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INTRODUCTION

Hepatic dysfunction is quite prevalent in critically ill patients, especially among
1 those with multiple organ failure, with a reported incidence of 10 to 40% [1,2]. Notably, hepatic dysfunction is linked to a higher mortality rate in critically ill patients, even without pre-existing liver disease. Indeed, the hepatic function is commonly used in clinical multifactorial scoring systems for prognostication in the intensive care unit (ICU) setting, for example, Acute Physiology and Chronic Health Evaluation II (cirrhosis as a factor) or Sequential Organ Failure Assessment score (bilirubin, and international normalized ratio as
2 components) [3]. Still, liver dysfunction and the role of the liver in the pathogenesis of systemic inflammatory response syndrome, sepsis, and multiorgan failure in the critically ill may be underrated because they are less obvious and less immediately life-threatening compared to respiratory, cardiovascular or renal dysfunction. Since no single physiologic variable allows for early detection of hepatic dysfunction, current diagnostic criteria are based
3 on laboratory tests, mostly serum bilirubin levels or international normalized ratio. Only a few specialized centres offer sophisticated measurements like the indocyanine green plasma disappearance rate, which reflects liver perfusion
4 and function in the critically ill [4]. Among other non-invasive tests, the measurement of liver stiffness by transient elastography (TE) is increasingly

used to evaluate hepatic dysfunction in critically ill patients. TE correlates well with liver dysfunction, and increasing stiffness values are also related to increased mortality in the ICU and non-hepatic organ failure patients [5]. Additionally, TE has shown promise in predicting the development of complications such as hepatic encephalopathy and hepatorenal syndrome in critically ill patients [6]. As a non-invasive test, TE can provide valuable information for monitoring liver function in critically ill patients, allowing for early detection and implementing appropriate interventions to prevent further deterioration of liver function and improve patient outcomes. However, even these non-invasive tests are not ideal and are associated with their limitations; hence, it becomes imperative for the practising physician to be aware of any existing limitations before applying and interpreting such tests.

LIVER STIFFNESS MEASUREMENT

Non-invasive tests to evaluate liver fibrosis may be broadly categorised as blood-based tests, tests assessing physical properties of the liver tissue and imaging modalities (Table 1). Serum markers for detecting liver fibrosis are non-specific and have poor accuracy [7]. Hence, other non-invasive tests, including liver stiffness measurement (LSM) and radiological imaging, are generally preferred. LSM can be performed using techniques based on magnetic resonance or ultrasonography. Ultrasound-based elastographic methods have been further classified as per the guidelines by the European Federation of Societies of Ultrasound in Medicine and Biology (EFSUMB) (Figure 1) [8-10]. Even though LSM using techniques like Acoustic Radiation Force Impulse Elastography with or without the Aixplorer® system (SuperSonic Imagine, France) offers the advantage of providing ultrasound images, FibroScan remains the most widely used and validated tool [7]. TE has been used not only

in managing patients with chronic liver disease but also in acute liver failure and those without any underlying liver disease (Table 2).

FIBROSCAN IN PATIENTS WITHOUT PREEXISTING CHRONIC LIVER DISEASE

Acute liver dysfunction in critically ill patients

Hepatic function is often impaired in critically ill patients for several reasons, such as endotoxemia, changes in circulation (cardiac failure), and external factors (increased intraabdominal or intrathoracic pressure due to an impending abdominal compartment or mechanical ventilation, respectively).

7 Hypoxic hepatitis occurs with an incidence of 10% in critically ill patients and is associated with an in-hospital mortality rate of 50% [11]. Pro-fibrogenic cells like hepatic stellate cells (HSCs) and myofibroblasts are quickly activated to make extracellular matrix components and hyaluronic acid, an indirect sign of collagen formation in the liver. The combination of hepatocyte oedema, bilirubin elevation and intrahepatic collagen deposition can increase liver stiffness. Koch A et al. examined critically ill patients in a medical ICU to assess liver stiffness and its clinical impact and predictive power to predict mortality [12]. They measured liver stiffness at admission, Day 3, Day 7, and weekly during the ICU course in critically ill medical patients. ICU patients had significantly higher liver stiffness than standard care patients without liver disease. ICU patients without cirrhosis had median liver stiffness values of about 10 kPa, indicative of severe hepatic fibrosis in the general population. Values > 12.5 kPa, which generally indicate established liver cirrhosis, were present in 33% of medical, non-cirrhotic ICU patients at admission. At admission, septic and non-septic patients had similar liver stiffness. However,

in an extensive subgroup analysis, abdominal sepsis patients had higher liver stiffness than pulmonary sepsis patients [12].

LSM reflects liver function upon admission to the ICU. On days 3 and 7, liver stiffness correlated with kidney, lung, and heart/circulation biomarkers but not with liver biomarkers. High-volume fluid resuscitation, vasopressors, and organ support therapies like mechanical ventilation and continuous veno-venous hemofiltration may change the significance of elevated liver stiffness in medical ICU patients, indicating non-hepatic organ failure in follow-up examinations. Also, patients with liver stiffness values greater than or equal to 18 kPa had substantially reduced survival rates during ICU treatment and long-term observation [12]. Despite this, there is a dearth of information on transient elastography's ability to predict "challenging end-points" like mortality.

Heart failure

8 Heart failure (HF) is a complex disease associated with multisystem organ failure and recurrent hospital admission, with 30–45% of patients hospitalized with acute decompensated heart failure (ADHF) dying within one year [13]. Congestive hepatopathy (CH) results from chronic passive venous congestion as central venous pressure (CVP) elevation in right-sided HF (RHF) is transmitted to the hepatic veins of the liver. ADHF further increases CVP with a resultant increase in hepatic congestion, and this relationship may have prognostic significance [14]. Right heart catheterization (RHC), though a gold standard method, is invasive and costly for assessments in RHF patients, necessitating the search for an accurate, non-invasive test. In HF, increased liver stiffness (LS) may reflect residual congestion secondary to volume,

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pressure overload, and/or inadequate liver perfusion with low cardiac output in patients hospitalized with ADHF. LS is reversibly associated with CVP with a direct strong relationship, increases exponentially with cardiac functional deterioration and improves dramatically after diuretic therapy (decongestion) [15].

A study that compared LS in patients with normal cardiac function, stable left HF (LHF), stable RHF, and ADHF found that all HF groups had significantly higher LS than controls, with the ADHF group having substantially higher RAP and LSM than the stable LHF group (median 11.2 vs 4.7 kPa, P = 0.01) [16]. In a cross-sectional study, Hopper et al. demonstrated that increased LSM correlated with increased bilirubin, gamma-glutamyl transferase and alkaline phosphatase in HF and ADHF groups [17]. During the clinical course of CH, liver markers vary and are typically unreliable despite more significant shifts in body volume, supporting LSM as a superior tool. LS may be particularly beneficial when the hemodynamic status cannot be readily assessed at the bedside on physical examination, and the assessment of LS by transient elastography is rapid, simple, and objective. Recent studies have shown that RHC and LSM have a baseline correlation [18].

Additionally, inadequate decongestion on discharge for ADHF is associated with increased morbidity and mortality. Nevertheless, many patients are discharged with residual congestion due to the lack of an objective measurement of HF. Compared with other non-invasive HF markers, LSM may more accurately demonstrate decongestion. Yoshitani et al. compared total bilirubin, aspartate aminotransferase, alanine transaminase, and gamma-glutamyl transferase before and after diuresis and found no significant change,

whereas body weight, LSM, and brain natriuretic peptide (BNP) all significantly decreased [19].

Saito et al. used FibroScan to categorize ADHF patients into low LSM (<8.8 kPa) and high LSM (≥8.8 kPa) groups based on the median LSM on admission, with primary end-points being death, cardiovascular disease and readmission rates [20]. They observed after a median follow-up of 153 days, the high LSM group had significantly higher rates of composite events (P = 0.001) and readmission rates (P = 0.022). High LSM was the only independent risk factor for cardiac events, not echocardiographic or serologic data. Soloveva et al. also evaluated FibroScan-based LSM on admission and before discharge, finding a significantly higher probability of adverse outcomes associated with LSM >13 kPa on admission and ≥5 kPa at discharge [21]. Discharge LSM independently predicted HF readmission and was associated with worse composite end-points and all-cause death. A recent meta-analysis also suggested that LS may be a novel, independent prognostic marker of cardiovascular outcomes in patients hospitalized with ADHF when assessed without liver disease, supporting LSM as a clinically relevant tool to assess adequate decongestion before discharge. Further, measuring LS may help identify patients at risk of developing cardiac cirrhosis due to heart failure, as higher systemic venous pressure is well-recognized as a significant risk factor of cardiac cirrhosis. Cardiac cirrhosis can only be ruled out if LS completely normalizes after removing water retention. Thus, LS could be a helpful non-invasive surrogate marker of hydrostatic pressure to offer additional prognostic information in patients hospitalized with ADHF and a guiding tool for optimal therapy during acute decompensated HF (Table 3).

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Left ventricular assist device placement

Left ventricular assist devices (LVADs) are increasingly becoming common therapy in managing advanced cardiac failure. Secondary RV failure in LVAD occurs in 5-44% of patients. It is attributed to the inability of the failing right heart to handle enhanced left-sided cardiac output, an excessive left-ward shift of the interventricular septum, and altered haemodynamic worsening tricuspid regurgitation. This typically occurs within 2 weeks of LVAD placement and is associated with increased ICU requirements and poor prognosis. No single marker or risk algorithm has significant predictive value for post-LVAD complications. However, measurements such as BNP, CVP, pulmonary artery pulsatility index, right ventricular stroke work index, and the CVP to pulmonary capillary wedge ratio are commonly used to evaluate the need for RVAD implantation and tricuspid valve replacement before surgery.

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Using FibroScan to assess LVAD candidates, Nishi and colleagues found that LSM were significantly higher in patients requiring RVADs. ROC analysis identified a cut-off ≥7.0 kPa for increased RVAD need [22]. Patients with major adverse events (MAEs), including mortality, post-operative bleeding, cerebrovascular events and infection, had significantly higher LSM than those without (22.4 ± 17.4 vs 8.0 ± 5 kPa, $P < 0.05$). Maes were notably more significant in patients with LSM ≥ 12.5 kPa (80% vs. 25% in LSM < 12.5 kPa). While multiple markers of HF were evaluated, including pre-operative haemodynamic measurements, BNP, and transaminases, LSM was the only independent risk factor for MAEs. While this does not preclude liver fibrosis from impacting LSM, it highlights the predictive ability of elastography as an independent risk factor for adverse events following LVAD placement and as a tool to augment existing predictors of poor outcomes.

Kashiyama et al. have also studied LS after LVAD implantation, depicting that LS was significantly elevated in patients with RV failure after LVAD compared to those without RV failure [23]. Because LS is immediately influenced by changes in CVP, serial assessments of LS would contribute to perioperative optimization of right-sided filling pressure without a pulmonary catheter study. Interestingly, the cases with higher LS than expected from pre-operative CVP were more likely to develop RVF or require RVAD implantation after LVAD implantation, which implies that LS may indicate not only CVP but also other factors such as RV failure or RV compliance. In patients with greater LS, there may be a more negative effect by an increased preload rather than a positive effect by a decrease in afterload on the RV by LVAD support. This suggests that RV with impaired compliance may increase RV filling pressure easily by elevating preload by LVAD flow.

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General Critical Care

The most important clinical end-point for critically ill ICU patients is overall survival. Lindvig K et al. conducted a study in the emergency room to assess initial LSM by elastography to predict 30-day mortality [24]. Increased LS, defined as >8 kPa, was detected in 22.6% (48/213) patients. Patients with a TE value > 8 kPa had a 30-day mortality rate of 20.8%, compared to 3.7% in patients with an LS < 8 kPa. Additionally, LS > 8 kPa was an independent predictor of death. In another study, LS was prospectively evaluated in 108 critically ill patients. LS was measured at admission, day 3, day 7, and weekly during their ICU stay. They observed that critically ill patients had significantly increased LS compared to sex- and age-matched standard-care patients (n = 25). Even in non-cirrhotic patients, LS values >18 kPa at ICU admission were

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associated with increased ICU and long-term mortality. In a recent meta-analysis by Wang J et al., the relative risk for all-cause mortality was 4.15 for patients with a high LS, which increased by 1.06 for each unit increment of LS. Intriguingly, LS appeared to predict all-cause mortality regardless of the aetiology [25].

Pregnancy

Twenty-five percent of pregnant women experience an increase in LS, which occurs almost exclusively in the third trimester and quickly returns to normal within a day after giving birth. However, the cause for the increase in LS remains unknown. Since liver inflammation or apoptosis often takes more than a day to resolve, the sudden drop in LS following delivery suggests a mechanical source, such as hemodynamic alterations, including inferior vena compression. Hormonal changes, a rise in the volume of blood, and modifications to the liver's functioning are a few more possibilities for LS elevation during pregnancy [26]. To completely comprehend the underlying mechanisms, more studies are required. Therefore, increased LS during pregnancy should not be confused with liver fibrosis or illness.

On the other hand, LS has a strong correlation with pregnancy-related problems like preeclampsia. A German study looked at two categories of complications: preeclampsia (n = 22) and intrahepatic cholestasis of pregnancy (ICP) (n = 40). With a mean LS of 17.9 kPa for preeclampsia and 6.9 kPa for ICP (AUROC 0.82), both groups showed elevated LS compared to healthy pregnancies in the third trimester. LS and leucocytes were separate predictors of preeclampsia in the multivariate model. Preeclampsia was twice as likely to develop in women with LSM greater than 8 kPa [27]. These findings suggest

that LSM could potentially serve as a valuable biomarker for predicting the development of preeclampsia during pregnancy. Nevertheless, further research is needed to validate these results and determine the underlying mechanisms linking LS to preeclampsia. Additionally, understanding how LS is associated with preeclampsia could provide valuable insights into the pathophysiology of this condition and potentially lead to new therapeutic approaches.

Acute liver failure

Acute Liver failure (ALF) is a severe clinical syndrome associated with high mortality if no immediate state-of-the-art intensive care or liver transplantation is performed. At the onset of ALF, predicting mortality remains difficult. Clichy and King's College criteria are widely recognized scoring systems to predict death in ALF patients. Nevertheless, further improvements are needed since the prognosis depends on quick and appropriate treatment initiation. Liver biopsy should always be a consideration in patients with ALF to rapidly confirm the diagnosis or measure iron or copper levels. However, a rapid decline of coagulation parameters due to liver failure can be a limiting factor for biopsy, and one may rely only on transjugular options in such cases. Hence, it is necessary to establish other methods to predict the likelihood of spontaneous remission or the need for liver transplantation.

LS elevation in this setting of ALF is suspected to be due to liver oedema, inflammatory infiltration, and tissue necrosis rather than fibrosis. Nevertheless, HSCs differentiate into contractile myofibroblasts, leading to tissue repair alongside cellular collapse and fibrosis [28]. Dechêne A et al. showed that fibrogenesis is a part of ALF at several levels and can contribute to increased LS. The fibrosis might serve as a wound-healing process by

transiently conserving the organ's structure until functional hepatocytes and accessory cells replace the defective tissue areas. The resolution of fibrosis is linked to the apoptosis of activated HSCs [29]. LS may be reduced in patients compromised through short-term liver damage such as toxicity or mycotoxicosis.

On the other hand, LS increased in patients with continuous liver injury, like in those with viral hepatitis. Measuring LS in patients with ALF can be used as a precise and early biomarker of fulminant hepatitis along with total bilirubin, prothrombin time, and platelet count. It correlates with ALT and total bilirubin in acute hepatitis [30]. A better prognosis estimation can be achieved by measuring LS at two time points (for example, days 0 and 7 of hospital admission). This could also be a potential tool to estimate prognosis. However, further studies are necessary to decide on a stiffness threshold.

FIBROSCAN IN PATIENTS WITH CHRONIC LIVER DISEASE

Chronic liver disease

Hepatic decompensation

Cirrhosis of the liver is one of the primary causes of death globally. It is characterized by two clinically distinctive conditions: compensated and decompensated cirrhosis. Decompensation is the onset of severe clinical symptoms, such as ascites, haemorrhage, hepatic encephalopathy, hepatorenal syndrome, or jaundice, all associated with a poor prognosis. Therapy aims to prevent clinical decompensation, which has a much worse prognosis than compensated liver cirrhosis. The hepatic venous pressure gradient (HVPG), which is the difference between the pressure in the "wedged"

or "occluded" hepatic vein and the pressure in the "free" hepatic vein, is believed to be the most accurate method for measuring the presence and severity of portal hypertension, except in cases such as heart failure in which HVPG and portal pressure can be different. This technique is relatively costly, unavailable at the bedside and in non-specialized institutions, requires appropriately trained personnel, and may be associated with procedural complications. There is a remarkable correlation between the HVPG and LS below 10 mmHg, with the latter being a reproducible and easy-to-perform non-invasive assay for assessing portal hypertension. For HVPG >10 mmHg, the cut-off of 21 kPa for LSM demonstrated high specificity (over 90%) [31]. However, the reference standard and LSM relationship diverge for larger values. In addition to the structure-dependent component of LS caused by liver fibrosis, the pressure balance between inflow and outflow from the hepatic sinusoidal system influences LSM, giving it a dynamic element. The 2015 Baveno VI consensus recommended using LS > 20–25 kPa to detect clinically significant portal hypertension (CSPH) in untreated hepatitis C or hepatitis B virus-related compensated advanced chronic liver disease (cACLD) patients [32]. In another recent meta-analysis of chronic viral hepatitis patients, LS cut-offs <13.6 kPa ruled out CSPH (pooled sensitivity 96%; CI 95% 93–97%) and >22 kPa ruled in CSPH (pooled specificity 94% (95% CI 86–97%), confirming the Baveno VI agreement.

In a cohort analysis of 343 individuals with chronic liver disease, 60 of whom had liver cirrhosis, each incremental unit in the natural logarithm (Ln) of LS was associated with 14.7 times increased risk of liver-related events ($P < 0.001$). With LS values >30 kPa, liver cirrhosis usually becomes clinically apparent, ascites will be omnipresent, and serum markers better predict death within the 12-month range. However, in another large meta-analysis with 35,249

participants, LS displayed a nonlinear relationship with the risk of liver-related events. These findings suggest a modest increase in the risk of liver-related events and death associated with increased LS. However, further research is needed to develop models that can accurately predict personalized risk stratification based on LS and other variables such as albumin, bilirubin, and prothrombin time.

Differentiate cirrhotic aetiologies

Disease aetiology significantly affects the liver's response to inflammation. Hepatitis C virus (HCV) patients with identical elevated transaminases and fibrosis stage showed lower LS values than lobular alcohol liver disease (ALD) patients. Hence, inflammatory localization (portal versus lobular) may also determine LS. Also, the liver size to LS ratio between HCV and ALD is significantly different. While liver size in patients with HCV dropped consistently as fibrosis progressed, it rose in patients with ALD up to an LS of 30 kPa before beginning to fall.

Simultaneous liver-spleen elastography can help distinguish cirrhosis from intrahepatic non-cirrhotic portal hypertension. Prehepatic pathologies, such as portal vein thrombosis, are associated with elevated SS/LS ratios. A post-hepatic pathology, such as liver congestion in heart failure, will result in an SS/LS ratio as low as 0.3. Consequently, the finding of a disproportionate increase in SS versus LS in a patient with portal hypertension (PH) symptoms and the finding of LS 20 kPa in a patient suspected of cirrhosis due to PH should prompt further investigations to rule out porto-sinusoidal vascular disease and other causes of non-cirrhotic intrahepatic PH [33]. SS/LS ratios may provide additional non-invasive and valuable information for the differential diagnosis of liver disease.

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Additionally, SS can be used to differentiate between acute and chronic liver damage, as SS is significantly higher in patients with chronic liver damage than acute ones with the same LS values. SS had better AUROC values in predicting oesophagal variceal bleeding (EVB) than spleen diameter, platelet count, and LS (0.857, 0.746, 0.720, and 0.688, respectively) [34]. In a recent study by Wang et al., similar SS cut-off values for EVB (SS = 45.5 kPa and AUROC = 0.923 vs LS = 29.6 kPa and AUROC = 0.860) were identified, with SS being superior to LS in predicting EVB [35]. Prospective long-term studies are required to validate further the utility of these elastography parameters and their performance.

Prediction of complications

Complications may frequently occur in patients with liver cirrhosis, necessitating ICU admission. These complications are associated with increased morbidity and mortality. Hence, identifying patients at risk and early detecting these complications may aid in instituting therapeutic measures and improving clinical outcomes. A meta-analysis evaluating the diagnostic accuracy of TE for portal hypertension reported a high accuracy for diagnosing portal hypertension and oesophagal varices with an AUROC of 0.93 and 0.84, respectively [36]. High LSM, as evaluated by TE, has also been shown to correlate with the development of hepatocellular cancer, the most dreaded complication and the most common cause of death among CLD patients [37,38].

Response to treatment

It is still unknown how, in the future, individual patient profiles of cirrhotic patients by LSM and SSM may contribute to optimizing therapeutic management (for example, by transjugular intrahepatic portosystemic shunt, TIPS or portal pressure lowering medications). Kim et al. explored SS for this

purpose because LS cannot be utilized to monitor PH under a non-selective beta blocker (NSBB). Before and after titrating NSBB (carvedilol), they assessed SS in 106 individuals with cirrhosis and high-risk oesophageal varices. By evaluating the HVPG at the same time points, they could also assess the hemodynamic response to NSBB. The hemodynamic response could be accurately predicted using the computed prediction model (Model = 0.0490-2.8345SSM) and 0.530 as the cut-off value (AUROC 0.803). The model retained a strong capacity for discrimination in the validation cohort (AUROC 0.848) [39]. Studies on LSM after TIPS insertion revealed an overall decline, but no significant correlation was detected between the decline in LS and that in portal pressure [40]. More recently, it has been proposed that only some patient's LS would drop after TIPS; patients with an early LS decline would demonstrate a positive outcome after TIPS, whereas patients with an early LS increase after TIPS would have a negative prognosis [41]. LS increase after TIPS could be due to an inflammatory response, triggering acute on chronic liver failure and death in this population.

Post liver transplant

Prognostication

18 The standard of care for patients with end-stage liver disease and those with inoperable liver malignancies is liver transplantation. Hepatic fibrosis is an important predictor of clinical outcomes in liver transplantation (LT) recipients. Advanced hepatic fibrosis is a surrogate for graft cirrhosis and hepatic decompensation and has been linked to both liver-related and non-liver-related outcomes. LSM can perform a role in the context of liver graft

transplantation. Using transient elastography, Nacif LS et al. compared the mortality risk of end-stage cirrhotic patients with and without hepatocellular carcinoma on the liver transplant waiting list [42]. Similar to the well-known model for end-stage liver disease (MELD) score, increased LS was associated with greater mortality. The average MELD score was 14.7 + 6.4, while the average LS was 32.7 + 22.5 kPa. The surviving group had a mean LS of 31.6 + 22.2 kPa compared to 50.8 + 9.9 kPa (P = 0.098) and higher MELD scores (P = 0.035). Thus, elastography could be an indispensable non-invasive instrument for diagnosing cirrhosis and hepatocellular carcinoma and predicting mortality, although more prospective data are needed.

Acute transplant rejection

Acute allograft rejection is still a significant post-operative complication following liver transplantation, affecting approximately 30% of recipients. It is an inflammatory process involving endothelial and biliary epithelial cells, typically within the first week after transplantation. Late episodes, i.e., those that occur after the first year, suggest insufficient immunosuppressive therapy. Acute rejection is generally diagnosed using clinical, laboratory, and histopathologic criteria. Additionally, the inflammatory process that characterizes allograft rejection may exacerbate hepatic stiffness. LS >7.9 kPa was defined as graft damage by Nacif LS et al., while LS < 5.3 kPa ruled out graft damage (AUROC = 0.93; P 0.001) [42]. In a separate study, LS cut-off values >8.5 kPa predicted moderate to severe acute rejection (100% specificity, AUROC = 0.924), whereas LS < 4.2 kPa ruled out any acute rejection [43]. Identical outcomes were also observed in the AMUSE trial [44].

LIMITATIONS

Like any other clinical test, FibroScan has its own set of limitations. Even though TE is reported to be an operator-independent procedure with low inter-observer variability [45], poor operator technique may increase variability in the results [46]. Hence, at least 10 measurements are required to ensure the reliability of the results. Patient positioning is also crucial for capturing correct readings [47]. Ideally, it is performed using an intercostal approach with the patient lying supine with the right arm in maximum abduction [47].

Several physiological or patient factors may also affect the accuracy of TE. Fatty meals [48], water intake [49], excessive exercise, and morbid obesity (BMI > 30 kg/m2) may all affect its accuracy, and hence, it is recommended that FibroScan be performed in a fasting patient [5,45,50]. Even alcohol consumption may also affect LSM measurement using FibroScan; therefore, repeat TE after a week of abstinence [51]. Apart from liver fibrosis, the LS may be altered in several other clinical conditions, including cholestasis, congestion, hepatitis, liver necrosis, malignancy and liver storage disorders, which may lead to false positive results [46,50-52].

Different cut-offs for LSM are recommended for the diagnosis of different liver diseases. On the one hand, cut-offs of < 7 kPa and > 12 kPa are recommended to rule out and rule out hepatitis B and hepatitis C-related cACLD. In contrast, cut-offs of < 7 kPa and > 12 kPa are recommended to rule out and rule out alcohol and non-alcoholic fatty liver disease-related cACLD [7,53]. Additionally, these cut-offs are still evolving as more literature becomes available.

Most of the data regarding TE has originated from studies conducted in relatively stable patients with chronic liver disease, and there is a dearth of data regarding its efficacy among critically ill patients. Several factors may affect the accuracy of TE, especially in critically ill and it is estimated that LSM cannot be accurately measured in about 30% of ICU patients [12]. Moreover, its efficacy may be further affected during the ICU course because of volume overload and the need for mechanical ventilation. FibroScan testing may be compromised in critically ill patients because of ascites, difficult positioning, feeding, invasive mechanical ventilation and hemodialysis [7,12,47,48,54]. Even phases of respiration in which readings have been obtained may affect the reliability of LSM [55].

For the SS, in addition to the technical restriction indicated for LS assessment, the operator cannot locate the splenic parenchyma in some individuals due to the spleen surface being smaller than the liver. However, with operator expertise, it has decreased over time. Another technical consideration for SS measurement by TE is that SS is performed using a probe approved solely to measure LS. Indeed, the FibroScan acquisition parameters were tuned for stiffness assessment for liver tissues, particularly in low-frequency excitation. Thus, utilizing the FibroScan on the spleen may overestimate stiffness values [56].

CONCLUSIONS

Detection of liver fibrosis is an important component of liver function evaluation as it correlates with severity and prognosis across different aetiologies causing liver dysfunction. Even though liver biopsy remains the gold

standard for assessing the extent and severity of liver fibrosis, it has several limitations, including its invasive nature, high cost, need for clinical expertise, and relatively high complication rates. These complications may be more severe in critically ill patients, necessitating the preferable use of non-invasive and easily repeatable tests like TE for evaluating liver fibrosis. These tests may help in staging and monitoring fibrosis and its related complications and provide a reasonable alternative to more invasive testing. Evolving literature suggests several clinical applications; however, its application has limitations, which must be considered while performing TE, especially in ICU patients.

1.	*with a reported incidence of 10 to 40*	Pancreatoenteral anastomosis or direct closure of the pancreatic remnant after a distal pancreatectomy: a single-centre experience	Originality
2.	*liver in the pathogenesis of systemic inflammatory response*	Incidence and prognosis of early hepatic dysfunction in critically ill patients—A prospective multicenter study	Originality
3.	*early detection of hepatic dysfunction, current diagnostic criteria are based on laboratory tests, mostly serum bilirubin*	Safety and efficacy of regional citrate anticoagulation in continuous venovenous hemodialysis in the presence of liver failure: the Liver Citrate Anticoagulation Threshold (L-CAT) observational study	Originality
4.	*reflects liver perfusion and function in the critically*	Increased liver stiffness denotes hepatic dysfunction and mortality risk in critically ill non-cirrhotic patients at a medical ICU	Originality
5.	*by the European Federation of Societies of Ultrasound in Medicine and Biology (EFSUMB*	Echoskopie	Originality
6.	*patients with chronic liver disease but also in*	Use of a monoclonal antibody in the detection of HBsAg in the liver by immunofluorescence.	Originality
7.	*in critically ill patients and is associated with an*	Inflammation biomarkers and delirium in critically ill patients	Originality
8.	*Heart failure (HF) is a complex disease associated with multisystem organ failure*	Use of liver stiffness measurements in acute decompensated heart failure: new applications of a non-invasive technique	Originality
9.	*or inadequate liver perfusion with low cardiac output*	Association of liver stiffness and cardiovascular outcomes in patients with heart failure: A	Originality

		systematic review and meta-analysis	
10.	*due to the lack of an objective measurement of*	Surgical gestures as a method to quantify surgical performance and predict patient outcomes | npj Digital Medicine https://www.nature.com/articles/s41746-022-00738-y?error=cookies_not_supported&code=b3ca7ed4-e683-4b54-912b-f948b98b7c51	Originality
11.	*outcomes in patients hospitalized with ADHF when assessed*	Association of liver stiffness and cardiovascular outcomes in patients with heart failure: A systematic review and meta-analysis	Originality
12.	*pulmonary artery pulsatility index, right ventricular stroke work index, and*	Review of heart transplantation and left ventricular assist https://www.uscjournal.com/articles/heart-transplant-and-ventricular-assist-cardiac-surgery-and-heart-failure-perspective	Originality
13.	*increase RV filling pressure easily by elevating preload*	Evaluation of right ventricular function using liver stiffness in patients with left ventricular assist device†	Originality
14.	*values >18 kPa at ICU admission were associated with increased ICU and long-term mortality.*	Increased liver stiffness denotes hepatic dysfunction and mortality risk in critically ill non-cirrhotic patients at a medical ICU	Originality
15.	*The hepatic venous pressure gradient (HVPG), which is the difference between the*	Endoscopic Ultrasound-guided Portal Pressure Gradient Measurement Is Technically Successful and Safe Without Deep Sedation: A Proof-of-Concept Case Series	Originality
16.	*valuable information for the differential diagnosis of liver*	Application of Real-Time Tissue Elastography with a Low	Originality

		Frequency Convex Array Probe: A Noninvasive Approach to Differential Diagnosis of Liver Tumors https://www.hindawi.com/journals/isrn/2014/378243/	
17.	*These complications are associated with increased morbidity and mortality.*	EVALUATION OF NUTRITIONAL STATUS AND DIETARY MANAGEMENT OF IN-PATIENT DIABETICS IN UNIVERSITY OF NIGERIA TEACHING HOSPITAL, ITUKU-OZALLA, ENUGU STATE, NIGERIA SOIL SCIENCE Project Topics https://eduproject.com.ng/soil-science/evaluation-of-nutritional-status-and-dietary-management-of-in-patient-diabetics-in-university-of-nigeria-teaching-hospital-ituku-ozalla-enugu-state-nigeria/index.html	Originality
18.	*The standard of care for patients with end-stage liver*	About ALTN | SCRI - Singapore Clinical Research Institute https://www.scri.edu.sg/crn/asian-liver-transplantation-network/about-altn/	Originality
19.	*with the patient lying supine with the right arm*	The factors associated with longitudinal changes in liver stiffness in patients with chronic hepatitis B https://www.e-cmh.org/journal/view.php?number=1157&viewtype=pubreader	Originality
20.	*Even though liver biopsy remains the gold standard for*	Glutaredoxin-1 regulates the Keap1-Nrf2 pathway	Originality
21.	*of liver fibrosis, it has several limitations, including its invasive nature,*	Acoustic Radiation Force Impulse Imaging is a Useful Tool for Predicting Fibrosis Level in Patients with Chronic Hepatitis B Infection	Originality