing its value in both clinical practice and research settings, including community and academic hepatology.

Recent Findings: VCTE reliably assesses liver fibrosis severity and clinically significant portal hypertension and enables ongoing monitoring of therapeutic response. It also predicts liver-related events and mortality. Recognizing its limitations and potential confounders is essential to ensure diagnostic accuracy, and its performance can be further enhanced by integrating clinical and biochemical variables.

Summary: Despite inherent limitations, improvements in probe design, standardized protocols, and composite algorithms have expanded its clinical utility. The 2022 Baveno consensus

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established clear guidance for using VCTE to identify clinically significant portal hypertension, ultimately aiming to prevent first decompensation and improve patient outcomes.

Keywords

Vibration controlled transient elastography (VCTE); Non-invasive test (NIT); Compensated advanced chronic liver disease (cACLD); Clinically significant portal hypertension (CSPH); Liver fibrosis measurement (LSM)

Introduction

Fibrosis is the result of chronic liver disease associated with inflammation from any etiology. Fibrosis goes through four stages (F1 to F4), with F4 also known as cirrhosis, the most advanced stage associated with morbidity and mortality [1, 2]. Because fibrosis stage is a key determinant of prognosis, accurate assessment is essential for risk stratification, therapeutic decision-making, and longitudinal monitoring for disease progression or regression.

Historically, liver biopsy has been considered the gold standard for assessing fibrosis. However, invasiveness and sampling error associated with biopsy limit its use in clinical care of feasibility for serial evaluation [3]. Over the past two decades, both serum-based and imaging-based non-invasive tests (NITs) have become integral to hepatology practice. Endorsed by major society guidelines, these modalities are now widely applied for initial assessment, follow-up, and evaluation of treatment response, substantially reducing the need for liver biopsy in both clinical and research settings [4, 5]. Among imaging-based NITs, vibration-controlled transient elastography (VCTE) commercially known as FibroScan® (Echosens, Paris, France), is the most widely studied and utilized tool. VCTE provides a liver stiffness measurement (LSM) in kilopascals (kPa) for fibrosis staging. It also provides controlled attenuation parameter (CAP) measurement in decibels (dB) to quantify steatosis [6]. VCTE has been extensively validated in liver diseases due to several different etiologies with cut-off values to determine the fibrosis stage [7]. Continued refinements, including optimized probes, standardized acquisition protocols, and integration with other non-invasive markers, have further enhanced its diagnostic accuracy.

Other elastography modalities include shear wave elastography (SWE) and magnetic resonance elastography (MRE), the latter offering high diagnostic accuracy, but its broader use is restricted by cost and availability [8–10]. Together, these advances have redefined liver disease assessment, making non-invasive, repeatable, and accessible fibrosis and steatosis evaluation a cornerstone of modern hepatology. For the purposes of this review, the term VCTE will be used to refer to FibroScan.

Vibration-Controlled Transient Elastography: General Principles

VCTE utilizes M-mode ultrasonography to monitor the propagation speed of a mild-amplitude, low-frequency shear wave (50 Hz), generated by a mechanical vibrator integrated into the probe. The shear wave velocity (V) is used to calculate the elastic modulus (E) of liver tissue via the relation $E = 3\rho V^2$, where ρ represents tissue density, assumed constant

across tissues [11, 12]. The resultant LSM spans from 2.5 to 75 kiloPascal (kPa) and serves as an indicator of fibrosis severity. The assessed tissue volume is approximately 3 cm³, located 25 to 65 mm beneath the skin surface, representing at least 100 times the volume of a standard liver biopsy sample. Reliable LSM requires at least 10 valid acquisitions with an interquartile range (IQR) less than 30% of the median value [13, 14].

For adult patients, two probes are available: the M probe, suitable for skin-to-liver capsule distances less than 25 mm, and the XL probe, designed for greater depths (35–75 mm) typically seen in obese individuals. A pediatric S probe has also been developed, with S1 and S2 configurations tailored to thoracic circumferences below 45 cm and between 45 and 75 cm, respectively [15, 16]. The XL probe achieves high success rates (> 95%) in obtaining valid LSM in patients with obesity (BMI) ≥ 40 kg/m². Recent data supports using M2 probe in those with BMI ≥ 32 kg/m², with a reported 78% prevalence of skin-to-liver capsule distance ≥ 25 mm in this group [16].

CAP embedded in VCTE, is a technique that measures hepatic steatosis by quantifying how sound waves lose energy as they pass through the liver tissue [17, 18]. Measurements range from 100 to 400 dB/m, with high interobserver reproducibility (concordance correlation coefficient 0.82–0.84) [19, 20]. Thresholds for steatosis grading vary based on population studies, underlying disease, and fibrosis severity, with notable overlaps and discordance in high CAP values (> 300 dB/m) [21, 22]. Recent approaches optimize cutoffs to balance sensitivity and specificity at 90%, with thresholds around 263–285 dB/m for $\geq 5\%$ steatosis, and a proposed standard of 275 dB/m across etiologies [23]. CAP is superior to blood-based methods and can monitor therapy response, with a ≥ 35 dB/m change indicating improvement [24–26]. CAP interpretation should consider probe type, fasting status, stiffness, and IQR/median range.

Role of VCTE in Fibrosis Assessment

Since its introduction in 2003, VCTE is used commonly used as a noninvasive radiological biomarker for staging fibrosis in patients with liver disease [27]. To make comparisons easier across studies, different liver fibrosis staging systems using the Metavir scoring system were converted into a single, standardized framework: no fibrosis (F0), any fibrosis (F1 or higher), significant fibrosis (F2 or higher), advanced fibrosis (F3 or higher), and cirrhosis (F4) [28]. While some variability exists, the correlation between liver stiffness and biopsy findings has been strong enough to support the use VCTE as a reliable tool [29]. VCTE has demonstrated good diagnostic accuracy across various liver diseases, particularly in staging fibrosis.

One challenge with VCTE-based techniques is that the cut-off values for staging fibrosis can vary depending on the underlying cause of liver disease. According to AASLD guidance, LSM <8 kPa can confidently exclude advanced fibrosis in patients with chronic liver disease. [23] Recently, Baveno VI consensus defined *compensated advanced chronic liver disease*(cACLD), to include patients with advanced fibrosis (F3) and cirrhosis (F4), [30] with both stages implying advanced fibrosis. [31] Further, this consensus group also introduced a “rule of five” (Figure 1). In this framework, an LSM of ≤ 5 kPa is considered

normal, <10 kPa, reliably excludes cACLD, 10–15 kPa raises suspicion for cACLD, and >15 kPa diagnoses cACLD, 20–25 kPa or higher with a platelet count <150,000, suggests clinically significant portal hypertension (CSPH). [31, 32].

Use of VCTE for the Assessment of Chronic Liver Diseases

Metabolic Dysfunction-Associated Steatotic Liver Disease

Metabolic dysfunction-associated steatotic liver disease (MASLD) contributes significantly to the morbidity and mortality due to end-stage liver disease and complications including hepatocellular carcinoma [33], cardiovascular disease and non-liver malignancy [34]. FIB-4 score has emerged as a simple NIT, based on patient age, AST, ALT and platelet counts, to estimate the likelihood of advanced fibrosis. Multiple society guidelines recommend a two-tiered approach using FIB-4 as first-line NIT, followed by VCTE for patients classified by FIB-4 as having an indeterminate risk or high risk of advanced fibrosis [4, 35–37]. However, this approach results in 12% referral to hepatology. With VCTE as the first step strategy, the referral rate to hepatology is 19% with a very low false negative rate of 3–4% for advanced fibrosis (F3-F4) [38].

Notwithstanding, the sequential FIB-4 and VCTE stratify the risk of liver-related complications in MASLD, and that VCTE has similar prognostic accuracy as liver biopsy [39, 40]. In addition, the measurement of liver stiffness and CAP score can serve to track and motivate patients to enact lifestyle modifications that can improve MASLD severity [41] as well as to predict long term survival and liver complications in patients with MASLD [42].

Patients with type 2 diabetes mellitus (T2DM) and moderate to severe obesity (BMI > 35 kg/m²) have a high prevalence of MASLD [43], advanced fibrosis (AF) and metabolic dysfunction-associated steatohepatitis (MASH) [44–46]. These at-risk groups should undergo targeted screening using sequential FIB-4 followed by VCTE studies or combined VCTE based NITs such as FAST (Fibroscan-AST) or FIB-5 scores (FIB-4 + Fibroscan) [47]. Bariatric surgery is associated with a positive impact on the degree of hepatic steatosis and inflammation in MASLD [48, 49]. VCTE can be used for monitoring and has shown good diagnostic accuracy in detecting advanced stage and grade of MASLD following bariatric surgery [50]. The use of semaglutide in subjects with T2D and MASLD has been shown to be associated with a significant decline of liver steatosis as monitored by serial VCTE, however the average follow up period in this study was only 6.4 months [51].

Alcohol-Related Liver Disease and Met-ALD

VCTE is the most reliable noninvasive method for the diagnosis of advanced fibrosis and cirrhosis in alcohol-related liver disease (ALD). It performed better than Fibrotest (0.81 and 0.88), APRI (0.65 and 0.75) and FIB-4 (0.70 and 0.73) [52]. An individual patient data meta-analysis yielded liver stiffness cutoffs of 7.0 kPa (area under the receiver operating characteristic curve 0.83 [SE 0.02; 95% CI 0.79–0.87]) for F ≥ 1 fibrosis, 9.0 kPa (0.86 [0.02; 0.82–0.90]) for F ≥ 2, 12.1 kPa (0.90 [0.02; 0.86–0.94]) for F ≥ 3, and 18.6 kPa (0.91 [0.04; 0.83–0.99]) for F = 4 [53, 54]. As the LSM is strongly

influenced with liver inflammation in ALD, LSM cutoff values should consider AST and bilirubin concentrations, especially in patients with ongoing active alcohol use. LSM by VCTE predicts decompensation and all-cause mortality in patients with compensated ALD both at diagnosis and when used for monitoring [55]. Future investigations are needed to investigate the role of VCTE in alcohol-associated hepatitis (AH), particularly with respect to prognostication and assessment of treatment response.

Viral Hepatitis

Based on a meta-analysis, the revised World Health Organization (WHO) guidelines for significant fibrosis and cirrhosis in chronic hepatitis B (CHB) recommend LSM > 7.0 kPa to identify adults with significant fibrosis ($\geq F2$) and > 12.5 kPa to identify those with advanced fibrosis and cirrhosis, and who are a priority for antiviral treatment [56].

LSM can be a useful tool in predicting hepatocellular (HCC) development in patients with CHB. In a prospective study of 1,130 patients with non-biopsy-proven CHB were followed between May 2005 and December 2007, with a median follow-up period of 30.7 (24.0–50.9.0.9) months. HCC developed in 57 patients at a rate of 2.0%/person-year, with 1, 2, and 3-years cumulative incidence rates of HCC were 0.80%, 3.26%, and 5.98%, respectively. On multivariate analysis, together with old age, male sex, heavy alcohol consumption (> 80 g/day), serum albumin, and hepatitis B e antigen positivity, patients with a higher LSM (> 8 kPa) were at a significantly greater risk of HCC development [57]. In another systemic review and meta-analysis, the risk of HCC development was elevated in CHB patients LSM of ≥ 11 kPa on VCTE examination. Taken together, these findings suggest that VCTE-based LSM values may aid in the risk prediction of HCC development in CHB patients [58].

Much of the early experience with LSM was derived from hepatitis C population, when prior to the introduction of pangenotypic treatments, fibrosis staging was required by insurance and state Medicaid plans before approval of antiviral therapy. VCTE demonstrated excellent diagnostic performance for identifying HCV-related cirrhosis but showed reduced accuracy in detecting earlier stages of fibrosis [59, 60]. Despite a significant reduction in LSM after sustained virological response (SVR), patients with advanced fibrosis (LS ≥ 8 kPa at 48 weeks after SVR) remain at risk for liver-related complications particularly HCC development [61, 62]. Therefore, screening for HCC and portal hypertension should continue despite decrease in LSM if the patient had cACLD before starting the treatment. Moreover, LSM ≥ 20 kPa and male sex are independent predictors of HCC development in this population [62].

Cholestatic Liver Diseases

VCTE has better diagnostic accuracy in autoimmune liver disease patients, especially PBC patients. The cutoff values for staging advanced fibrosis and cirrhosis ranged from 9.6 to 10.7 and 14.4 to 16.9 KPa respectively for PBC patients in a recent meta-analysis [63, 64].

In an international, multicenter, retrospective follow-up study of 3,985 patients with primary biliary cholangitis (PBC) seen at 23 centers in 12 countries, LSM by VCTE was found to be a major, independent, validated predictor of PBC outcome [65]. Tracking longitudinal changes in LSM using VCTE provides valuable insights into PBC prognosis, offering a

robust predictive measure for the risk of serious adverse events [66]. The authors conclude LSM is a strong predictor of clinical outcomes and could be a useful surrogate endpoint in PBC trials [65, 66].

There are no validated non-invasive markers for liver fibrosis in patients with primary sclerosing cholangitis (PSC). In a prospective study of 73 consecutive patients with PSC, LSM by VCTE was compared with liver biopsy. Cutoff values for fibrosis stages $\geq$ F1, $\geq$ F2, $\geq$ F3, and F4 were 7.4 kPa, 8.6 kPa, 9.6 kPa, and 14.4 kPa, respectively. The adjusted diagnostic accuracy values for severe fibrosis and cirrhosis were 0.83 and 0.88, respectively [67]. VCTE can differentiate severe from non-severe liver fibrosis and serial longitudinal changes can provide prognostic information in patients with PSC.

Autoimmune Hepatitis

Though guidelines recommend biopsy to establish diagnosis and make treatment decisions in patients with autoimmune hepatitis (AIH) [68, 69]. VCTE shows high diagnostic accuracy for staging liver fibrosis in patients with AIH. VCTE outperforms non-invasive markers such as FIB-4 and APRI in differentiating the stages of fibrosis in AIH patients, AUROC of 0.885 for stage F2, 0.897 for stage F3, and 0.878 for stage F4 [70]. In a meta-analysis, the summary AUCs for AF and cirrhosis were 0.88 and 0.92, respectively, while the cutoff values for AF and cirrhosis in AIH were 8.2–12.1 and 12.3–19.0 respectively [71]. Taken together, these findings support VCTE's excellent diagnostic performance in staging liver fibrosis in patients with AIH.

Role of VCTE in Special Populations

Children and Adolescents

The prevalence of MASLD is increasing in adolescents and young adults due to the obesity and alcohol pandemics in a study using the National Health and Nutrition Examination Survey (NHANES) database (2017–2018) [72]. Current data support the use of LSM and CAP as a first-line tool in the diagnosis and evaluation of adolescent MASLD, to better stratify high-risk patients [73].

Biliary atresia (BA), a unique pediatric liver disease in children is characterized by progressive inflammatory obliterative cholangiopathy. If left untreated, fibrosclerosing obliteration progresses in both intrahepatic and extrahepatic bile ducts, which inevitably leads to liver cirrhosis. VCTE is valuable, non-invasive tool for assessing liver fibrosis in children with BA. The cut-off value of LSM (15.15 kPa) can distinguish cirrhotic patients from non-cirrhotic patients and correlates well with the biochemical changes of liver fibrosis and development of portal hypertensive complications [74, 75].

Sickle cell liver disease (SCLD) is a lifelong and progressive disease which results from a cumulative hepatic injury. VCTE may have a role in monitoring its disease progression [76].

Fontan-Associated Liver Disease

Fontan procedure is associated with a spectrum of liver diseases including hepatic fibrosis, cirrhosis, portal hypertension and hepatic neoplasia including HCC. LS measurement using

NITs such as VCTE and SWE may be of use in follow-up of patients undergoing the Fontan operation for early recognition of hepatic changes [77]. In a retrospective single-center study, involving 91 adult post-Fontan patients, LSM by VCTE and elapsed time since surgery was found to be a useful non-invasive method for diagnosis of Fontan-associated liver disease (FALD) (AUC: 0.877; sensitivity, 95.4%; specificity, 80.0%; positive predictive value, 96.9%; negative predictive value, 72.7%). LSM by VCTE was associated with clinically relevant events (OR = 1.07; 95%CI: 1.01–1.13; $P = 0.021$) and all-cause mortality (OR = 1.23; 95%CI: 1.02–1.47; $P = 0.026$) suggesting its possible role in prognosis [78].

Liver Transplant Recipients

The risk of MASLD is significant in the post-transplant period, with prevalence of metabolic syndrome ranging in 43–59%, T2DM 10–64% and obesity 24–64% [79]. Monitoring of graft function for steatosis and recurrent fibrosis is therefore paramount. Traditionally, surveillance or protocol biopsies have been performed. LSM measurements by VCTE combined with NITs is a promising alternative tool.

In a prospective study of liver transplant recipients, patients underwent liver biopsy and VCTE. The AUROC was 0.94 (0.89–0.99) for VCTE, 0.65 (0.50–0.79) for FAST, 0.90 (0.83–0.97) for Agile-3, and 0.90 (0.83–0.97) for Agile-4. The false-positive rates in LSM-based scores were higher among patients with diabetes mellitus, higher AST levels, and lower platelet count. The authors concluded that the lack of improvement in diagnostic performance results from the impact of immunosuppression on bio-clinical profile and underscores the importance of developing LSM-based scores that are specific to LT patients [80]. Furthermore, thrombocytopenia might persist post-transplant, which further compromises utilization of VCTE based scores that utilize platelet count as a variable [81]. A separate study suggested that LSM values < 8 kPa after LT for MASH are strongly correlated with absence of significant/advanced fibrosis [82].

Non-Cirrhotic Portal Hypertension

The data on non-invasive assessment using LSM by VCTE for predicting CSPH are limited in patients with non-cirrhotic portal hypertension (NCPH). A recent study of 155 patients with idiopathic NCPH and 273 patients with cirrhosis showed that LSM < 10 kPa strongly predicts porto-sinusoidal vascular disease (PSVD) in patients with signs of portal hypertension, whereas PSVD is highly unlikely at LSM > 20 kPa [83].

A recent European study showed the promising performance of spleen stiffness (SS) in predicting high-risk varices in patients with NCPH achieving an AUROC of 0.88 (0.75–100). This study reported a sensitivity of 93.3%, specificity 60.0%, and a negative predictive value of 90.9% at a cut-off of 35.4 kPa [84]. It is worth noting that SS is not routinely performed in many centers in the United States. In another study wherein transient liver and spleen elastography were performed using VCTE and the ratio between SSM and LSM (SSM/LSM index) achieved a good sensitivity and specificity for diagnosis of NCPH at a cut-off of 2 [85].

Monitoring of Drug Response and Toxicity

Long-term use of methotrexate therapy in can be associated with liver fibrosis. Although high-quality studies comparing VCTE with standard liver biopsy for monitoring methotrexate induced liver fibrosis are lacking, the evidence from multiple small cohort studies and case series suggest VCTE maybe a useful tool [86, 87]. A recent Australasian position statement recommends that VCTE should be routinely done in following patients on long-term methotrexate, repeated every 3 years if kPa < 7.5 and yearly if kPa > 7.5 [87].

While statins are well established in reducing cardiovascular risk, their impact on MASLD severity in patients with T2DM remains less well defined. In a cross-sectional analysis of adults with T2DM and MASLD from the 2017–2018 NHANES cycle, VCTE was used as a NIT to assess fibrosis. Statin use was associated with significantly lower odds of advanced fibrosis as measured by VCTE (OR 0.35, 0.13–0.90, $p=0.03$), underscoring the potential role of LSM in evaluating treatment-related effects on liver disease severity [88].

VCTE tends to overestimate advanced fibrosis and cirrhosis in patients with class 3 obesity, which may influence resmetirom eligibility in clinical practice [89]. In contrast, data from a German steatotic liver disease-registry evaluated resmetirom eligibility using different criteria including biopsy proven MASH, FibroScan-AST (FAST) score ≥ 0.67 and VCTE 8–15 kPa. Based on the VCTE 8–15 kPa, 28.5% patients were deemed eligible compared with 34% when biopsy findings were used [90].

Role of VCTE in Predicting Disease Progression and Mortality Outcomes

VCTE is a promising NIT for diagnosing clinically significant portal hypertension (CSPH). LSM cut-off at 22.8 kPa has a high accuracy for diagnosing CSPH. In a study of 4192 US adults aged ≥ 18 years enrolled in the NHANES (2017–2018), compared with LSM < 10 (absence of cACLD), LSM 10–19.9.9 (likely ACLD), and ≥ 20 kPa (likely CSPH) conferred a 3.4 (1.0–13.8.0.8) and 5.2 (1.2–22.3) folds risk of mortality [40]. VCTE, like other NITs such as FIB-4 and APRI has moderate accuracy for liver fibrosis diagnosis and esophageal varices prediction in patients with hepatocellular carcinoma [91]. It has been suggested that VCTE should be integrated into clinical practice for noninvasive diagnosis of CSPH [92].

Pitfalls and Challenges of VCTE in Clinical Practice

Despite its advantages, VCTE accuracy may be limited in acute hepatitis, hepatic congestion, cholestasis, and AH. Understanding these limitations is crucial for ensuring accurate diagnosis and management of liver diseases.

Acute Hepatitis

Inflammation can overestimate LSM and misleading results [93]. A strong correlation between aminotransferase levels and LSM has been observed, with LSM values typically returning to normal once the acute liver injury resolves [94, 95]. In a study on 18 patients admitted for acute viral hepatitis, liver stiffness exceeded established thresholds for significant fibrosis or cirrhosis (up to 75.4 kPa) at the time of peak aminotransferase elevation. During follow-up, a marked and statistically significant decline in liver stiffness was observed (median 17.1 to 5.4 kPa), corresponding with a parallel reduction in

aminotransferase levels ($P < 0.0001$) [96]. In conclusion, the extent of necroinflammatory activity needs to be carefully considered in future studies aimed at further validating VCTE, particularly in patients with absent or low-stage liver fibrosis.

Active Alcohol Use

VCTE has been evaluated and shown to be a useful tool for assessing liver fibrosis in ALD [97]. However, the optimal timing of testing whether during active alcohol consumption or following a period of abstinence remains uncertain. In ALD, the diagnostic thresholds for advanced fibrosis or cirrhosis are often higher than in other chronic liver diseases, likely due to the confounding effects of hepatic inflammation associated with alcohol associated hepatitis [98]. Multiple studies have demonstrated that liver stiffness values tend to decline during periods of alcohol withdrawal or abstinence, suggesting that acute alcohol use may transiently increase liver stiffness and lead to falsely elevated measurements at cost of positive predictive value. These findings support deferring VCTE until at least 2 to 4 weeks after alcohol cessation for more accurate assessment of fibrosis [99, 100].

A prospective study evaluated changes in LSM among patients with ALD at baseline and following alcohol abstinence. The study found a significant reduction in LSM after one month of abstinence, particularly in patients with baseline $LS > 7$ kPa and elevated transaminase levels. Compared to ongoing drinkers, abstinent patients experienced a significantly greater decline in LSM at 4 weeks (-2.6 ± 5.5 kPa vs. -2.2 ± 3.6 kPa; $p = 0.004$) [100].

However, many earlier studies did not clearly report the interval between the last alcohol intake and the timing of VCTE or biopsy, complicating the interpretation of their results. In a European multicenter study of 259 patients hospitalized for alcohol detoxification, 45 (17%) were diagnosed with cACLD based on liver biopsy performed at baseline. VCTE was conducted at baseline, one month, and two months. Among patients with baseline LSM values between 10 and 25 kPa and no histological evidence of cACLD, more than 50% exhibited a reduction in LS to < 10 kPa at follow-up. The study also demonstrated that VCTE can reliably exclude cACLD when LS is < 10 kPa and confirm its presence when LSM exceeds 25 kPa [101].

While the use of VCTE in AH remains controversial due to the potential overestimation of fibrosis due to inflammation, LSM can still be reliably utilized in patients with ALD when the assessment is deferred until at least 12 – 4 weeks of abstinence. Future studies should investigate the use of VCTE in assessing changes in the Lille score to guide treatment response in AH. Furthermore, integrating biochemical markers into VCTE-based algorithms may enhance diagnostic precision and improve clinical utility in this population.

Congestive Hepatopathy

In animal models, liver stiffness increased significantly with elevated central venous pressure, as demonstrated by reversible changes in both live pigs and isolated pig livers [102]. In a prospective study in patients with heart failure LSM were significantly elevated compared to healthy controls, particularly in those with right sided or acute decompensated heart failure [103]. These findings suggest that elevated central venous pressure, rather than

fibrosis, can directly influence liver stiffness and must be considered when interpreting VCTE results; therefore, liver biopsy combined with venous pressure measurements should be considered as the standard of care in this setting.

Cholestasis

Severe cholestasis particularly from extrahepatic obstruction has been shown to independently and significantly elevate liver stiffness values. In a study involving 15 patients with extrahepatic cholestasis, LSM was elevated (up to 15.2 kPa), falsely suggesting advanced fibrosis or cirrhosis; however, following successful biliary drainage, values significantly declined to near-normal levels (mean 7.1 kPa), demonstrating that cholestasis independently inflates LSM readings in VCTE regardless of true hepatic fibrosis [104].

Similarly, in other studies, LSM were found to be elevated in patients with choledocholithiasis or obstructive jaundice, with significant reductions observed after biliary decompression, supporting the conclusion that cholestasis alone can transiently increase liver stiffness irrespective of histologic fibrosis [105, 106]. Taken together, these studies emphasize the importance of considering and ruling out significant cholestasis, especially from extrahepatic causes before relying on LSMs, as doing so helps avoid overestimating fibrosis in this subset of patient.

Obesity

Approximately 70–80% of individuals with MASLD are overweight or obese, and this rises to 80–90% in biopsy-proven NASH cases [107]. However, VCTE derived LSM and CAP show limitations in patients with BMI ≥ 30 kg/m² [108, 109]. High BMI, greater skin-to-liver distance, sub-cutaneous fat, and waist circumference are independent predictors of measurement failure with the M-probe [110, 111], prompting development of the XL probe. This probe significantly reduces failure rates (1.1% vs. 16%) and improves LSM reliability in obese patients (BMI ≥ 28 kg/m²), though it requires lower liver stiffness cutoffs [112]. Using VCTE with the XL probe offers a feasible, noninvasive alternative to biopsy in obese and elderly patients [113]. Despite using optimal probe in a study conducted on 74 bariatric surgery patients, LSM had limited ability to detect significant fibrosis (AUROC 0.65), whereas CAP better identified hepatic steatosis (AUROCs 0.74–0.82) [114]. Importantly, VCTE tends to overestimate fibrosis in class 3 or morbid obesity. In a study of 245 MASLD patients, ≥ 2 -stage discordance between VCTE and biopsy occurred in 38.6% of class 3 obesity, versus 24.6% (class 2) and 18.4% (class 0–1) [89]. These results emphasize careful interpretation in severe obesity despite improved feasibility with the XL probe.

Novel Applications of Transient Elastography

NITs are playing a growing role in identifying patients with MASH who are at increased risk for cirrhosis and clinical decompensation. As new therapies become available and trials expand, early identification of appropriate candidates and the ability to monitor disease progression without repeated biopsies is essential [115, 116].

The diagnostic value of VCTE improves when LSM and CAP readings are interpreted alongside routine lab values (Table 1 and 2). One such tool, the FAST (FibroScan-AST)

score, integrates LSM, CAP, and aspartate aminotransferase (AST) to identify patients with active MASH (NAFLD Activity Score ≥ 4) and advanced fibrosis (stage F2 or greater). The score was developed using 350 patients and validated in a cohort of 1,026. It demonstrated good accuracy in both groups, with C-statistics of 0.80 (95% CI: 0.76–0.85) and 0.85 (0.83–0.87), respectively. A cutoff of 0.35 and 0.67 maximized sensitivity and specificity respectively. In the original cohort, this yielded a positive predictive value (PPV) of 0.83 and a negative predictive value (NPV) of 0.85. External validation showed NPV of 0.73–1.0, while PPV varied (0.33–0.81), reflecting differences in study populations [117]. Additional studies across U.S. and Asian populations confirmed the FAST score's role in identifying MASH with significant fibrosis, though in some settings LSM alone performed similarly or better [118, 119]. A Phase 2b clinical trial evaluating treatment response showed that a reduction of 0.22 in the FAST score was associated with histologic improvement, highlighting its use in therapy monitoring [120]. These results confirm the FAST score as a reliable, non-invasive tool for identifying high-risk MASH with significant fibrosis in clinical practice.

More recently, Agile 3 + and Agile 4 scores have emerged to stratify advanced fibrosis ($F \geq 3$) and cirrhosis ($F = 4$), respectively, both scores combine LSM with routine clinical data including AST/ALT ratio, platelet count, age, sex, and diabetes status. In a study on 3,761 patients across seven cohorts showed that Agile 3 + and Agile 4 outperformed FIB-4 and LSM, AUROC of 0.86–0.90 and 0.89–0.93 respectively [121]. A pooled analysis of six studies ($n = 6,955$) reported Agile-3 to have 88% sensitivity and 65% specificity for excluding advanced fibrosis, and 68% sensitivity with 87% specificity to confirm F3/F4 [122]. In a multicenter analysis, Agile 3 + and Agile 4 maintained strong performance (AUROC 0.85), comparable to LSM and outperforming FIB-4 ($p < 0.0001$) and reduced rates of indeterminate results (Agile 3+: 14% vs. FIB-4: 31%; Agile 4: 23% vs. LSM: 38%) [123].

A similar pattern was observed in a study of 246 patients with biopsy-confirmed MASH and advanced fibrosis. Agile 3 + and Agile 4 achieved excellent accuracy (AUROC 0.909 and 0.968, respectively) and reduced indeterminate cases compared to other methods. Agile 4, using a threshold of 0.60, reached 93.5% accuracy for cirrhosis and remained reliable in patients with obesity. In the same study the FAST score (AUROC 0.679) outperformed APRI, FIB-4 and LSM but left about one-third of patients in the gray zone [124].

SmartExam, a new VCTE feature, uses automated depth adjustment and continuous data capture to improve LSM and CAP reproducibility. While promising, it still requires further validation in diverse populations [125]. More recently, an AI-based model, ALADDIN-F2-VCTE, developed from 1,331 biopsy-proven MASH cases, predicted $\geq F2$ fibrosis with an AUC of 0.791, outperforming FAST, Agile 3+, and VCTE alone [126].

In summary, Agile 3+, Agile 4, and FAST are practical, well-validated scoring systems that aid in identifying advanced fibrosis and cirrhosis in MASLD. Agile 4 performs strongly for cirrhosis and may help assess portal hypertension, especially in obese MASH patients. While FAST shows moderate accuracy for fibrotic MASH, its ease of use supports treatment monitoring. Tools like SmartExam and ALADDIN represent the next frontier in improving

diagnostic confidence. Further research and real-world application will determine their place in routine care.

Conclusion

VCTE has revolutionized the noninvasive assessment of liver disease. Its ease of use at the point of care, rapid turnaround, and accurate, reproducible evaluation of fibrosis and steatosis across diverse hepatic pathologies have markedly reduced reliance on liver biopsy. VCTE enables earlier diagnosis and longitudinal monitoring of disease and treatment response. While factors such as hepatic congestion, inflammation, cholestasis, and severe obesity may confound results, advances in probe technology, standardized criteria, and integration with serum biomarkers and composite scores have improved diagnostic accuracy. Beyond liver stiffness, spleen stiffness measurement enhances its role in assessing portal hypertension and predicting major adverse liver outcomes. Emerging applications in artificial intelligence and clinical trials promise to expand its utility in patient stratification, prognostication, and precision care in hepatology. With increasing applications and utility of this simple widely available tool, it would not be wrong to say that VCTE or Fibroscan is emerging as a mandatory tool for hepatology practice/s, like a stethoscope of an internal medicine physician.

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Data Availability

No datasets were used for this manuscript.

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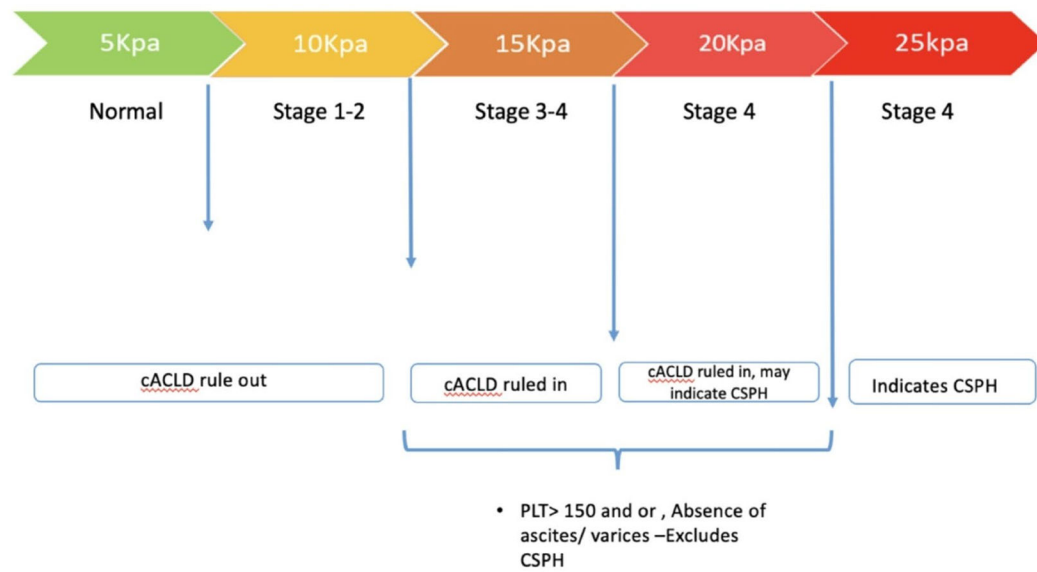
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Compensated advanced chronic liver disease (cACLD) , clinically significant portal hypertension (CSPH), Kilopascal (Kpa), Platelets (PLT)

Fig. 1.
Liver Stiffness-Based Risk Stratification for Advanced Fibrosis and Portal Hypertension
Using the “Rule of 5”

Table 1

Diagnostic accuracy of fibroscan (VCTE) in chronic liver diseases

Etiology	Fibrosis Stage	AUROC	Optimal LSM Cutoff (kPa)	Sensitivity	Specificity	PPV	NPV
HCV (Ref: 58)	≥F2	0.83	7.9	74	78	80	70
	≥F3	0.90	8.8	74	64	60	80
	F4	0.95	11.7	85	82	88	78
MASLD (Ref: 37)	≥F2	0.83 (0.8–0.86)	7.2	79	75		
	≥F3	0.87 (0.84–0.90)	9.2	85	82		
	F4	0.94 (0.91–0.96)	14.0	92	92		
ALD (Ref: 53,54)	≥F2	0.86 (0.82–0.90)	9.0				
	≥F3	0.90 (0.86–0.94)	12.1	(high)	(high)		
	F4	0.91 (0.83–0.99)	18.6				
AIH (Ref: 69)	≥F2	0.88	6.3	85	77	90	66
	≥F3	0.90	8.2	80	85	84	81
	F4	0.88	12.7	88	88	96	67
PBC (Ref: 64)	≥F2	~ 0.90 (est)	N/A	76	93		
	≥F3	0.91	9.3	88	90		
	F4	0.97	15.2	91	95		

Novel applications: combining Non-Invasive testing biomarkers with transient elastography in MASLD

Table 2

NIT (with TE)	Study	Cohort of MASH	N	Clinical Variables used with CAP and LSM	AUC (AUROC) and p Value compared to LSM
FAST Score	Newsome PN (2020)	At-risk MASH (F ≥ 2)	(N= 1376)	(MASH biopsy + LSM + labs) AST	0.80–0.85 ($p < 0.05$)
Agile 3+	Sanyal AJ (2023)	Advanced fibrosis (F ≥ 3)	(N = 3761)	(MASH biopsy + LSM + labs) AST/ALT, Platelets, Age, Sex, Diabetes	0.86–0.90 ($p < 0.05$)
Agile 4	Sanyal AJ (2023)	Cirrhosis (F = 4)	(N = 3761)	(MASH biopsy + LSM + labs) AST/ALT, Platelets, Age, Sex, Diabetes	0.89–0.93 ($p < 0.05$)
Aladdin	Dunn W (2025)	Cirrhosis (F = 4)	(N= 1331)	(MASH biopsy + LSM + labs) AST/ALT, Age, BMI, LDL, Hb A1c cholesterol, protein, albumin, GGTP	0.791 ($p < 0.005$)

FibroScan-AST Score (FAST), FibroScan-derived liver stiffness (LSM), controlled attenuation parameter (CAP), aspartate aminotransferase (AST), ALT Alanine Aminotransferase