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Review Article

Evolving B-mode ultrasound-based techniques for assessing metabolic dysfunction-associated steatotic liver disease: Now and beyond

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ABSTRACT

Metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as the leading cause of chronic liver disease worldwide, coinciding with the growing burden of obesity and type 2 diabetes mellitus. While liver biopsy remains the gold standard for assessing hepatic steatosis and fibrosis, its invasiveness, sampling variability, and limited feasibility have necessitated the establishment of non-invasive diagnostic alternatives. Among non-invasive alternatives, conventional B-mode ultrasound (US) has retained a central role as the first-line imaging modality owing to its wide availability, low cost, and reasonable sensitivity and specificity, particularly in moderate-to-severe steatosis. However, traditional B-mode US has several limitations, including operator dependence, poor sensitivity in mild steatosis, and reduced accuracy in obese individuals. Semi-quantitative scoring systems and emerging technologies such as attenuation imaging, shear wave elastography, and vibration-controlled transient elastography, have been recently introduced to improve diagnostic accuracy. Additionally, artificial intelligence (AI) is increasingly being integrated into US platforms to enhance image interpretation, standardize assessments, and reduce interobserver variability. This review provides a comprehensive appraisal of the diagnostic performance, strengths, and limitations of conventional B-mode US and its advanced products in the context of MASLD. US-based techniques are also compared with magnetic resonance spectroscopy and histological assessment, highlighting the evolving role of AI in US diagnostics. Given the global rise of MASLD, optimizing and standardizing US-based approaches are essential to improve early detection, risk stratification, and monitoring strategies. With continued technological refinement and integration of AI, US remains a cornerstone of MASLD diagnosis in clinical practice.

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1. Introduction

Steatotic liver disease (SLD) encompasses a spectrum of disorders characterized by excessive fat accumulation within hepatocytes, which could progress to fibrosis.[1] Globally, SLD represents one of the leading causes of liver-related morbidity and mortality.[1] SLD includes various entities such as metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed non-alcoholic fatty liver disease (NAFLD), and metabolic dysfunction-associated steatohepatitis (MASH), formerly non-alcoholic steatohepatitis (NASH).[2] In June 2023, a multisector Delphi consensus introduced a revised nomenclature, officially replacing NAFLD with MASLD.[3] Currently, 38% of all adults and 7%–14% of children and adolescents have MASLD.[4] By 2040, the MASLD prevalence rate for adults is projected to increase to more than 55%.[4,5] This surge parallels the worldwide epidemics of obesity and type 2 diabetes mellitus (T2DM),[5,6] with insulin resistance and associated metabolic dysfunction playing central roles in its pathogenesis.[7] The prevalence of MASLD is anticipated

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to rise further in the coming decade.[1] Advanced liver disease manifestations, including cirrhosis, hepatic decompensation, hepatocellular carcinoma, and extrahepatic sequelae such as T2DM, cardiovascular disease (CVD), chronic kidney disease (CKD), and certain malignancies, represent major clinical consequences.[8] The risk of extrahepatic malignancies is also elevated in individuals with MASLD, with obesity and diabetes serving as prominent contributing factors.[9] Although liver biopsy remains the diagnostic gold standard for MASLD, its application is limited by procedural invasiveness, potential complications, and sampling variability.[10] These constraints underscore the need for accurate, non-invasive diagnostic tools for early identification and intervention. Conventional B-mode ultrasound (US), owing to its wide availability and cost-effectiveness, is currently endorsed as the first-line imaging modality for detecting hepatic steatosis.[11] This review presents a comprehensive evaluation of the role of conventional B-mode US and novel US-based technologies in the diagnosis of MASLD.

2. Diagnosis of MASLD

Most individuals with MASLD are asymptomatic at presentation.[12] However, emerging evidence suggests that a subset of patients may experience subtle symptoms and diminished health-related quality of life (HRQoL), even at early disease stages.[13,14] The diagnosis of MASLD involves a combination of clinical, laboratory, and imaging findings to identify hepatic steatosis and exclude other causes of liver disease.[3] Central diagnostic criteria include imaging-based detection of hepatic steatosis, typically through US, computed tomography (CT), or magnetic resonance imaging (MRI), or histological confirmation by liver biopsy. Additionally, at least one cardiometabolic risk factor must be present, such as obesity, T2DM, hypertension, dyslipidemia, or insulin resistance.[15] Routine laboratory investigations, including serum aminotransferases (*e.g.*, ALT and AST) and metabolic markers (*e.g.*, fasting glucose and lipid profile), assist in evaluating hepatic injury and metabolic dysfunction. Non-invasive fibrosis assessment tools, such as the Fibrosis-4 (FIB-4) index and the NAFLD Fibrosis Score (NFS), are commonly employed to stratify fibrosis risk, though these modalities have limitations in sensitivity and specificity.[15,16] Moreover, composite scores such as Agile 3+ and Agile 4 have been developed to enhance risk stratification.[17] The NFS was originally derived and validated in a cohort of 733 biopsy-confirmed MASLD patients.[18] In the validation group, this tool achieved an area under the curve (AUC) of 0.82 for identifying advanced fibrosis, with a negative predictive value of 88% and a positive predictive value of 82% based on threshold scores of -1.455 and 0.676, respectively.[18] A meta-analysis of 13,046 patients with MASLD demonstrated that the NFS and FIB-4 index provided the highest diagnostic performance for advanced fibrosis, with pooled areas under the receiver operating characteristic curve (AUROCs) of 0.84 (95% CI: 0.82–0.86) for both tools.[19] While both scores showed strong negative predictive value, performance varied depending on population characteristics, prevalence of advanced fibrosis, and chosen cut-offs, highlighting the heterogeneity across studies. Despite the advent of non-invasive approaches, liver biopsy remains the diagnostic gold standard for staging fibrosis and confirming MASH. Histological hallmarks include steatosis, lobular or portal inflammation, and hepatocellular ballooning. Nevertheless, liver biopsy is constrained by invasiveness, potential adverse events, sampling variability, and patient reluctance.[20] These challenges underscore the critical need for accurate, non-invasive diagnostic alternatives. A comprehensive and integrated approach, merging clinical assessment, laboratory parameters, and advanced imaging, is essential to ensure timely and effective diagnosis and management of MASLD.

3. Screening applications of B-mode US in MASLD

3.1. Assessment of hepatic steatosis

B-mode US assessment of hepatic steatosis in MASLD encompasses a spectrum of techniques, broadly categorized as qualitative, semi-quantitative, and quantitative. Among these, qualitative assessment, predominantly employing conventional B-mode imaging, remains the most widely utilized method in clinical practice. It relies on the visual appraisal of hepatic echogenicity, in which increased parenchymal echogenicity relative to the kidneys or spleen suggests fat accumulation. However, this method is intrinsically subjective and exhibits restricted sensitivity in identifying mild steatosis.[21,22] Semi-quantitative techniques, such as the Hamaguchi score and the hepatorenal index (HRI), offer a more structured evaluation by integrating echogenicity with additional sonographic features, including diaphragm clarity and comparative renal-liver echogenicity. Quantitative US modalities aim to provide objective, reproducible metrics of hepatic fat content. These include advanced tools such as attenuation measurement function, also referred to as attenuation imaging (ATI) or attenuation coefficient measurement depending on the US platform, and ultrasound-guided attenuation parameter (UGAP), as well as the controlled attenuation parameter (CAP), which measures US attenuation via transient elastography. Additional methods, including the backscatter coefficient (BSC) and speed of sound analysis, quantify hepatic steatosis by evaluating changes in US wave propagation and scattering properties. Although qualitative and semi-quantitative methods are preferred for their accessibility and simplicity in routine practice, quantitative techniques provide enhanced accuracy and are progressively utilized in research and advanced diagnostic contexts. Each method has unique benefits and drawbacks, highlighting the necessity of customizing the imaging strategy to the clinical situation.[21,22] Accurately staging liver fibrosis using B-mode US alone remains difficult, even during longitudinal follow-up, as early fibrotic changes do not significantly alter hepatic morphology or echogenicity. Consequently, US elastography has emerged as a valuable non-invasive modality for assessing tissue stiffness and estimating the extent of liver fibrosis.[23]

3.2. Qualitative B-mode US as a tool in screening for MASLD

B-mode US is a widely accessible, non-invasive, and cost-effective imaging modality commonly employed for the assessment of hepatic steatosis. In the context of MASLD screening, it serves as a valuable first-line tool to identify individuals at risk who may require further diagnostic evaluation.[24,25] On US, hepatic steatosis typically manifests as a diffuse increase in liver parenchymal echogenicity, with relative hypoechogenicity of the right renal cortex, reflecting heightened hepatic reflectivity.[22] The sensitivity of B-mode US for detecting mild steatosis ranges from 53% to 76%, whereas its diagnostic accuracy is notably higher for moderate to severe steatosis.[26,27] Screening efforts are particularly targeted toward individuals at greater risk of clinically significant fibrosis (stage $\geq$ F2), aiming to enable timely therapeutic interventions.[28] Asymptomatic cases of advanced fibrosis can often be detected through systematic screening in high-risk populations, including patients with T2DM,[29,30] individuals with obesity and associated metabolic complications,[31] those with a family history of cirrhosis,[32] or individuals with a history of heavy alcohol consumption.[33]

Early identification of such at-risk individuals allows for timely lifestyle and medical interventions, potentially averting future liver-related complications.[34] Emerging evidence also suggests that even unrelated household members may be predisposed to MASLD and advanced fibrosis due to shared environmental exposures, gut microbiota, and behavioral risk factors.[35] In response, several authoritative guidelines have been issued by societies such as the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Association of Clinical Endocrinology (AACE), and multidisciplinary groups including the European Association for the Study of Obesity (EASO), the European Association for the Study of Diabetes (EASD), and the European Association for the Study of the Liver (EASL).[20,36–39] Most recently, in January 2024, the American Diabetic Association (ADA) updated its MASLD guidelines, aligning with contemporary recommendations from the AGA and the American College of Cardiology (ACC).[40]

4. Diagnostic performances of B-mode US

4.1. Role of B-mode US in diagnosis of MASLD

A study reported that B-mode US exhibits a pooled sensitivity of 84.8% and specificity of 93.6% for detecting hepatic steatosis, with an AUROC of 0.93.[22] Notably, in cases where hepatic fat content exceeded 20%, sensitivity and specificity increased to 100% and 90%, respectively.[22] Despite its favorable performance, conventional US has several limitations. These include the subjective nature of image interpretation, absence of standardized sonographic parameters for grading steatosis severity, and reduced sensitivity in mild steatosis.[41] Additionally, steatosis involving less than 20% of hepatocytes may be missed on US.[42] The most widely adopted grading system qualitatively categorizes hepatic steatosis into three levels (grades 1–3), based on visual comparisons of liver echogenicity relative to the renal cortex, clarity of hepatic vasculature and diaphragm, and degree of posterior beam attenuation.[22] Grade 1 (mild) is characterized by a mild, diffuse increase in hepatic echogenicity with preserved visualization of intrahepatic vessels and the diaphragm. Grade 2 (moderate) involves a more pronounced echogenicity with partial obscuration of the diaphragm and vascular margins. Grade 3 (severe) is defined by marked hyper-echogenicity with poor or absent visualization of the diaphragm, intrahepatic vessels, and posterior segments of the right hepatic lobe.[43] Focal fatty sparing may also be observed in grades 2 and 3.[43] The diagnostic performance of US for moderate-to-severe steatosis in adults remains acceptable, with pooled sensitivity and specificity ranging from 85.7% to 99.1% and 85.2%–91.9%, respectively.[44] Most studies included in the meta-analysis used $\geq$25% as the threshold for moderate-to-severe steatosis.[44] Fig. 1 illustrates the key advantages and limitations of B-mode US in MASLD diagnosis.

4.2. Semi-quantitative B-mode US role in MASLD

The Hamaguchi method is a semi-quantitative scoring system that employs four subjective parameters derived from B-mode US to assess hepatic steatosis, yielding a cumulative score ranging from 0 to 6. A score greater than 2 demonstrates excellent diagnostic performance, with an AUROC of 0.98 and sensitivity and specificity of 91.7% and 100.0%, respectively.[45] Notably, the Hamaguchi score has proven effective in minimizing interobserver variability, with a reported interobserver agreement of 0.95.[45] Similarly, the HRI quantifies hepatic steatosis by calculating the echogenicity ratio between the liver and the right renal cortex, based on pixel brightness in B-mode images. This method is largely unaffected by the presence of fibrosis or steatohepatitis and shows strong interobserver reliability, with an agreement coefficient of 0.956.[41] However, its accuracy is contingent upon normal renal cortical echogenicity, limiting its applicability in patients with intrinsic renal parenchymal disease or increased renal echogenicity.[46] Across all grades of steatosis, the HRI consistently demonstrates high diagnostic accuracy, with AUROC values exceeding 0.90.[41,46]

4.3. Quantitative metrics: ATI and attenuation measurement for MASLD assessment

ATI estimates the extent of US beam attenuation by utilizing corrected echo intensities, thereby neutralizing the effects of focus-related beam profiles and compensating for gain variations inherent in the original.[47] When benchmarked against histologically confirmed steatosis, ATI demonstrates moderate to strong correlations, with reported correlation coefficients ranging from 0.47 to 0.72.[48,49] Comparisons with MRI-proton density fat fraction (PDFF) yield slightly higher correlation coefficients, ranging from 0.51 to 0.89.[50,51] In a pooled analysis across studies evaluating ATI for $\geq$ S1 steatosis, the AUROC reached 0.91, with pooled sensitivity and specificity of 88% and 83%, respectively.[52]

Attenuation measurement (ATT), in contrast, involves the propagation of dual-frequency US waves along the same axis, with attenuation quantified by calculating the slope of the signal ratio.[53] ATT is incorporated into Fujifilm US platforms (Fujifilm, Tokyo, Japan). When validated against liver biopsy and MRI-PDFF, ATT demonstrated correlation coefficients of 0.47 and 0.80, respectively.[53] For steatosis grades $\geq$ S1, $\geq$ S2, and = S3, the AUROC values ranged between 0.74 and 0.93, 0.87–0.96, and 0.90–0.96, respectively, with corresponding optimized cutoff thresholds of 0.62–0.68, 0.67–0.74, and 0.73–0.78.[53]

5. Comparison with other diagnostic modalities (magnetic resonance spectroscopy and liver biopsy)

5.1. B-mode US versus magnetic resonance spectroscopy (MRS) in diagnosis of MASLD

B-mode US and MRS are two essential imaging techniques for diagnosing MASLD, each presenting unique benefits and drawbacks. US is the chosen initial diagnostic modality due to its extensive availability, cost-effectiveness, and non-invasive characteristics. It identifies hepatic steatosis through distinctive indicators, including heightened hepatic echogenicity, an elevated HRI, and diminished visualization of intrahepatic vessels or the diaphragm, making it especially valuable for initial screening and monitoring moderate-to-severe steatosis in clinical settings.[24,25] However, US is limited by various factors, including operator dependence, diminished sensitivity for identifying mild steatosis (often <20%–30% fat content), and impaired accuracy in obese persons due to technological difficulties.[15,16] Additionally, conventional US lacks quantitative capability, instead providing semi-quantitative grading (*e.g.*, scores from 0 to 3) rather than exact hepatic fat percentages.

Conversely, MRS is considered a standard tool for hepatic fat estimation, providing enhanced sensitivity and specificity. It can precisely quantify liver fat fractions, identify mild steatosis ($\geq$5% fat content), and differentiate between lipid subtypes; these attributes are particularly beneficial for research endeavors and detailed clinical evaluations.[54] Notably, MRS is unaffected by obesity and yields highly reproducible measurements, making it ideal for longitudinal monitoring or precise fat quantification. Despite these advantages, MRS has limited clinical utility due to its

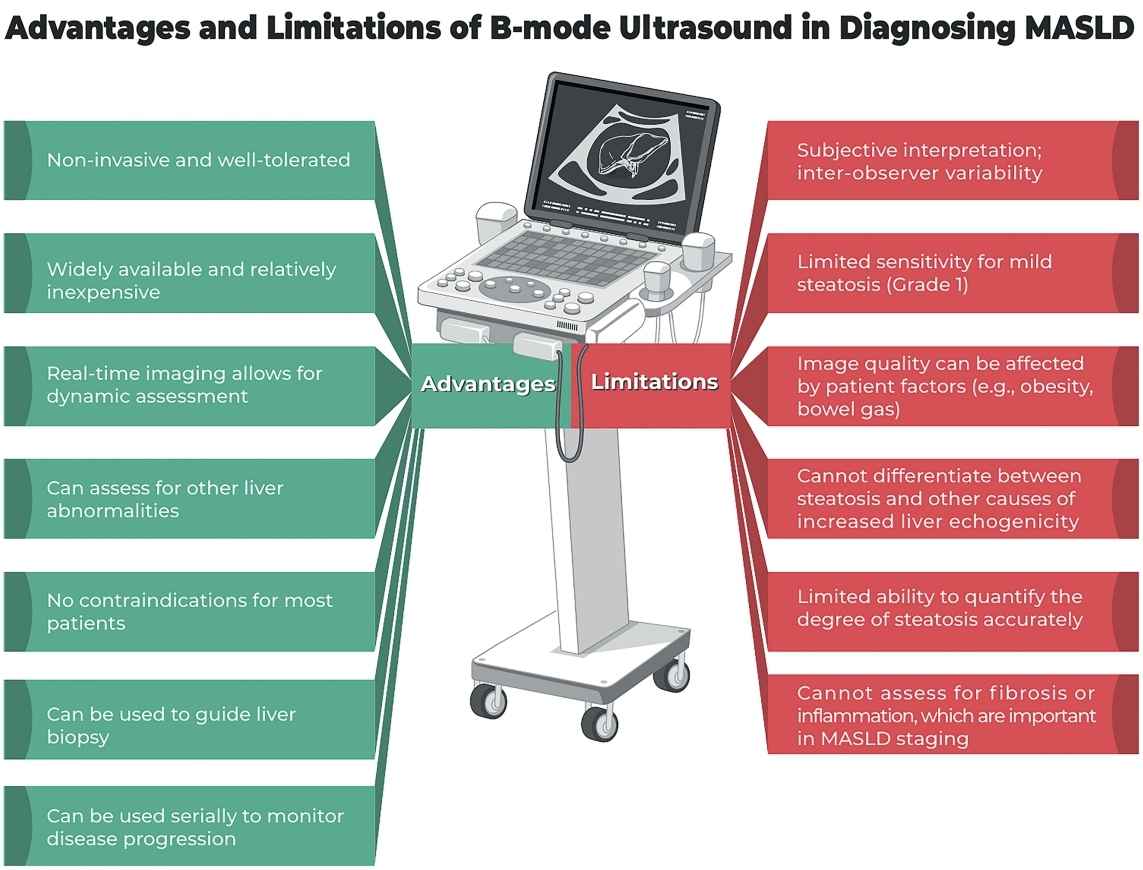

Fig. 1. The advantages and limitations of B-mode ultrasound in diagnosing MASLD. Abbreviation: MASLD, metabolic dysfunction-associated steatotic liver disease.

high cost, restricted availability (mainly in tertiary or research settings), and prolonged acquisition times.[8] Comparative studies emphasize the complementary roles of these modalities: US is appropriate for population-level screening and routine clinical use, whereas MRS is reserved for research settings, clinical trials, equivocal cases, or situations requiring exact quantification.[10,54] Emerging evidence supports their synergistic application—US facilitates efficient risk stratification, while MRS confirms findings, monitors subtle changes, and guides personalized therapeutic decisions.[55] In summary, the choice between US and MRS should be guided by clinical context, diagnostic precision requirements, and available resources. While US meets most routine diagnostic needs, MRS remains essential for advanced and investigational applications.[54,55] Moreover, MRI-PDFF demonstrates excellent diagnostic accuracy for quantifying hepatic fat and has been shown to outperform liver biopsy in monitoring longitudinal changes in steatosis.[56] Multiple systematic reviews and meta-analyses have consistently confirmed its high performance, with pooled AUROC values for detecting $\geq$ S1 steatosis often exceeding 0.95 (95% CI: 0.93–0.97).[57] As a non-invasive modality, MRI-PDFF overcomes key limitations of MRS and liver biopsy. Although MRS provides accurate hepatic fat quantification, its application is limited by technical complexity, dependence on operator expertise, and sampling confined to a few tissue voxels.[58] Table 1 summarizes the characteristics of B-mode US, MRS, and MRI-PDFF in MASLD diagnosis.

MRI-PDFF has also emerged as a reliable biomarker for monitoring therapeutic response in MASH, with a $\geq$30% reduction in fat content correlating with histologic improvement in disease activity and regression of fibrosis.[59] A recent systematic review identified MRI-based techniques and US-derived indices as the most accurate imaging tools for MASLD and MASH diagnosis, reporting AUROC values up to 0.93 for magnetic resonance elastography, 0.90 for MRI-PDFF, 1.00 for MRS, and 0.94 for US-based methods, although significant heterogeneity across studies was noted.[60] Despite its superior diagnostic performance, the high cost and limited accessibility of MRI-PDFF preclude its use as a front-line screening tool for large populations.[20] Table 2 shows the diagnostic accuracy of US, CT, and MRI/MRS reported in some studies evaluating the liver steatosis.[44,51,61–67]

5.2. B-mode US versus liver biopsy in diagnosis of MASLD

A thorough comprehension of both non-invasive imaging techniques and liver biopsy is crucial in the diagnostic assessment of MASLD. Notwithstanding advancements in imaging, histological examination continues to be the most conclusive technique for diagnosing and staging MASLD. Histological characteristics indicative of MASLD/MASH encompass centrilobular (zone 3) steatosis, lobular and/or portal inflammation, hepatocellular ballooning, and differing levels of fibrosis.[68] Additional findings, such as acidophil bodies, iron deposition, vacuolated nuclei, Mallory–Denk bodies, and cytoplasmic megamitochondria within ballooned hepatocytes, may further support the diagnosis.[69] Nevertheless, accurate grading of disease activity and staging of fibrosis can be challenging.[70] The METAVIR scoring system, initially developed for viral hepatitis, has increasingly been applied in MASLD to assess inflammatory activity (A0–A3) and fibrosis stage (F0–F4), offering important prognostic insights.[71] Its widespread adoption reflects

Table 1
Comparison between B-mode ultrasound versus MRS and MRI-PDFF in diagnosing MASLD.

Aspect	B-mode ultrasound	MRS	MRI-PDFF
Primary role	Detection of hepatic steatosis	Quantification of hepatic fat content	Quantification of hepatic fat content
Imaging principle	Sound waves to assess tissue echogenicity	Magnetic fields and radiofrequency pulses to measure fat and water signals	Magnetic fields and advanced algorithms to measure fat fraction
Key diagnostic feature	Increased liver echogenicity	Direct measurement of fat-to-water ratio	Direct measurement of fat fraction in the liver
Sensitivity	Moderate to high for moderate-severe steatosis	High for all degrees of steatosis	High for all degrees of steatosis
Specificity	Lower for mild steatosis	High for all degrees of steatosis	High for all degrees of steatosis
Advantages	Non-invasive, widely available, and cost-effective	Non-invasive highly accurate for fat quantification	Non-invasive highly accurate, and reproducible
Limitations	Operator-dependent, less accurate for mild steatosis, and limited by obesity or fibrosis	Expensive, limited availability, and required expertise	Expensive, limited availability, and required advanced equipment
Quantification of fat	Qualitative or semi-quantitative (grading)	Quantitative (precise fat-to-water ratio)	Quantitative (precise fat fraction)
Clinical utility	First-line screening tool for steatosis	Gold standard for fat quantification in research	Gold standard for fat quantification in clinical practice
Complementary techniques	Elastography for fibrosis assessment	Often used in research settings	Often combined with elastography for fibrosis assessment
Cost and accessibility	Low cost, widely accessible	High cost, limited to specialized centers	High cost, limited to specialized centers
Patient factors	Limited by obesity or fibrosis	Not limited by obesity or fibrosis	Not limited by obesity or fibrosis

Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; MRS, magnetic resonance spectroscopy.

the growing emphasis on standardized histological assessment across chronic liver diseases.[69,71]

Among histological parameters, steatosis demonstrates the highest interobserver reproducibility, whereas assessments of lobular inflammation and hepatocellular ballooning show greater variability.[72] Ballooning, in particular, is a pivotal marker of disease progression in MASH and is associated with an elevated risk of adverse outcomes.[73] Due to substantial variability among expert hepatopathologists in evaluating this feature, artificial intelligence (AI)-based histological models are increasingly employed to standardize and improve diagnostic consistency.[74]

Liver biopsy provides an integrated assessment of hepatic architecture, inflammation, cellular injury, and fibrosis, and is typically indicated in cases requiring confirmation of advanced fibrosis, resolution of inconclusive non-invasive tests, clinical trial enrollment, or evaluation for alternative etiologies.[36,75] Despite its diagnostic value, liver biopsy is not suitable for population-level screening due to its invasive nature. Instead, validated non-invasive methods are often sufficient for detecting clinically significant fibrosis.[75] Nevertheless, histologically confirmed fibrosis remains the most robust predictor of liver-related morbidity and mortality, and thus continues to serve as the gold standard in clinical research.[36,76]

US-guided liver biopsy has demonstrated superior safety compared to blind techniques.[77] Ensuring an adequate specimen is critical to minimize sampling variability; longer biopsy cores and a higher number of complete portal tracts are directly correlated with diagnostic reliability.[78] Current guidelines recommend sampling at least 11 complete portal tracts, which generally necessitates a 20 mm core obtained with a 16-gauge needle.[79] Although smaller-caliber needles (*e.g.*, 18-gauge) may slightly reduce complication rates, 16-gauge needles consistently yield superior specimen quality with comparable safety profiles.[79,80] The most frequent complication, post-procedural pain, affects 30%–50% of patients but is typically mild and self-limiting.[81] More serious adverse events, such as bleeding, occur in up to 10% of cases, with severe bleeding reported in fewer than 2%.[80] Mortality is exceedingly rare, estimated at fewer than 1 in 1000 procedures.[82]

6. Emerging US technologies in MASLD

6.1. Vibration-controlled transient elastography (VCTE)

Shear wave elastography (SWE) techniques, either VCTE or acoustic radiation force impulse (ARFI) techniques, allow non-invasive quantification of liver stiffness, which is directly related to liver fibrosis.[83] Notably, ARFI-based techniques with DAX transducers were more accurate than VCTE in detecting advanced fibrosis, and this difference reached statistical significance in the intention-to-diagnose analysis.[84] Liver stiffness measurement (LSM) using VCTE is a widely established non-invasive technique that shows strong correlation with the severity of hepatic fibrosis. Its main clinical application is the assessment of fibrosis and steatosis in chronic liver diseases, including MASLD.[85] VCTE estimates liver stiffness by measuring the velocity of shear waves transmitted through hepatic tissue, which are detected at a depth of 25–65 mm and converted into quantitative LSM values (expressed in kilopascals) according to Hooke's law.[86]

In MASLD, VCTE has consistently demonstrated high diagnostic accuracy for advanced fibrosis, with pooled AUROC values ranging from 0.85 to 0.89 (95% CI: 0.82–0.91).[85] While accuracy is generally robust, inter-study variability has been observed, influenced by factors such as obesity, presence of diabetes, and operator experience. Importantly, VCTE devices are also equipped with the CAP, which provides simultaneous quantification of hepatic steatosis, with AUROC values of 0.82–0.88 for $\geq$ S1 disease in MASLD cohorts.[85,87]

Table 2
The diagnostic accuracy of US, CT, and MRI/MRS in evaluating the liver steatosis.

Type of imaging modality	Study (Reference)	Number of patients	Sensitivity (%)	Specificity (%)	Other data
US	Retrospective[61]	Suspected patients underwent liver biopsy and US measurement on the same day ($n = 101$)	76.0 (grade S1–S3); 96.0 (grade S2–S3)	86.0 (grade S1–S3); 74.0 (grade S2–S3)	Cutoff values: 0.69 dB/cm/MHz (grade S1–S3); 0.72 dB/cm/MHz (grade S2–S3)
US	Retrospective[51]	Patients having suspected steatotic liver ($n = 100$)	91.5 (for mild fatty liver); 93.3 (for moderate fatty liver)	80.0 (for mild fatty liver); 87.1 (for moderate fatty liver)	Cutoff values: 0.615 dB/cm/MHz (for mild fatty liver); 0.715 dB/cm/MHz (for moderate fatty liver)
US	Retrospective[62]	Patients with chronic liver diseases ($n = 119$)	67.9 (grade $\geq$ S1); 79.3 (grade $\geq$ S2); 92.2 (grade $\geq$ S3)	85.7 (grade $\geq$ S1); 91.1 (grade $\geq$ S2); 88.6 (grade $\geq$ S3)	Cutoff values: 0.63 dB/cm/MHz (grade S1–S3); 0.73 dB/cm/MHz (grade S2–S3); 0.75 dB/cm/MHz (grade $\geq$ S3)
CT	Meta-analysis[44] on 46 studies	Different patients including liver donors, non-alcoholic fatty liver, and patients having liver resection ($n = 1721$)	46.0 (for steatosis $\geq$0%); 57.0 (for steatosis $\geq$10%); 72.0 (for steatosis $\geq$25%)	94.0 (for steatosis $\geq$0%); 88.0 (for steatosis $\geq$10%); 72.0 (for steatosis $\geq$25%)	-
CT	Prospective[63]	Patients with liver resection ($n = 46$)	74.0 (for steatosis $\geq$5%)	70.0 (for steatosis $\geq$5%)	-
CT	Prospective[64]	Liver donors ($n = 161$)	50.0 (for steatosis $\geq$5%); 73.0 (for steatosis $\geq$30%)	77.0 (for steatosis $\geq$5%); 91.0 (for steatosis $\geq$30%)	-
MRI/MRS	Multicenter study/ secondary analysis of biopsy proven non-alcoholic steatohepatitis cohorts[65]	Patients with biopsy proven non-alcoholic fatty liver ($n = 110$)	74.0 (for steatosis grade = 2); 60.0 (for steatosis grade = 3)	90.0	PDFF threshold: 17.5% (grade = 2); 23.3% (grade = 3)
		Patients with non-alcoholic steatohepatitis ($n = 113$)	83.0 (for steatosis grades = 2–3); 84.0 (for steatosis grade = 3)	90.0	PDFF threshold: 16.3% (grades = 2–3); 21.7% (grade = 3)
MRI/MRS	Prospective[66]	Patients with biopsy proven non-alcoholic fatty liver ($n = 89$)	86.0 (for steatosis grade $\geq$1); 64.0 (for steatosis grade $\geq$2); 71.0 (for steatosis grade = 3)	83.0 (for steatosis grade $\geq$1); 96.0 (for steatosis grade $\geq$2); 92.0 (for steatosis grade = 3)	PDFF threshold: 6.4% (grade $\geq$1); 17.4% (grade $\geq$2); 22.1% (grade = 3)
MRI/MRS	Retrospective[67]	Patients with biopsy proven non-alcoholic fatty liver ($n = 70$)	93.0 (for steatosis grade $\geq$2)	85.0 (for steatosis grade $\geq$2)	PDFF threshold: 15% (grade $\geq$2)

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; PDFF, proton density fat fraction; US, ultrasound.

This dual-functionality renders VCTE particularly valuable in the clinical management of MASLD. Both the AASLD and the EASL endorse VCTE as a first-line imaging modality for non-invasive fibrosis evaluation in MASLD.[87,88] Clinical studies have demonstrated its high sensitivity and specificity for diagnosing advanced fibrosis and cirrhosis (F3–F4), particularly in outpatient settings where liver biopsy is not routinely performed.[38] VCTE (7.1–7.9 kPa) and MRE (3.62–3.80 kPa) with the suggested cut-offs showed favorable accuracy for diagnosing advanced fibrosis.[89] Furthermore, VCTE has shown prognostic utility comparable to liver biopsy in predicting liver-related events, including decompensated cirrhosis and hepatocellular carcinoma.[37,38]

Certain limitations affect VCTE performance. Obesity and the presence of ascites may compromise US wave transmission, reducing measurement reliability.[90] In such scenarios, magnetic resonance elastography may offer superior diagnostic accuracy.[91] Additionally, factors such as acute hepatic inflammation, alcohol consumption, obesity, and extrahepatic cholestasis can result in overestimation of liver stiffness.[87,92]

6.2. CAP

The CAP represents a recent advancement in diagnostic imaging, utilizing VCTE to provide quantitative assessment of hepatic steatosis.[93] CAP is an algorithm available on the FibroScan system (Echosens, Paris, France) for quantification of liver fat content. The system calculates the attenuation slope in decibels per meter (dB/m). CAP values range from 100 to 400 dB/m, and they are obtained together with the value of liver stiffness.[94] Moreover, it is one of the most extensively studied methods for non-invasively quantifying liver fat. Despite its growing clinical utility, CAP is not without limitations. Notably, its measurement failure rate ranges from 0% to 24%,[95] with higher failure rates observed in patients with obesity.[96,97] A meta-analysis reported that CAP cannot adequately grade steatosis in patients with MASLD, but its value in the MASLD screening setting needs to be studied.[98] Consequently, recent comparative studies have challenged CAP's superiority. For instance, Collin Remi and colleagues[99] reported that the HRI, derived from conventional US, yielded higher diagnostic accuracy than CAP, with AUROCs of 0.91 and 0.79, respectively. Although

CAP has undergone extensive validation and shows excellent diagnostic performance, its limited availability—particularly in resource-constrained settings—restricts its widespread implementation.[100] Consequently, conventional B-mode US remains the first-line screening modality for MASLD due to its broad accessibility, low cost, and long-established role in clinical practice.

6.3. SWE

US-based elastography has gained considerable traction as a non-invasive tool for evaluating liver stiffness and staging fibrosis in chronic liver diseases, including MASLD.[101,102] SWE quantifies liver tissue viscoelastic properties, with stiffness values shown to correlate with hepatic fat content, rendering it a promising modality for detecting both fibrosis and steatosis.[103,104] FibroScan (Echosens, Paris, France), a widely validated US-based transient elastography (TE) device, has demonstrated reliable correlation with histological findings.[95] TE is based on vibration controlled transient elastography and differs from conventional point or two dimensional SWE techniques. It offers the advantages of widespread availability and usability at the point of care. However, it has several limitations. These include the absence of gray-scale imaging to guide the precise location of measurements and limited ability to avoid large vessels or hepatic lesions, although some structures can be inferred from time-motion and A-mode displays. Additionally, TE requires periodic recalibration of the device's internal spring mechanism, typically every 6–12 months, depending on the probe type.[105] Furthermore, TE's diagnostic reliability may be reduced in individuals with obesity, and it is generally unsuitable for patients with ascites.[105] Measurement outputs are reported in kilopascals (kPa), typically ranging from 2.5 to 75 kPa.[106] Still, SWE is particularly advantageous in patients with MASLD who are obese, a population in which conventional techniques such as VCTE may yield suboptimal or inconsistent results due to probe limitations or altered acoustic transmission.[84] However, severe hepatic steatosis can lead to overestimation of liver stiffness, potentially impairing SWE's diagnostic accuracy.[84,107] SWE can be used to rule out (<8 kPa) and rule in (>12–15 kPa) advanced liver fibrosis in patients with MASLD.[108] Moreover, SWE demonstrates better diagnostic performance for detecting advanced fibrosis stages (≥F2) than for early-stage disease (F0–F1).[101,107] While SWE remains useful, higher measurement failure rates have been reported in obese individuals, although robust data are lacking for those with class 3 obesity.[109] Besides, two-dimensional SWE (2D-SWE), a newer elastographic modality, has shown potential as a non-invasive alternative to liver biopsy in assessing fibrosis, particularly in obese MASLD patients.[109] By integrating elastography into conventional B-mode US systems, 2D-SWE facilitates real-time evaluation of liver stiffness with simultaneous anatomical imaging and user-defined region-of-interest selection.[109,110] Nonetheless, its performance in patients with class 3 obesity remains uncertain,[92] and currently, no ideal non-invasive test has demonstrated consistent accuracy for grading fibrosis severity in this subgroup.[111,112]

6.4. Combi-elastography

Combi-elastography is a novel approach that utilizes both shear wave measurement and real-time tissue elastography measurement simultaneously using a single probe. It overcomes the drawbacks of US-based methods used in isolation.[113] Additionally, the acquisition of features from both types of elastography allows greater histological insight and analysis. Indeed, a recent study using combi-elastography formulated the fibrosis index (F index) for determining fibrosis severity, and the activity index (A index) for assessing hepatic inflammation.[114] The diagnostic performance of combi-elastography-derived indices for detecting fibrosis in MASLD patients is rarely reported. Prior studies using the liver fibrosis index either had a small cohort or were not conducted with liver biopsy as reference.[115] The F index is a strong, independent predictor of early recurrence of hepatocellular carcinoma. However, its efficacy in MASLD has yet to be reported.[116]

6.5. Contrast-enhanced US (CEUS)

Conventional ultrasonography has inherent limitations in the evaluation of intrahepatic space-occupying lesions, particularly in the context of hepatic steatosis, where its diagnostic specificity is often reduced.[117] Image quality may also be compromised by factors such as intestinal gas, patient obesity, and suboptimal acoustic windows. In this regard, CEUS represents a promising advancement, offering microvascular-level imaging to assess hepatic microcirculation and to support the differential diagnosis of focal liver lesions.[117] CEUS evaluates perfusion dynamics by using microbubble (MB) contrast agents, which are strictly intravascular and enhance the visualization of blood flow and tissue perfusion kinetics.[118] This is particularly relevant in steatotic liver disease, as fat accumulation can significantly alter hepatic parenchymal vascularity.[119] Despite its potential, there are limited studies worldwide on the application of CEUS for differentiating intrahepatic lesions in the setting of steatotic liver. Notably, Luo *et al.*[117] reported that CEUS demonstrated good diagnostic concordance with contrast-enhanced CT when evaluating space-occupying lesions in fatty liver. Furthermore, in preclinical models, CEUS has shown superior sensitivity in tracking the progression of fatty liver disease and in accurately identifying MASH.[120] These findings underscore the potential of CEUS as a valuable adjunctive tool for characterizing hepatic lesions in steatotic environments, although further clinical validation is warranted.

7. US platforms and the impact on reproducibility in MASLD

Several quantitative US (QUS) techniques using radiofrequency data, including sound velocity, US attenuation, and BSCs, have been used to quantitate liver fat content.[121] Tissue attenuation imaging (TAI) and tissue scatter distribution imaging (TSI) results exhibited significant correlations with those of MRI-PDFF.[122] TAI provides a measure of US energy loss in tissue, while TSI provides a measure of US energy retention within tissue.[122] To enable the clinical use of TAI and TSI as quantitative imaging biomarkers, rigorous technical evaluation is required. Repeatability and reproducibility are essential for novel techniques to be widely accepted.[123] Meanwhile, US is an extremely operator-dependent technique. Therefore, it is important to demonstrate the repeatability and reproducibility of TAI and TSI between radiologists with different levels of experience for the technique to be widely employed.[124] Recently, several US platforms have incorporated algorithms for estimating the attenuation coefficient (AC), with encouraging evidence supporting their utility in quantifying hepatic fat content.[125] AC assessment is frequently performed alongside LSMs, guided by standardized protocols designed to enhance reliability.[108] Among the recommended parameters, the interquartile range-to-median ratio (IQR/M) is considered the most critical for evaluating variability across sequential measurements. Notably, studies have demonstrated that failure to meet this criterion can markedly reduce the accuracy of stiffness assessments.[126,127] For liver stiffness, the use of the median from five valid acquisitions is the standard recommendation.[108] In contrast, quality control criteria for AC estimation, such as optimal acquisition number, preference for mean versus median values,

and use of IQR/M or alternative metrics like the standard deviation-to-average ratio (S/A), remain poorly defined.[128,129] Furthermore, the impact of varying these parameters on the diagnostic accuracy of AC in estimating hepatic fat remains uncertain. The newly developed parameter, ultrasound-derived fat fraction (UDFF), can effectively detect and quantify hepatic steatosis. The calculation of this parameter combines the AC (detection of energy loss per unit distance in the tissue) and the BSC (detection of differential scattering per unit volume per unit steradian angle), which quantitatively measures both the liver echo enhancement and the posterior beam attenuation.[124] UDFF is quantified as the percentage of liver steatosis. Therefore, it can be directly compared with MRI-PDFF to provide similar clinical applications.[130] Moreover, UDFF is more convenient and cost-effective than PDFF. Additionally, it is a quantitative parameter that is not as susceptible to operator influence as conventional US.[130]

8. AI advancements in US image analysis and risk stratification in MASLD

AI is rapidly transforming the landscape of MASLD diagnosis, risk stratification, and management. The complexities of MASLD, including the need for non-invasive diagnostic tools, standardized disease assessment, and improved diagnostic accuracy, are being increasingly addressed through machine learning and deep learning methodologies.[131,132] The role of AI in MASLD includes the following:

- AI algorithms are enhancing the interpretation of conventional B-mode US and elastography by improving the detection of hepatic steatosis and fibrosis.
- AI models outperform traditional techniques in predicting fibrosis stage and quantifying hepatic fat content by analyzing US images with greater precision. Radiomics-based AI analysis further enables the extraction of high-dimensional quantitative features from MRI and CT, identifying imaging patterns associated with MASLD severity and facilitating more accurate staging. AI systems are also advancing automated liver segmentation, thereby minimizing operator variability and streamlining imaging workflows.[131]
- In histopathology, AI has been trained to assess liver biopsy samples with improved consistency, reducing interobserver variability in the evaluation of key features such as fibrosis, inflammation, steatosis, and hepatocellular ballooning. The latter, a hallmark of disease progression in MASLD, remains difficult to assess manually, and AI-driven tools are being developed to improve its identification and grading. AI-powered digital pathology platforms now enable whole-slide image analysis, yielding reproducible and objective assessments of liver histology.[133,134]
- AI models are increasingly integrating clinical, biochemical, and imaging data for comprehensive risk stratification. These systems can predict advanced fibrosis, disease progression, and liver-related outcomes, while simultaneously reducing reliance on invasive biopsy by supporting the development of multimodal non-invasive biomarkers. AI tools frequently combine serum markers, imaging inputs, and demographic data to assess disease activity.
- In the realm of precision medicine, AI is being employed to forecast individual responses to lifestyle modification, pharmacotherapy, and bariatric interventions—facilitating tailored therapeutic planning. AI algorithms also allow for the identification of MASLD phenotypic subgroups, enabling a more nuanced approach to disease management.[132] Furthermore, AI is being integrated with digital health platforms, including mobile applications that track lifestyle metrics (*e.g.*, physical activity and nutrition) and metabolic parameters in MASLD patients, thus promoting early intervention and treatment adherence.
- Integration of AI into electronic health records (EHRs) offers real-time clinical decision support by suggesting individualized referrals, investigations, or therapeutic adjustments based on patient-specific data.[135]

AI limitations: While AI has generated significant enthusiasm within the scientific community, its integration into healthcare is not without challenges and concerns. A key issue is the potential for bias in AI models, particularly when they are developed using datasets from single centers with variable data quality.[136] These biases can lead to inaccurate predictions and reduced generalizability.[136] Additional challenges include the dependency on high-quality, standardized datasets; limited generalizability due to variation in imaging protocols, histological techniques, and clinical input; and a need for external validation in diverse real-world settings.[137] Another notable limitation is the risk of AI 'hallucinations', where large language models generate incorrect or misleading outputs that appear plausible.[137] Such errors, if misinterpreted as factual, can have serious consequences for patient care, underscoring the critical need for careful human oversight in clinical decision-making. Moreover, it is essential to ensure that the benefits to patients clearly and transparently exceed the commercial obligations of companies developing AI models (beneficence principle) and that access to AI tools is equitable for all (justice principle).[138] Ethical and regulatory considerations—such as patient data privacy, algorithmic transparency, and potential bias—must also be addressed before AI can be routinely adopted in clinical hepatology.[139]

Future perspectives in AI: Looking ahead, the development of multimodal AI frameworks that integrate imaging, histology, and multi-omics data (*e.g.*, genomics and proteomics) may offer holistic, precision-driven diagnostic and prognostic tools for MASLD. Aligning these technologies with international guidelines (*e.g.*, AASLD and EASL) will be crucial to ensuring their clinical relevance. Equally important is the democratization of AI access in underserved and low-resource settings, where MASLD prevalence is rising but diagnostic infrastructure remains limited. In conclusion, while AI holds transformative potential in MASLD management, its benefits will only be fully realized through continued research, rigorous validation, and responsible clinical integration.[131,140]

9. Conclusions and future perspectives

MASLD has become the most prevalent chronic liver disease worldwide, necessitating reliable, accessible, and non-invasive diagnostic strategies. While liver biopsy remains the reference standard for staging fibrosis and diagnosing MASH, its invasive nature and limited practicality underscore the importance of imaging-based alternatives. US continues to serve as the cornerstone of initial MASLD evaluation due to its wide availability, low cost, and reasonable diagnostic performance, particularly for moderate-to-severe hepatic steatosis. Recent advances in US-based modalities, including semi-quantitative scoring systems, SWE, and CAP, have significantly improved diagnostic accuracy and risk stratification. However, technical limitations, especially in patients with obesity and mild disease, highlight the need for ongoing refinement and validation of these tools. CEUS and emerging AI-driven solutions offer additional potential to enhance diagnostic precision, reproducibility, and clinical workflow

efficiency. Despite encouraging progress, no single non-invasive modality currently provides a comprehensive assessment of steatosis, inflammation, and fibrosis in all clinical scenarios. A multiparametric approach, integrating clinical, biochemical, imaging, and where appropriate, histological data, remains essential. Future research should focus on standardizing imaging protocols, validating AI-assisted diagnostic models, and ensuring equitable access to advanced technologies, particularly in resource-limited settings. Ultimately, the future of MASLD diagnosis lies in harmonizing conventional and novel imaging strategies with digital innovations to improve early detection, guide personalized treatment, and reduce the burden of liver-related complications globally.

While B-mode US remains the first-line screening tool for SLD due to its safety, accessibility, and cost effectiveness, it has inherent limitations. QUS is utilized for more precise assessment of fat content, particularly when mild steatosis is suspected. These QUS methods can serve as effective, non-invasive tools for monitoring liver condition changes following lifestyle modification and treatment. Integrated approaches using these US-based techniques should be incorporated into the comprehensive clinical assessment and diagnosis of MASLD patients. More cohort studies and clinical trials are encouraged to validate emerging B-mode US techniques for more accurate MASLD assessment. Further efforts are also needed to integrate these quantitative techniques with AI and machine learning algorithms to improve the detection of low-grade hepatic steatosis and fibrosis, and ultimately reduce the need for biopsies.

Authors' contributions

Walaa Abdelhamed: Writing – original draft. **Mohamed Elbadry:** Writing – review & editing, Conceptualization. **Mohamed El-Kassas:** Writing – review & editing, Conceptualization, Supervision.

Declaration of competing interest

The authors declare that there is no conflicts of interest.

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