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Editorial

Potential Factors Confounding Quantitative Measurements in Ultrasound Elastography of the Liver

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1. Introduction

Ultrasound elastography has emerged as a significant noninvasive method for assessing the mechanical characteristics of tissues—demonstrating clinical applicability, among others, in hepatology, oncology, and musculoskeletal imaging. Despite its potential, the reliability and comparability of quantitative elastographic studies are susceptible to various confounding factors that can conceal real tissue stiffness. These effects originate from both technical and biological sources, including operator-dependent variability and differences in acquisition methodologies. Moreover, tissue heterogeneity, anisotropy, and viscoelastic properties undermine the simplistic assumptions—such as linear elasticity and isotropy—that form the basis of several elastography techniques. Discrepancies in device calibration and proprietary processing algorithms also hinder standardisation across platforms, complicating longitudinal assessments and multicentre studies.

Familiarity with potential confounders is essential for the implementation of ultrasound elastography in everyday clinical practice. The method encompasses a range of techniques that have advanced swiftly in recent years. Staying updated with all recent developments can be challenging; hence, this editorial aims to summarise the most important information from European Federation of Societies for Ultrasound in Medicine and Biology, Japan Society of Ultrasonics in Medicine, Society of Radiologists in Ultrasound, and World Federation for Ultrasound in Medicine and Biology guidelines on the topic [1,2,3,4,5,6]. The cited documents are the quintessence of almost two decades of research on elastographic methods.

2. Stiffness Measurement and Reliability Metrics

The result of an ultrasound elastography examination is a liver stiffness measurement (LSM), expressed as wave speed in metres per second or stiffness in kilopascals. This measurement does not directly translate to the degree of fibrosis—as liver stiffness is influenced by several factors, including obesity, ascites, hepatic venous outflow tract obstruction, sinusoidal obstruction syndrome, hepatic congestion of cardiac/pulmonary vascular origin, obstructive cholestasis, hepatic infiltration, inflammatory hepatitis, postprandial state, or critical illness [7]. It is also worth noting that fibrotic liver remodelling and the accompanying processes depend on the underlying pathology; therefore, LSMs vary between diseases.

In terms of the principle of operation, we distinguish three main measurement methods: vibration-controlled transient elastography (VCTE), point shear wave elastography (pSWE), and two-dimensional shear wave elastography (2D-SWE). VCTE measures liver stiffness in a volume that approximates a 4 cm long by 1 cm wide cylinder—the depth of which depends on the probe used, ranging from 15 to 85 mm below the skin surface for the S+ and XL+ probes, respectively. When a measurement is unsuccessful, the device does not return a value. The entire examination is considered to have failed when no values are obtained after 10 attempts [2].

pSWE uses an excitation pulse called an acoustic radiation force impulse (ARFI) to induce shear waves in the liver within a region of interest (ROI) of approximately 1 cm^3. Shear wave speed is determined in metres per second from the displacements observed over time at various sites. To convert shear wave speed from metres per second to Young's modulus in kilopascals, it is assumed that the liver density is homogeneous and is 1 g/mL and the tissue's elastic response is linear, which is generally untrue. These assumptions cause a constant method-specific calculation error [2].

In 2D-SWE, several ARFIs are conducted across the field of view, executed as a singular image or conducted in real time. An ROI can be placed within the field of view to acquire measurements from that specific spot [2].

The acquisition protocol is very similar for all three methods, but there are some differences worth noting. For all methods, fasting for at least 4 hours and resting for 10 minutes before examination are recommended. The patient assumes a supine position, with the right arm above the head. The measurement is performed via intercostal access and, for pSWE and 2D-SWE, after obtaining a B-mode image without shadowing of the lung or ribs. The trans-

ducer and ROI should be perpendicular to the liver capsule. For 2D-SWE, the ROI size should be at least 10 mm. For pSWE and 2D-SWE, measurements should be taken 15–20 mm below the liver capsule to avoid reverberation artefacts. The optimal measurement depth is 4–4.5 cm, ensuring that it does not exceed 6–7 cm usually. Large blood vessels, bile ducts, and masses should be avoided. The measurement is performed on a breath-hold during the neutral expiratory phase. VCTE requires a probe appropriate to the patient's body size. All measurements should be performed at a single location (liver segment) on different images. It is recommended to perform 10 measurements for VCTE, 5–10 for pSWE, and 3–5 for 2D-SWE. For all methods, the results should be expressed as the median value, together with the interquartile range divided by the median. For results in kilopascals, the interquartile range divided by the median should be $\leq$30%, and for results in metres per second $\leq$15%. For 2D-SWE, the coefficient of variation should also be reported, which is <0.25 for stiffness between 8.8 and 11.9 kPa and <0.1 for stiffness $\geq$12 kPa [4].

Attention should be paid to vendor-specific reliability indicators not included in the guidelines. Here, we can mention the use of confidence maps, wavefront displays, or coefficients such as reliability of the measurement, stability index, and percentage of the net effective shear wave velocity. When performing examinations, please refer to the manufacturer's recommendations for the model of ultrasound machine used.

Despite following the above recommendations, the literature reports a failure rate of up to 15% of cases [1,7]. The following list of causes, also summarised in Table 1, may enable the identification and sometimes elimination of the factors responsible.

3. Device- and Software-Related Factors

Stiffness results obtained from VCTE, pSWE, and 2D-SWE are not comparable due to differences in technique and calculation methods [4]. In the juvenile demographic, there is inadequate evidence to endorse one noninvasive imaging modality for liver disease assessment over another for evaluating liver fibrosis or steatosis [7].

The Ultrasound Shear Wave Speed Technical Committee of the Radiological Society of North America and the Quantitative Imaging Biomarker Alliance endeavoured to quantify the disparities among commercially available systems using elastic phantoms. A statistically significant variation in the measurements between systems was demonstrated and positively linked with the depth of the measurement [1]. It is estimated that the variability between and within vendors is approximately 10%, so a significant change in stiffness is considered to occur when it exceeds 10% [2].

Curved transducers are employed in liver imaging using pSWE and 2D-SWE, and optimal results are obtained when the ROI is directly aligned with the transducer, as the angle influences the measurements. Also, the convex transducer demonstrates significantly elevated LSM values compared to those acquired with the linear transducer, attributable to the differing frequency ranges [1]. The main disadvantages of VCTE include the absence of grayscale visual guidance for measurement localisation, difficulty in locating masses and huge vessels at the measurement site, and the need to recalibrate the device's spring every 6–12 months [2].

4. Acquisition Protocol and Operator Experience

The currently recommended examination protocol can be found in the 2024 World Federation for Ultrasound in Medicine and Biology guidelines [4]. The operator's experience with liver ultrasonography influences the ability to perform stiffness measurements, especially in the case of higher liver fibrosis stages and patients with an abnormally high body mass index [3,6]. For VCTE, an operator who has performed fewer than 500 examinations has a 2.6 times higher chance of obtaining unreliable results [1]. There is no consensus on the number of examinations required for pSWE and 2D-SWE to be considered an experienced operator. Suggested requirements include >300 abdominal ultrasound examinations and >50 supervised elastography examinations [1]. It is recommended to perform 10 acquisitions with pSWE and 5 with 2D-SWE for beginners and to decrease the number of acquisitions when the operator's expertise is improved. The LSM is optimised when the ARFI is perpendicular to the liver capsule to limit its refraction [2]. Colour-coded maps in 2D-SWE allow for increased accuracy when measuring in homogeneous areas and enable the avoidance of artefacts [4]. At present, numerous manufacturers are employing artificial intelligence (AI) to assist users in selecting the optimal ROI site. The effect of AI on accuracy requires more validation. A two-step approach during examination is proposed: (1) establish a dependable LSM and (2) execute three reliable LSMs. This provides superior differentiation between reliable LSMs and those with inadequate accuracy, which should be excluded from liver fibrosis assessment in clinical practice [4].

5. Patient-Related Factors

In general, predictors of unreliable results with VCTE, pSWE, and 2D-SWE are similar [1]. VCTE can be difficult in patients with obesity or those with a narrow intercostal space and cannot be performed in patients with ascites [4]. Morbid obesity restricts the efficacy of elastography techniques and diminishes measurement precision, even when employing XL+ probes for VCTE or low-frequency probes for pSWE [1]. Prevalent factors hindering measurement with 2D-SWE include measurement depths exceeding 4–5 cm, suboptimal ultrasound windows, reverberation artefacts, pulsatile motion, inadequate breath control, significant ascites, an intercostal wall thickness of 25 mm or

Table 1. Summary of the impact of various confounding factors.

Confounding factors	Affected methods	Direction of bias	Mitigation strategy
Ascites	VCTE, pSWE, 2D-SWE	Prevents VCTE Reduces the accuracy of pSWE and 2D-SWE	Reduction of ascites
Binge drinking	VCTE, pSWE, 2D-SWE	Overestimation of stiffness	Examination after 1 to 4 weeks of abstinence
Chronic kidney disease	VCTE	Higher stiffness in patients with baseline fluid overload	Examination after hemofiltration
Food consumption	VCTE, pSWE, 2D-SWE	Overestimation of stiffness	Examination at least 180 minutes after a meal
Hepatic infiltration	VCTE, pSWE, 2D-SWE	Overestimation of stiffness	Measurement of the parenchyma away from focal lesions
Hepatic venous outflow obstruction or congestion	VCTE, pSWE, 2D-SWE	Overestimation of stiffness	Removing the cause
Inflammatory hepatitis	VCTE, pSWE, 2D-SWE	Overestimation of stiffness	Examination after normalisation of inflammatory markers
Narrow intercostal space	VCTE, pSWE, 2D-SWE	Prevents VCTE or causes overestimation of stiffness Can reduce the accuracy of pSWE and 2D-SWE	Correct positioning of the patient
Obesity	VCTE, pSWE, 2D-SWE	Reduces the accuracy or prevents examination	LSM after tissue compression, weight reduction
Obstructive cholestasis	VCTE, pSWE, 2D-SWE	Overestimation of stiffness	Removal of the cause
Steatosis	VCTE, pSWE, 2D-SWE	Overestimation of stiffness Can reduce the accuracy of pSWE and 2D-SWE	Weight reduction

2D-SWE, two-dimensional shear wave elastography; pSWE, point shear wave elastography; VCTE, vibration-controlled transient elastography; LSM, liver stiffness measurement.

greater, a body mass index of 30 kg/m^2 or higher, histological steatosis, and a waist circumference of 102 cm or more [1].

6. Physiological Factors

Increased stiffness is observed after intense physical exercise; therefore, at least 10 minutes of rest before the ultrasound elastography examination is recommended. Measurements taken in the left lateral position are significantly higher than those obtained in the supine position. Breathing artefacts can significantly affect LSM, reducing the obtained values by up to 25% compared to those obtained with a breath-hold [2]. Inhaling deeply, performing a Valsalva manoeuvre, or doing a prolonged expiration alters hepatic venous pressures, which can affect LSM [2]. Food consumption elevates measurement results (irrespective of fibrosis) for around 120–180 minutes postmeal. Furthermore, meal consumption markedly elevates the median interquartile range values at 30 and 120 minutes in comparison to the baseline interquartile range. It may lead to misclassification and overestimation of the fibrosis degree, as documented in individuals infected with the hepatitis C virus [1]. This may lead to the overstaging of people as precirrhotic or cirrhotic, despite a normal fasting value confirmed by liver biopsy. Reports have indicated that the measurement decreases to accurate values approximately 180 minutes postconsumption [1]. The test should preferably be conducted following an overnight fast, with the avoidance of food, beverages (particularly caffeine), and smoking [1].

7. Disease-Related Factors

Liver stiffness is increased by hepatic inflammation (often shown by high transaminase levels), obstructive cholestasis, and hepatic congestion. Additionally, acute toxic hepatitis elevates readings. In individuals with inaccurately high LSMs caused by alcoholic hepatitis, liver stiffness diminishes after one to four weeks of abstinence [1]. In the context of alcoholic liver disease, continuous alcohol consumption does not appear to significantly elevate LSM; nonetheless, episodes of binge drinking may lead to increased LSM [4]. Other conditions that result in elevated liver stiffness, irrespective of liver fibrosis, include amyloidosis, lymphomas, and extramedullary haematopoiesis [1]. It is worth noting that in all of the above conditions, stiffness values within the normal range exclude significant liver fibrosis [2].

Histological inflammatory activity strongly influences LSMs obtained using VCTE, but not those derived from

2D-SWE in metabolic dysfunction–associated steatotic liver disease (MASLD); analogous results have been noted in cohorts of patients with diverse etiologies of chronic liver disease [4]. Additionally, the impact of steatosis on LSM yields inconsistent findings across different elastography methodologies in the literature. The ARFI experiences gradual attenuation as it passes through the tissue, with increased attenuation observed in a stiffer liver. Consequently, measures exhibit greater variability in patients with cirrhosis [1].

8. Follow-Up and Longitudinal Comparability Across Devices

Currently, it is recommended to follow up using the same equipment due to significant measurement differences between vendors [2]. In successfully treated patients with hepatitis B or C, a rapid decrease in liver stiffness is observed secondary to resolution of the inflammatory process. This may lead to the misinterpretation of low liver stiffness, despite the presence of significant fibrotic remodelling or cirrhosis in B-mode. Therefore, the delta change in stiffness is currently used in this group of patients, with the patient acting as their own control [2].

The American Association for the Study of Liver Diseases (AASLD) advises against using imaging-based noninvasive liver disease assessment as a standalone measure for assessing liver fibrosis changes. Instead, they recommend evaluating changes in liver stiffness over time within a clinical context, considering noninvasive liver disease assessment modifiers and additional evidence indicative of the patient's clinical trajectory. For patients treated for hepatitis B or C, the AASLD suggests that the LSM taken before antiviral therapy initiation is the most reliable longitudinal parameter for prognostication due to a lack of substantial evidence connecting LSM with clinical outcomes after viral suppression or eradication [7].

9. Current Noninvasive Risk Stratification Pathways

Current AASLD guidelines embed the use of ultrasound elastography in the clinical management of various liver diseases [7,8]. The AASLD advises the use of imaging-based tests to identify significant fibrosis (F2–4), advanced fibrosis (F3–4), and cirrhosis (F4) among patients with chronic hepatitis C, chronic hepatitis B, and nonalcoholic fatty liver disease (NAFLD). Current evidence demonstrates over 98% concordance between patients meeting the diagnostic criteria for NAFLD/nonalcoholic steatohepatitis and those classified under the new criteria for MASLD/metabolic dysfunction–associated steatohepatitis in extensive cohort studies. This suggests that the analyses and recommendations outlined in guidelines for patients with NAFLD/nonalcoholic steatohepatitis are likely applicable to individuals identified by the new terminology of MASLD and metabolic dysfunction–associated steatohepatitis. The AASLD also suggests employing imaging-based diagnostics to identify advanced fibrosis (F3–4) and cirrhosis (F4) in patients with alcoholic liver disease or chronic cholestatic liver disease [7]. Serum-based biomarker panels for hepatic fibrosis are not established in autoimmune hepatitis (AIH) and should not be utilised. VCTE can accurately diagnose advanced fibrosis or cirrhosis in patients with AIH; however, it should be postponed for a minimum of six months following effective AIH treatment to mitigate the confounding effects of hepatic inflammation. There is currently limited information on pSWE and 2D-SWE for AIH [8].

The AASLD recommends that imaging-based noninvasive liver disease assessment be included in the initial fibrosis staging procedure for people with chronic liver disease, as it is more precise than blood-based noninvasive assessments. Furthermore, for adults with chronic liver disease undergoing initial fibrosis staging, the AASLD advises the combination of blood- and imaging-based noninvasive liver disease assessments, especially for identifying significant fibrosis (F2–4) and advanced fibrosis (F3–4). The AASLD noninvasive liver disease assessment (NILDA) Writing Group formulated an algorithm designed for doctors requiring an accessible and straightforward decision assistance tool [7].

10. Conclusion

Ultrasound elastography is a noninvasive technique essential for assessing tissue mechanical characteristics, notably in hepatology. However, its reliability is affected by operator variability, measurement methods, and biological factors, which complicate stiffness assessments. Key methods include VCTE, pSWE, and 2D-SWE, each with unique protocols and measurement requirements. Operator experience significantly alters the quality of results, particularly in higher fibrosis stages. Patient-specific factors, such as obesity, body position, and disease-related conditions (e.g., inflammation), also influence measurements. Furthermore, the efficacy of elastography can be affected by physiological states such as posture, breathing, or fasting. Current guidelines recommend standardised protocols and emphasise the importance of consistent equipment for follow-ups to ensure reliable longitudinal assessments. The AASLD supports integrating elastography into clinical practice for evaluating liver fibrosis—highlighting its superiority over blood-based assessments, especially for patients with chronic liver disease.

Key Points

• Ultrasound elastography is a noninvasive technique used to assess tissue stiffness, and its reliability is influenced by various confounding factors.

• Each ultrasound elastography method has specific protocols and measurement requirements, with variations

in accuracy and reliability based on operator experience and patient conditions.

• Factors such as obesity, body position, and disease-related conditions (e.g., inflammation), as well as physiological states (e.g., fasting and hydration), can affect the accuracy of measurements.

• Current guidelines from organisations such as the AASLD emphasise the integration of ultrasound elastography into clinical practice and recommend standardised protocols and consistent equipment for follow-ups to ensure reliable longitudinal assessments, highlighting the method's superiority over blood-based assessments in chronic liver disease evaluations.

Abbreviations

2D-SWE, two-dimensional shear wave elastography; pSWE, point shear wave elastography; VCTE, vibration-controlled transient elastography; LSM, liver stiffness measurement; ARFI, acoustic radiation force impulse; ROI, region of interest; MASLD, metabolic dysfunction–associated steatotic liver disease; AASLD, American Association for the Study of Liver Diseases; AIH, autoimmune hepatitis; NAFLD, nonalcoholic fatty liver disease.

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Not applicable.

Author Contributions

MC: Conceptualisation, Writing—Original Draft. PP: Conceptualisation. JK: Conceptualisation. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

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Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used QuillBot to edit the text in order to improve readability, check grammar, and assess the work for potential plagiarism. After its use, the authors thoroughly reviewed, verified, and revised all content to ensure accuracy and originality.

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