International Journal Dental and Medical Sciences Research
Volume 6, Issue 3, May - June 2024 pp 279-287 www.ijdmsrjournal.com ISSN: 2582-6018

Role of Shear Wave Liver Elastography in Assessment of Liver Fibrosis with Correlation to Liver Function Test

Dr. Akash Saji Thomas[1], Dr.Ajay Upadhyay[2,], Dr.Darshi Sorathiya[3], Dr.Heer Modi[4]

[1]*3rd Year Resident , Dept of Radio-Diagnosis,GCS Hospital and Medical Research Centre.Ahmedabad*
[2,]*Professor,Dept of Radio-Diagnosis,GCS Hospital and Medical Research Centre.Ahmedabad*
[3]*3rd Year Resident , Dept of Radio-Diagnosis,GCS Hospital and Medical Research Centre.Ahmedabad*
[4]*3rd Year Resident , Dept of Radio-Diagnosis,GCS Hospital and Medical Research Centre.Ahmedabad*

Date of Submission: 05-06-2024 Date of Acceptance: 15-06-2024

INTRODUCTION: Liver fibrosis, crucial in chronic liver disease progression, leads to severe conditions like cirrhosis and cancer, often resulting from chronic damage due to factors like viral hepatitis and alcohol abuse. Accurate fibrosis assessment, crucial for disease management, traditionally relies on invasive liver biopsies, which pose risks and limitations. Shear Wave Elastography (SWE), a non-invasive ultrasound-based modality, offers a safer alternative by measuring liver stiffness, correlating strongly with fibrosis stages.

METHODOLOGY: This cross-sectional study at the Department of Radio-Diagnosis in GCS Hospital and Medical Research Centre, Ahmedabad aimed to assess liver fibrosis using Shear Wave Elastography (SWE) and liver function tests (LFTs), enrolling adults with chronic liver disease based on specific criteria. Procedures included SWE, and LFTs, following ethical guidelines. Statistical analysis evaluated SWE's diagnostic performance. The study excluded certain groups, like pregnant women or those with acute liver failure, to ensure safety and accuracy.

RESULTS: Out of 24 participants, most had no liver fibrosis (F0: 10 participants), followed by mild fibrosis (F1: 8), and a minority with moderate fibrosis (F2: 1), with none showing severe fibrosis stages (F3 and F4). At the F0 stage, the mean liver stiffness is 6.81 kPa with a standard deviation (STD) of 1.49. SGPT(ALT) and SGOT(AST) show strong positive correlations with liver stiffness, evidenced by coefficients of 0.65 and 0.68, respectively, and low p-values (0.003 and 0.002), suggesting significant relationships. For normal liver size, there are 8 with F0, 5 transitioning from F0 to F1, 6 with F1, and 1 with F2. There's one case each of enlarged and shrunken livers with F0 fibrosis.

CONCLUSION: This study confirms SWLE's effectiveness in identifying different liver fibrosis stages and its strong correlation with ALT and AST. However, its broader clinical application requires considering diverse patient factors and further research with larger populations.

KEY WORDS: Shear Wave Liver Elastography, Liver Fibrosis, Liver Function Tests, Chronic Liver Disease, Non-Invasive Diagnostic Technique, Fibrosis Staging

I. INTRODUCTION

Liver fibrosis is a critical pathological stage in the progression of chronic liver diseases (CLDs), leading ultimately to cirrhosis, liver failure, or hepatocellular carcinoma.[1] It results from a prolonged wound healing process of the liver, typically in response to chronic damage caused by factors such as viral hepatitis, alcohol abuse, non-alcoholic fatty liver disease (NAFLD), and metabolic syndromes.[2]

The accurate assessment of liver fibrosis is essential for staging the disease, guiding treatment decisions, and monitoring disease progression or regression.[3,4]

Traditionally, liver biopsy has been considered the gold standard for diagnosing and staging liver fibrosis.[5] However, this invasive procedure is not without its drawbacks, including pain, bleeding, and not to mention the inter- and intra-observer variability.[6] These limitations underscore the need for non-invasive, reliable, and reproducible diagnostic methods.

In recent years, Shear Wave Elastography (SWE), a novel ultrasound-based imaging modality, has emerged as a significant non-invasive alternative for assessing liver stiffness, which correlates with fibrosis.[7] Unlike traditional ultrasound techniques, SWE measures the velocity of mechanically generated shear waves within the

liver tissue, translating these measurements into liver stiffness values.[8] These values have shown a strong correlation with the extent of fibrosis, offering a quantitative and non-invasive means of evaluating liver health.

Moreover, the role of liver function tests (LFTs) in assessing liver health cannot be understated. LFTs, which include measurements of bilirubin, albumin, and liver enzymes, among others, are routinely used to detect liver injury and dysfunction.[9] However, while LFTs are sensitive to liver injury, they are not specific to fibrosis and often do not correlate well with the stage of fibrosis. Therefore, a combined approach using SWE to assess fibrosis and LFTs to evaluate liver function could potentially provide a comprehensive view of liver health.[10]

The significance of this combined approach lies in its ability to offer a holistic view of liver health, enabling clinicians to make informed decisions regarding the management of patients with chronic liver disease. By providing a more accurate assessment of liver fibrosis and function, this approach could significantly impact the treatment, management, and monitoring of patients, potentially improving patient outcomes and quality of life.[11]

This study aims to investigate the role of Shear Wave Liver Elastography in the assessment of liver fibrosis and its correlation with liver function tests. By doing so, this research seeks to validate the effectiveness of SWE as a non-invasive diagnostic tool for liver fibrosis and to explore its potential as part of a comprehensive evaluation of liver health in patients with chronic liver diseases.

In the context of existing research, while several studies have validated the efficacy of SWE in assessing liver fibrosis, fewer have explored the relationship between elastography findings and traditional markers of liver function. This study endeavors to fill this gap, providing insights into the combined diagnostic value of SWE and LFTs. The findings of this study could contribute significantly to the field of hepatology by improving diagnostic accuracy, patient safety, and overall management of chronic liver diseases.

The impact of accurately assessing liver fibrosis extends beyond individual patient management to inform public health strategies and healthcare policies. By improving the diagnostic pathway, healthcare systems can better allocate resources, prioritize patient care, and potentially reduce the overall burden of chronic liver diseases.

This study's significance lies in advancing the non-invasive diagnosis of liver fibrosis, potentially replacing the need for invasive liver biopsies. By correlating Shear Wave Liver Elastography (SWE) with liver function tests (LFTs), we aim to provide a comprehensive, safer, and more patient-friendly assessment method. This could lead to earlier detection and improved management of chronic liver diseases, reducing complications and healthcare costs. Furthermore, the findings may enhance clinical decision-making and patient care, contributing to the broader understanding and treatment strategies for liver fibrosis, ultimately impacting public health positively.

The rationale behind this study stems from the urgent need for non-invasive, reliable methods to assess liver fibrosis, a critical indicator of chronic liver disease progression. Shear Wave Liver Elastography (SWE) presents a promising tool in this regard. However, its effectiveness and correlation with conventional liver function tests (LFTs) remain underexplored. By investigating this relationship, the study aims to validate SWE's diagnostic accuracy and its potential integration with LFTs, thus offering a holistic approach to liver health assessment, improving patient outcomes, and guiding more effective clinical management of liver diseases.

The primary aim of this study is to evaluate the role of Shear Wave Liver Elastography (SWE) in the non-invasive assessment of liver fibrosis and to understand its correlation with liver function tests (LFTs) in patients with chronic liver diseases.

Objectives:

1. To investigate the correlation between SWE measurements and conventional LFTs results to establish a combined diagnostic approach.
2. To determine the utility of SWE combined with LFTs in the monitoring and management of liver fibrosis.
3. To evaluate the potential of SWE to reduce the need for invasive liver biopsies, thereby improving patient safety and comfort.

II. METHODOLOGY

Study Design and Setting:

The study was conducted as a cross-sectional analytical study at the Department of Radio-Diagnosis of GCS Hospital and Medical Research Centre,Ahmedabad. The study duration spanned from June 2023 to May 2024, with patient enrolment based on predefined inclusion and exclusion criteria.

International Journal Dental and Medical Sciences Research
Volume 6, Issue 3, May - June 2024 pp 279-287 www.ijdmsrjournal.com ISSN: 2582-6018

Participant Recruitment and Selection:

Participants were recruited from the outpatient and inpatient departments, following an ethical approval by the Institutional Review Board.

Inclusion Criteria:

1. Age and Consent: Adults aged 18 years and above, capable of providing informed consent.
2. Clinical Diagnosis: Patients with a clinical diagnosis of chronic liver disease, irrespective of etiology (e.g., viral hepatitis, alcoholic liver disease, non-alcoholic fatty liver disease, etc.).
3. Availability for Follow-up: Patients must be available for follow-up assessments, including Shear Wave Elastography and Liver Function Tests, as scheduled in the study protocol.
4. Stable Condition: Patients in a stable clinical condition, without any acute exacerbations of liver disease or other acute medical conditions.

Exclusion Criteria:

1. Pregnancy: Pregnant women, due to the potential risks associated with the use of ultrasound elastography during pregnancy.
2. Acute Liver Failure: Patients presenting with acute liver failure or severe acute exacerbations of liver disease.
3. Previous Liver Transplantation: Patients who have undergone liver transplantation, as the transplanted liver may have different elastography and histological characteristics.
4. Recent Alcohol or Drug Abuse: Patients with recent history of significant alcohol or illicit drug abuse, which could affect liver function tests and elastography readings.
5. Inability to Perform SWE: Patients with conditions that preclude the proper performance or interpretation of Shear Wave Elastography, such as severe obesity or extensive liver surface nodularity.

Sample Size Determination:

The sample size was calculated based on previous studies' standard deviations and mean differences in liver stiffness measurements between fibrosis stages. Using a 5% level of significance and 80% power, the calculated sample size was 25 participants.

Shear Wave Elastography Procedure:

SWE measurements were performed using a high-resolution ultrasound system equipped with an elastography module. Patients were instructed to fast for at least six hours before the procedure. The examination was conducted with the patient lying in the dorsal decubitus position, with the right arm maximally abducted. Measurements were taken from the right lobe of the liver through intercostal spaces, ensuring minimal thoracic pressure. A region of interest (ROI) was placed on the liver parenchyma, avoiding large vessels and bile ducts. Ten valid measurements were recorded for each patient, and the median value was used for analysis.

Liver Function Tests:

Blood samples were collected from all participants on the same day as the SWE procedure. Standard LFTs including serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, and albumin were measured using automated analyzers.

Data Collection and Statistical Analysis:

Data were collected using structured case report forms, including demographic information, clinical data, SWE measurements, and LFT results findings. Statistical analyses were conducted using SPSS software. Descriptive statistics were used to summarize the data. The diagnostic performance of SWE in assessing liver fibrosis was evaluated using receiver operating characteristic (ROC) curves, calculating the area under the ROC curve (AUROC). Correlations between SWE values and LFTs were assessed using Spearman's rank correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations:

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board. All participants provided written informed consent before enrolment, ensuring confidentiality and the right to withdraw from the study at any time.

III. RESULTS

Table 1: Demographic and Clinical Characteristics of Study Participants

Category	Details
Total participants	24
Age (years)	45.2 ± 16.6
Sex (Male/Female)	15/9

Category	Details
Fibrosis grade (F0/F1/F2/F3/F4)	F0: 10, F1: 8, F2: 1, F3: 0, F4: 0
Liver size (Normal/Enlarged)	Normal: 20, Enlarged: 1
E Mean (kPa)	7.70 ± 1.59
Cs Mean	2.27 ± 1.80
SGPT(ALT) (U/L)	64.1 ± 69.4
SGOT (AST) (U/L)	142.0 ± 335.5
ALP (U/L)	91.8 ± 28.7
Total Protein (g/dL)	6.31 ± 0.99
Albumin (g/dL)	3.36 ± 0.64
Globulin (g/dL)	2.97 ± 0.67
A/G Ratio	1.18 ± 0.33

The study included 24 participants with an average age of 45.2 years, predominantly male (15 males and 9 females). Most had no liver fibrosis (F0: 10 participants), followed by mild fibrosis (F1: 8), and a minority with moderate fibrosis (F2: 1), with none showing severe fibrosis stages (F3 and F4). Liver size was typically normal (20 participants) with only one case of enlargement. Liver stiffness (E Mean) averaged 7.70 kPa. Biochemical parameters varied, indicating diverse liver function across participants, with notable averages in SGPT(ALT), SGOT(AST), ALP, total protein, albumin, globulin, and the A/G ratio.

Table 2: Comparison of Liver Stiffness Measurements by Shear Wave Elastography Across Fibrosis Stages

Fibrosis Stage	E Mean (kPa) Mean	E Mean (kPa) STD
F0	6.81	1.49
F0 to F1	7.74	1.13
F1	8.21	0.43
F2	12.34	N/A

The table 2 presents liver stiffness measurements across various fibrosis stages using Shear Wave Elastography. At the F0 stage, the mean liver stiffness is 6.81 kPa with a standard deviation (STD) of 1.49. Transitioning from F0 to F1, the mean increases to 7.74 kPa with a 1.13 STD. For F1, the mean slightly rises to 8.21 kPa, demonstrating minimal variation (STD of 0.43). Notably, at stage F2, liver stiffness jumps significantly to 12.34 kPa, but the standard deviation is not applicable (N/A), indicating a single measurement or uniform results across subjects at this stage.

Table 3: Correlation between Liver Stiffness Measurements and Liver Function Test Results

Liver Function Test	Pearson Correlation Coefficient	P-Value
SGPT(ALT)	0.65	0.003
SGOT (AST)	0.68	0.002
ALP (ALKALINE PHOSPHATASE) 135.00 u/l	0.58	0.014
PROTEIN (TOTAL)	0.06	0.825

Liver Function Test	Pearson Correlation Coefficient	P-Value
ALBUMIN	0.21	0.409
GLOBULIN	-0.19	0.446
A/G RATIO	0.33	0.189

Table 3 reveals the correlation between liver stiffness measurements and liver function tests, using Pearson Correlation Coefficients. SGPT(ALT) and SGOT(AST) show strong positive correlations with liver stiffness, evidenced by coefficients of 0.65 and 0.68, respectively, and low p-values (0.003 and 0.002), suggesting significant relationships. ALP has a moderate positive correlation (0.58) with a p-value of 0.014. In contrast, total protein, albumin, and globulin demonstrate weak or negligible correlations with liver stiffness, with Pearson coefficients ranging from -0.19 to 0.21 and non-significant p-values, indicating no meaningful association.

Table 4: Distribution of Liver Fibrosis Grades Among Participants

Fibrosis Grade	Number of Participants
F0	10
F1	8
F2	1
F0 to F1	5

Table 4 shows the distribution of liver fibrosis grades among participants: 10 with grade F0, 8 with F1, 1 with F2, and 5 transitioning from F0 to F1, indicating a majority with no or mild fibrosis.

Table 5: Comparison of Liver Size and Fibrosis Grade in Study Participants

Liver Size	F0	F0 to F1	F1	F2
Normal	8	5	8	1
Enlarged	1	0	0	0
Shrunken	1	0	0	0

Table 5 compares liver size with fibrosis grades among study participants. For normal liver size, there are 8 with F0, 5 transitioning from F0 to F1, 6 with F1, and 1 with F2. There's one case each of enlarged and shrunken livers with F0 fibrosis.

International Journal Dental and Medical Sciences Research
Volume 6, Issue 3, May - June 2024 pp 279-287 www.ijdmsrjournal.com ISSN: 2582-6018

Table 6: Association between Demographic Factors and Liver Stiffness Measurements

Demographic Factor	Association with Liver Stiffness (E Mean)
Age	Pearson Correlation: -0.171, P-Value: 0.424
Sex	Mean Difference (Male - Female): 0.972 kPa

Table 6 explores the relationship between demographic factors and liver stiffness measurements. Age shows a weak negative correlation with liver stiffness (Pearson -0.171) but is not statistically significant (P=0.424). Males, on average, exhibit liver stiffness 0.972 kPa higher than females.

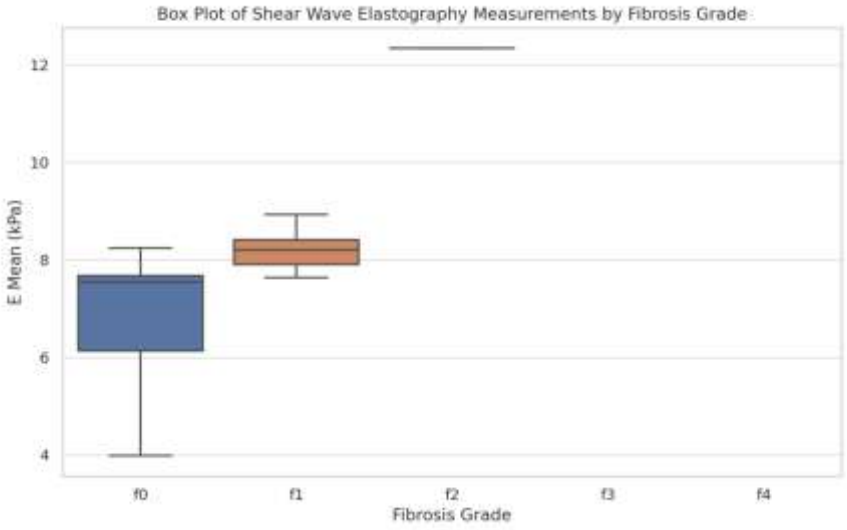

Figure 1: Shear Wave Elastography Measurements by Fibrosis Grade

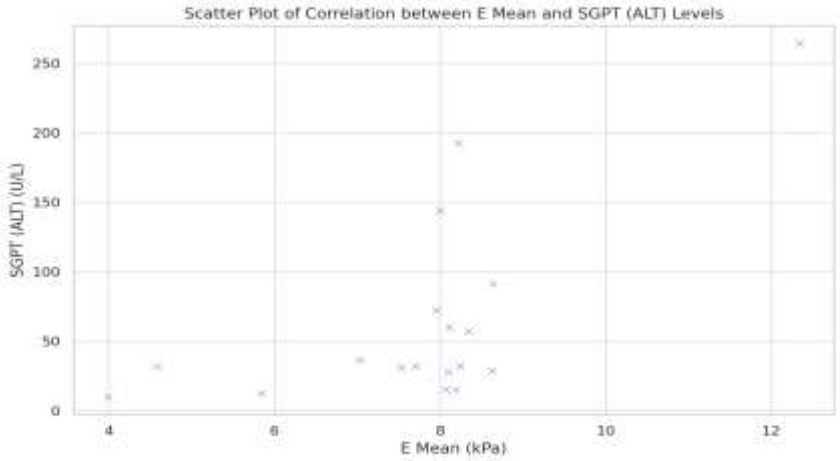

Figure 2: Scatter Plot of Correlation between E Mean and SGPT (ALT) Levels

International Journal Dental and Medical Sciences Research
Volume 6, Issue 3, May - June 2024 pp 279-287 www.ijdmsrjournal.com ISSN: 2582-6018

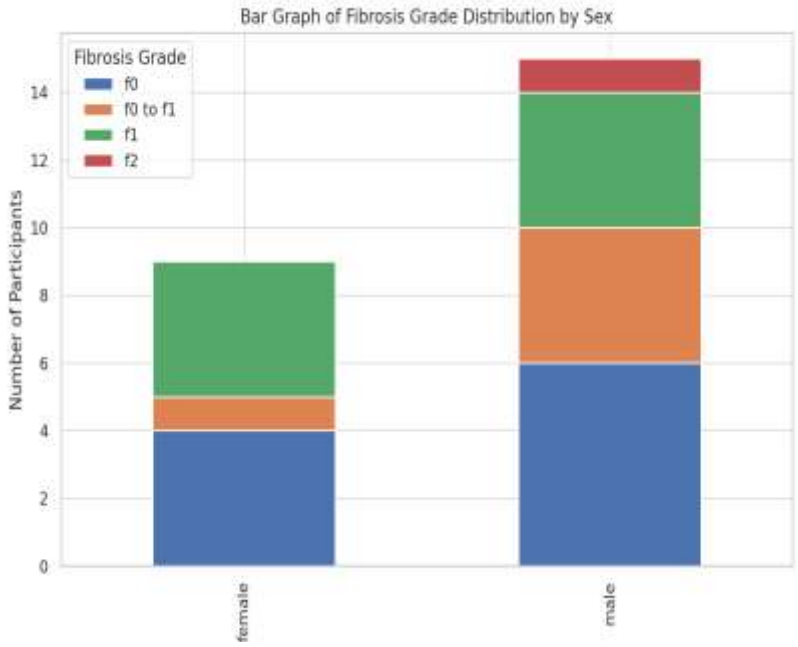

Figure 3: Bar Graph of Fibrosis Grade Distribution by Sex

IV. DISCUSSION

This study aimed to evaluate the role of Shear Wave Liver Elastography (SWLE) in assessing liver fibrosis and its correlation with liver function tests. The sample comprised 24 individuals, predominantly male, with a majority displaying no or mild liver fibrosis. The average liver stiffness, measured by the E Mean in kilopascals (kPa), correlated with the degree of fibrosis, reflecting established principles that stiffer liver textures are indicative of more severe fibrosis.

The data reveals a noticeable progression in liver stiffness from fibrosis stages F0 through F2. Notably, there is a significant leap in stiffness measurements from the F1 to the F2 stage, suggesting that SWLE can distinctly differentiate between mild and moderate fibrosis.[12] However, due to the small number of participants with higher fibrosis grades, these findings should be interpreted with caution.

In terms of liver function tests, SGPT (ALT) and SGOT (AST) levels exhibited a strong positive correlation with liver stiffness. This is consistent with the understanding that increased levels of these enzymes are indicative of liver damage, which in turn could be associated with increased fibrosis and therefore greater liver stiffness.[13] ALP showed a moderate correlation, which might suggest its lesser association with fibrosis compared to ALT and AST. However, the correlation of liver stiffness with total protein, albumin, and globulin levels was weak, indicating that these markers are not as effective in reflecting changes in liver stiffness due to fibrosis.[14]

Interestingly, the study also explored the relationship between demographic factors and liver stiffness. While there was a noticeable difference in liver stiffness between genders, with males showing higher stiffness on average, age did not show a significant correlation. This diverges from some previous studies where older age has been associated with increased liver stiffness.[15] The discrepancy might be due to the relatively small sample size or the specific age distribution within our study population.

Furthermore, the distribution of liver sizes across different fibrosis grades adds another layer to the understanding of fibrosis impact. The predominance of normal liver sizes across fibrosis stages might indicate that liver size, as determined by physical examination or imaging, is not a sensitive indicator of early-stage fibrosis.

When comparing these findings with those from previous studies, several parallels and divergences emerge. The progression of liver stiffness with increasing fibrosis stages mirrors findings from other studies, reinforcing SWLE's role as a reliable method for fibrosis assessment. For instance, the increase in E Mean values from F0 to F2 stages is consistent with literature demonstrating that liver stiffness increases with fibrosis severity.[16]

However, our study's correlation coefficients between liver stiffness and liver function tests (specifically SGPT and SGOT) are slightly higher than those reported in some other studies. This discrepancy could be due to differences in study populations, the severity of liver disease, or methodological differences in measuring liver stiffness and enzyme levels. It suggests that while ALT and AST are useful markers, their relationship with liver stiffness can vary depending on the cohort and the fibrosis etiology.[17]

In contrast to some literature, our study did not find a significant age-related increase in liver stiffness. This could challenge the notion that liver stiffness invariably increases with age, suggesting that factors other than aging per se, such as the presence and severity of liver disease, are more critical determinants of liver stiffness.[18] However, this finding should be interpreted with caution due to our small sample size and the narrow age range of participants.

The gender difference in liver stiffness, with males exhibiting higher values than females, aligns with some studies but not others.[19] This variance underscores the complexity of factors influencing liver stiffness, including hormonal differences, fat distribution, and potentially unrecognized liver disease. These findings advocate for gender-specific normal ranges in liver stiffness assessment, a point that has been raised in previous research but remains contentious.

Our study's limitations include its small sample size and the lack of participants with advanced fibrosis stages (F3 and F4). These factors limit the generalizability of our findings and the statistical power to detect differences or correlations

V. CONCLUSION

This study supports the utility of SWLE in assessing liver fibrosis, particularly in distinguishing between no, mild, and moderate stages. The strong correlation between liver stiffness and certain liver function tests (ALT and AST) reinforces their combined use in non-invasively assessing liver health. However, the lack of significant correlation with other liver function tests and demographic factors indicates that liver stiffness, as measured by SWLE, should be interpreted in a broader clinical context, considering other patient-specific factors and comorbidities. Future research should aim to include larger, more diverse populations and to explore the utility of SWLE in more advanced stages of liver disease.

Acknowledgement: We are sincerely thankful to all the participants who took part in our study
Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Review Board

REFERENCES

[1]. Parola M, Pinzani M. Liver fibrosis: Pathophysiology, pathogenetic targets and clinical issues. Molecular aspects of medicine. 2019 Feb 1; 65:37-55.
[2]. Pellicoro A, Ramachandran P, Iredale JP, Fallowfield JA. Liver fibrosis and repair: immune regulation of wound healing in a solid organ. Nature Reviews Immunology. 2014 Mar;14(3):181-94.
[3]. Sebastiani G. Non-invasive assessment of liver fibrosis in chronic liver diseases: implementation in clinical practice and decisional algorithms. World journal of gastroenterology: WJG. 2009 May 5;15(18):2190.
[4]. Duarte-Rojo A, Taouli B, Leung DH, Levine D, Nayfeh T, Hasan B, Alsawaf Y, Saadi S, Majzoub AM, Manolopoulos A, Hafar S. Imaging-based non-invasive liver disease assessment for staging liver fibrosis in chronic liver disease: A systematic review supporting the AASLD Practice Guideline. Hepatology. 2024 Mar 15:10-97.
[5]. Afdhal NH. Biopsy or biomarkers: is there a gold standard for diagnosis of liver fibrosis? Clinical chemistry. 2004 Aug 1;50(8):1299-300.
[6]. Mullish BH, Kumar N, Goldin RD, Manousou P. Liver biopsy. Evidence-based Gastroenterology and Hepatology 4e. 2019 Apr 23:395-407.
[7]. Agbim U, Asrani SK. Non-invasive assessment of liver fibrosis and prognosis: an update on serum and elastography markers. Expert review of gastroenterology & hepatology. 2019 Apr 3;13(4):361-74.
[8]. Barr RG. Shear wave liver elastography. Abdominal Radiology. 2018 Apr; 43:800-7.
[9]. Lala V, Zubair M, Minter D. Liver function tests. StatPearls. 2023 Jul 30.
[10]. Chin JL, Pavlides M, Moolla A, Ryan JD. Non-invasive markers of liver fibrosis: adjuncts or alternatives to liver biopsy?

Frontiers in pharmacology. 2016 Jun 20; 7:197597.

[11]. Zhang YN, Fowler KJ, Ozturk A, Potu CK, Louie AL, Montes V, Henderson WC, Wang K, Andre MP, Samir AE, Sirlin CB. Liver fibrosis imaging: A clinical review of ultrasound and magnetic resonance elastography. Journal of Magnetic Resonance Imaging. 2020 Jan;51(1):25-42.

[12]. Campos-Murguía A, Ruiz-Margáin A, González-Regueiro JA, Macías-Rodríguez RU. Clinical assessment and management of liver fibrosis in non-alcoholic fatty liver disease. World journal of gastroenterology. 2020 Oct 10;26(39):5919.

[13]. Friedman SL. Evolving challenges in hepatic fibrosis. Nature reviews Gastroenterology & hepatology. 2010 Aug;7(8):425-36.

[14]. Czul F, Bhamidimarri KR. Noninvasive markers to assess liver fibrosis. Journal of clinical gastroenterology. 2016 Jul 1;50(6):445-57.

[15]. Bazerbachi F, Haffar S, Wang Z, Cabezas J, Arias-Loste MT, Crespo J, Darwish-Murad S, Ikram MA, Olynyk JK, Gan E, Petta S. Range of normal liver stiffness and factors associated with increased stiffness measurements in apparently healthy individuals. Clinical Gastroenterology and Hepatology. 2019 Jan 1;17(1):54-64.

[16]. Eddowes PJ, Sasso M, Allison M, Tsochatzis E, Anstee QM, Sheridan D, Guha IN, Cobbold JF, Deeks JJ, Paradis V, Bedossa P. Accuracy of FibroScan controlled attenuation parameter and liver stiffness measurement in assessing steatosis and fibrosis in patients with nonalcoholic fatty liver disease. Gastroenterology. 2019 May 1;156(6):1717-30.

[17]. Eddowes PJ, Sasso M, Allison M, Tsochatzis E, Anstee QM, Sheridan D, Guha IN, Cobbold JF, Deeks JJ, Paradis V, Bedossa P. Accuracy of FibroScan controlled attenuation parameter and liver stiffness measurement in assessing steatosis and fibrosis in patients with nonalcoholic fatty liver disease. Gastroenterology. 2019 May 1;156(6):1717-30.

[18]. Bertolotti M, Lonardo A, Mussi C, Baldelli E, Pellegrini E, Ballestri S, Romagnoli D, Loria P. Nonalcoholic fatty liver disease and aging: epidemiology to management. World journal of gastroenterology: WJG. 2014 Oct 10;20(39):14185.

[19]. Garate-Carrillo A, Gonzalez J, Ceballos G, Ramirez-Sanchez I, Villarreal F. Sex related differences in the pathogenesis of organ fibrosis. Translational Research. 2020 Aug 1;222:41-55.