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Systematic Review

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Elastography for the Evaluation of Liver Fibrosis in Non-Alcoholic Fatty Liver Disease: A Systematic Review

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease worldwide, often progressing to fibrosis, cirrhosis, and liver failure. Liver biopsy, the traditional gold standard for fibrosis assessment, is invasive and impractical for routine monitoring. Elastography, a non-invasive technique measuring liver stiffness, has emerged as a promising alternative. This systematic review evaluates the diagnostic accuracy of transient elastography (TE), point shear wave elastography (pSWE), two-dimensional shear wave elastography (2D-SWE), and magnetic resonance elastography (MRE) for staging liver fibrosis in NAFLD. **Methods: :** Studies were included if they evaluated one or more of elastography techniques and used liver biopsy as the reference standard for fibrosis staging. A comprehensive literature search was conducted in PubMed and Google Scholar to identify studies that assessed elastography techniques to assess liver fibrosis. Five studies met the criteria after screening 4,136 records. Risk of bias was evaluated using the QUADAS-2 tool, and diagnostic accuracy was synthesized narratively. **Results**: All five studies demonstrated low to moderate risk of bias. SWE and TE showed good diagnostic accuracy (AUC > 0.75) for detecting significant fibrosis (≥F2), with 2D-SWE and MRE excelling in advanced stages (AUC > 0.90). MRE offered superior specificity, while SWE correlated strongly with biopsy findings, particularly in the right upper lobe. However, studies included mixed liver disease etiologies, limiting NAFLD-specific conclusions. **Conclusion**: Elastography, especially MRE and SWE, provides accurate, non-invasive fibrosis staging in NAFLD, reducing reliance on biopsy. Standardization of cut-offs and NAFLD-focused research are needed to enhance clinical utility.

INTRODUCTION

Chronic liver disease (CLD) is a significant global health challenge, affecting hundreds of millions of individuals world wide[1]. Accurate diagnosis and monitoring of fibrosis are crucial for effective disease management'[2]. NAFLD, characterized by abnormal fat accumulation in the liver, is a leading cause of CLD, affecting a substantial portion of the global population, particularly those with obesity and type 2 diabetes[3]. Its progressive nature can lead to non-alcoholic steatohepatitis (NASH), advanced fibrosis, cirrhosis, and liver failure[4].

Traditionally, liver biopsy has been the gold standard for assessing liver fibrosis [4]. However, its invasive nature, potential complications, and limitations in monitoring disease progression underscore the need for non-invasive diagnostic tools. Elastography has emerged as a promising non-invasive technique for evaluating liver fibrosis by measuring tissue stiffness, which increases with fibrosis progression[5]. Various elastography techni ques are available, each with its own strengths and limitations:

- **Transient elastography** (TE), including vibration-controlled transient elastography (VCTE), is a widely used ultrasound-based technique that measures the speed of a shear wave to assess liver stiffness[6].
- **Point shear wave elastography** (pSWE) utilizes acoustic radiation force impulse (ARFI) to generate and measure shear wave velocity at a specific liver location[6].
- **Two-dimensional shear wave elastography** (2D-SWE) provides a visual map of liver stiffness, offering a more comprehensive asse ssment'[2].
- **Magnetic resonance elastography** (MRE) uses magnetic resonance imaging to measure shear wave propagation, known for its accuracy but limited availability[7].

While these techniques have shown promise in detecting liver

fibrosis, challenges remain regarding accuracy, reliability, and accessibility. Factors such as obesity and inflammation can influence ultrasound-based elastography measurements, while MRE, though accurate, faces limitations in cost and availability[8].

This systematic review aims to critically evaluate the evidence on the effectiveness of different elastography techniques in assessing liver fibrosis specifically in patients with NAFLD. By synthesizing the available data on the diagnostic accuracy of TE, pSWE, 2D-SWE, and MRE, this review will provide valuable insights into their performance in staging liver fibrosis in adults with NAFLD. This information will help clinicians make informed decisions regarding the most appropriate non-invasive diagnostic approach for this growing patient population.

METHODS

Eligibility criteria

The eligibility criteria for this systematic review were defined to ensure that only the most relevant and metho dologically sound studies were included, adhering to established guidelines. The review aimed to evaluate the diagnostic accuracy of transient elastography (TE), shear wave elastography (SWE) including both point SWE and 2D-SWE and magnetic resonance elastography (MRE) for assessing liver fibrosis in adults with non-alcoholic fatty liver disease (NAFLD). Studies were included if they evaluated one or more of these imaging modalities and used liver biopsy as the reference standard for fibrosis staging. In addition, studies reported sufficient data to construct 2×2 contingency tables (true positives, false positives, true negatives, false negatives) or provided sensitivity and specificity values, and they were published in English. Conversely, studies were excluded if they were case reports, reviews, editorials, or conference abstracts. This approach ensured that only studies of the highest relevance and methodological quality were included in the final synthesis.

Literature search and selection

A comprehensive literature search was conducted to identify all relevant studies in PubMed and Google Scholar. The search strategies employed a combination of keywords and controlled vocabulary terms, including MeSH terms in PubMed and Emtree terms in Google Scholar, related to the study's focus on elastography techniques and NAFLD. The search utilized Boolean operators (AND, OR) to combine search terms. Specific keywords related to the intervention included "elastography," "transient elastography," "shear wave elastography," "magnetic resonance elastography," "FibroScan," "acoustic radiation force impulse," and "liver stiffness measurement". Keywords related to the condition of interest included "non-alcoholic fatty liver disease," "NAFLD," "steatohepatitis," and "NASH". The search strategy was tailored for each database as shown in our conversation history.

Pubmed Search Strategy (last searched on Jan 21, 2025)

("elastography" OR "transient elastography" OR "shear wave elastography" OR "magnetic resonance elastography" OR "FibroScan" OR "acoustic radiation force impulse" OR "liver stiffness measurement") and ("non-alcoholic fatty liver disease" OR "NAFLD" OR "steatohepatitis" OR "NASH")

Google Scholar Search Strategy (last searched on Jan 21, 2025)

('elastography'/exp OR 'transient elastography'/exp OR 'shear wave elastography'/exp OR 'magnetic resonance elastography'/exp OR 'fibroscan' OR 'acoustic radiation force impulse' OR 'liver stiffness measurement') and ('non-alcoholic fatty liver disease'/exp OR 'nafld' OR 'steato hepatitis'/exp OR 'nash')

The systematic review began with an initial search that retrieved 2,676 records from PubMed and 1,460 records from Google Scholar, totaling 4,136 records. Following the elimination of 351 duplicates, 3,785 records remained for further evaluation. These were screened based on their titles and abstracts, leading to the exclusion of 3,750 records that failed to satisfy the eligibility criteria. Subsequently, 35 records advanced to full-text retrieval assessment. After a thorough full-text review, 30 were excluded, resulting in 5 studies that fulfilled the inclusion criteria and were incor - porated into the final review [figure 1].

Two reviewers independently screened titles and abstracts as well as full-text articles, to identify potentially eligible studies, and any disagreements were resolved through discussion and consensus with a third author who served as the mediator. This rigorous screening process ensured that only the most relevant studies were included in the systematic review.

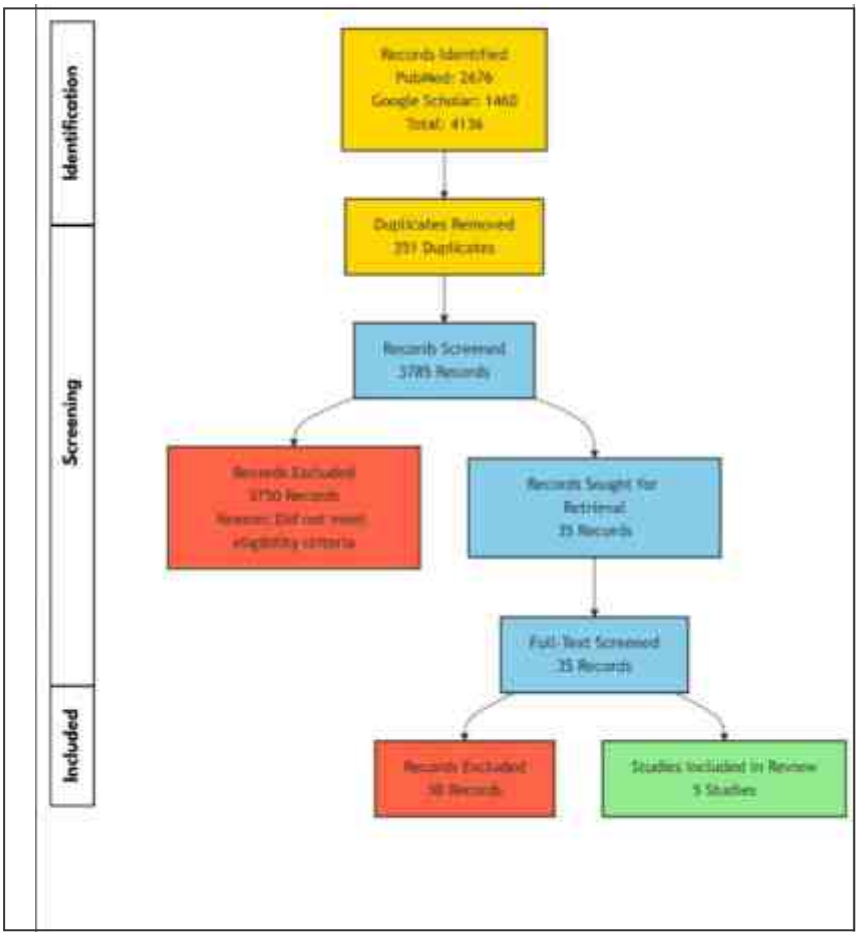

Figure 1: PRISMA Flow Diagram of the Study Selection Process

RESULTS

Characteristics of the studies

A total of five studies were included in this systematic review. The studies employed a variety of designs and methodologies, focusing on the diagnostic accuracy of elastography for liver fibrosis staging. These studies were conducted across different geographical locations and included participants with chronic liver diseases, although not exclusively NAFLD, which is a limitation, as detailed further in the synthesis. Patient demographics varied across the studies, with the age range of participants ranging from 18 to 76 years and a mix of both males and females, although some studies focused on specific populations like liver transplant recipients. The sample sizes ranged from 70 to 310 patients, and the studies used different elastography techniques, including Shear Wave Elastography (SWE) and Magnetic Resonance Elastography (MRE), and Transient Elastography (TE). The reference standards for fibrosis staging were histopathological analysis of liver biopsy specimens, using METAVIR or Batts and Ludwig scoring systems.

Table 1: Characteristics of Included Studies

First Author	Study Design	Location	Participants	Elastography Technique	Reference Standard
Patidar(9)	Prospective, single-center	India	Patients with nonfocal liver disease	SWE and TE	Liver biopsy (METAVIR)
Yoon(10)	Retrospective	South Korea	Liver donors and recipients	MRE and SWE	Liver biopsy (Korean guidelines)
Samir(11)	Prospective, single-center	USA	Patients with diffuse liver disease scheduled for biopsy	SWE	Liver biopsy (METAVIR)
Jeong(12)	Retrospective	South Korea	Patients with various chronic liver diseases	SWE	Liver biopsy (Batts and Ludwig)
Zeng(13)	Prospective	China	Patients with chronic hepatitis B (CHB)	2D-SWE	Liver biopsy (METAVIR)

Risk of Bias Assessment

The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool was used to assess the risk of bias in the included studies(14). This tool evaluates potential biases across four domains: patient selection, index test, reference standard, and flow and timing. All five studies demonstrated alow risk of bias across all domains. This indicates that the findings of these studies are likely to be reliable and unbiased, contributing to the strength of the evidence for the use of SWE in assessing liver fibrosis in NAFLD.

Table 2: Risk of Bias Assessment of the Included Studies, using QUADAS 2 tools

First Author	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias
Patidar et al.(9)	Low	Low	Low	Low	Low
Yoon et al.(10)	Moderate	Low	Low	Low	Low
Samir et al.(11)	Low	Low	Low	Low	Low
Jeong et al.(12)	Moderate	Low	Low	Low	Low
Zeng et al.(13)	Low	Low	Moderate	Low	Low

Narrative Synthesis

The narrative synthesis of the results focused on the key findings related to the diagnostic accuracy of elastography techniques for staging liver fibrosis, and how these techniques compare with other non-invasive serum markers. The study by Patidar et al. found that both SWE and TE had good diagnostic performance for liver fibrosis staging, and that elastography-guided biopsies helped in determining the most accurate site of biopsy due to the heterogenous nature of fibrosis(9).

The research by Yoon et al. compared MRE and SWE, showing a moderate correlation in liver stiffness measure ments (LSM), although SWE had higher rates of unreliable measurements in cirrhotic livers(10). Samir et al. found that SWE measurements from the upper right lobe of the liver had the highest correlation with fibrosis stage, which is important in determining the region of interest when performing SWE(11). Jeong et al. concluded that SWE is useful and accurate for predicting significant and advanced fibrosis, with comparable accuracy to serum markers like hyaluronic acid and type IV collagen(15). Zeng et al. found that 2D-SWE had high diagnostic accuracy for assessing liver fibrosis in patients with chronic hepatitis B, which could be of relevance to NAFLD patients, but only if they have this co-morbidity(13).

Across studies, SWE showed good diagnostic accuracy for detecting significant fibrosis (≥F2), with areas under the ROC curves (AUC) generally above 0.75, which indicates it may be a valuable tool in NAFLD. The use of elastography, especially SWE, is supported by these studies in the detection of liver fibrosis, and it may help clinicians avoid invasive procedures such as liver biopsies, although the utility of serum markers was not inferior in one study(12). However, the limitations of these studies, such as not focusing exclusively on NAFLD and varying methodo logies, do suggest there is a need for more research in this area.

Table 3: Key Findings and Narrative Synthesis of the Included Studies

First Author	Elastography Modality	Key Findings	Diagnostic Accuracy	Correlation with Fibrosis
Patidar et al.	SWE & TE	Elastography-guided biopsy improves accuracy; fibrosis is heterogeneously distributed. Both TE and SWE performed well in fibrosis staging.	SWE comparable to TE in fibrosis staging; good for F2, F3, F4, fair for F1, F2.	Excellent correlation between biopsy segments and mean velocities. More correlation in inferior segments (5/6).
Yoon et al.	MRE & SWE	Moderate correlation between MRE and SWE; SWE showed higher LSM values and variability, particularly in cirrhotic livers.	MRE: AUC of 1.0, SWE: AUC of 0.989 for differentiating F0 from other stages, but SWE had lower specificity than MRE (90.5%)	Moderate correlation between MRE and SWE.
Samir et al.	SWE	SWE measurements from right upper lobe correlate best with fibrosis stage; left lobe correlation is poor. SWE is good at differentiating lower (F0-F1) and higher (F2-F4) stages of fibrosis.	AUC of 0.77 for differentiating <F2 vs. ≥F2; 0.84 after spectrum bias adjustment.	Highest correlation in right upper lobe (r=0.41).
Jeong et al.	SWE	High diagnostic accuracy of SWE for detecting significant (≥F2) and advanced (≥F3) fibrosis. Comparable to HA and type IV collagen.	AUC of 0.908 for significant fibrosis and 0.893 for advanced fibrosis, higher than APRI.	Liver stiffness measurements (LSM) using SWE strongly correlated with severity of hepatic fibrosis (r = 0.774).
Zeng et al.	2D-SWE	High diagnostic accuracy for liver fibrosis in chronic hepatitis B; high negative predictive values for excluding fibrosis.	AUC > 0.90 for significant, severe fibrosis, and cirrhosis. High NPV for excluding liver fibrosis; low PPV for confirming severe fibrosis and cirrhosis	Correlation with fibrosis stage; GGT and albumin also influence LSM

DISCUSSION

A key strength of elastography lies in its non-invasive nature, overcoming the limitations of liver biopsy, which include sampling variability and potential complications. The use of real-time imaging with some elastography techniques, like SWE, allows for the avoidance of large vessels and targeted sampling. Our study adds to the evidence base supporting the clinical adoption of elastography to reduce the need for liver biopsies.

Our findings on the diagnostic accuracy are in line with several studies in the existing literature. For example, a meta-analysis of transient elastography (TE) studies showed pooled sensitivity of 87% and specificity of 91% for detecting cirrhosis [16]. Similarly, studies using SWE have reported good diagnostic accuracy, with an area under the ROC curve (AUROC) of 0.89 for detecting significant fibrosis[17]. However, it's important to acknowledge the heterogeneity in reported cut-off values for different fibrosis stages across various studies, which could be due to differences in patient populations, histologic scoring systems (Ishak vs. METAVIR), and the specific elastography equipment used. Hartl et al in their study reported transient elastography has an excellent diagnostic accuracy for differentiating severe from non-severe fibrosis after 6months of immunosuppressive treatment in autoimmune hepatitis [18].

Several sources highlight the variability in results between different elastography systems. This variability underscores the importance of standardization of US-based hardware and software[12]. Additionally, different ultrasound systems developed by different manufacturers may produce varying liver stiffness measurements for the same degree of fibrosis. Some studies have shown that the XL probe used in transient elastography (TE) can lead to lower cut-off values when compared to the M probe, requiring different cut-off values to be established for each probe [16,19].

Each elastography technique possesses distinct advantages and limitations that influence its clinical applicability in NAFLD. VCTE is a widely validated and relatively inex pensive technique, offering the benefit of portability and rapid bedside assessment, with a substantial body of supporting evidence[20]. However, its limitations include higher failure rates in obese patients, susceptibility to BMI and steatosis grade, and the assessment of only a small liver volume, potentially affected by localized inflammation or congestion' [21]. SWE, particularly 2D-SWE, can be integrated into conventional ultrasound systems, enabling real-time assessment with simultaneous B-mode imaging, which may be advantageous in obese individuals compared to VCTE [22]. Nevertheless, SWE is operator-dependent and its accuracy can also be influenced by steatosis. MRE generally exhibits the highest diagnostic accuracy for liver fibrosis and offers the advantage of assessing the entire liver, with less susceptibility to BMI, steatosis, or ascites, and a high technical success rate[23]. However, MRE is more

The findings from our systematic review, when considered alongside the broader literature, have significant clinical implications for the management of NAFLD. Elastography plays an increasingly vital role in identifying patients at high risk of advanced fibrosis (≥F2 or ≥F3), who are most likely to benefit from intensive lifestyle interventions, future pharmacological therapies, and referral to specialist care[25]. Furthermore, elastography can be instrumental in screening high-risk populations, such as individuals with type 2 diabetes or multiple metabolic risk factors, for the presence of significant liver fibrosis[26]. Future research should focus on several key areas. Standar dization of elastography protocols and the establishment of universally accepted cut-off values for different fibrosis stages across various techniques and patient subgroups are essential.

LIMITATIONS

Our study, like most others, has limitations. We acknowledge that the lack of interobserver variability assessment of the liver biopsies and the lack of assessment of interobserver variability of elastography measurements could be a limitation. Cross-sectional studies limit our understanding of how liver stiffness changes over time, hindering the assessment of disease progression or regression and treatment response. Heterogeneity in study populations, with varying liver diseases and fibrosis patterns, makes it challenging to apply uniform cut-off values across different disease etiologies. Additionally, liver biopsy, the reference standard, is subject to sampling errors and inter-observer variability in interpretation, potentially leading to misclassification of fibrosis stage.

CONCLUSION

Our systematic review likely highlights the significant role of elastography in the non-invasive evaluation of liver fibrosis in NAFLD. When compared with the current literature, it is evident that elastography, particularly MRE, demonstrates high diagnostic accuracy for staging fibrosis. While VCTE and SWE are more widely accessible, their performance can be influenced by factors such as obesity and steatosis. Elastography generally outperforms simple serum biomarkers and holds considerable promise for monitoring disease progression and treatment response. Its increasing integration into clinical practice guidelines underscores its value in identifying high-risk patients and guiding manage - ment strategies for NAFLD-related liver fibrosis. Continued research efforts aimed at standardization, validation in longitudinal settings, and optimal integration into clinical pathways will further enhance the utility of elastography in combating the growing burden of NAFLD.

Future research should aim to address the limitations by establishing standardized cut-off values for different fibrosis stages and aetiologies. There is also a need for studies that compare different elastography techniques directly and evaluate their long-term impact on patient outcomes.

Automated analysis and multiparametric approaches are also important avenues for further research. Finally, longitu dinal studies are needed to see how elastography can monitor disease progression.

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