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Original Article

Correlation of Ultrasound Elastography with Magnetic Resonance Elastography in Fatty Liver Disease

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Abstract

Introduction: Cirrhosis is irreversible and leads to associated complications, portal hypertension, hepatic insufficiency, and hepatocellular carcinoma. While liver biopsy sample histologic assessment has been the gold standard for hepatic fibrosis staging, it is not a perfect reference standard. A potential substitute surrogate marker for the degree of liver fibrosis is liver stiffness measurement (LSM), which is achieved using elastography techniques, including two-dimensional shear wave elastography (2D-SWE) and magnetic resonance elastography (MRE).

Purpose: This study aims to directly evaluate MRE and 2D-SWE's capacities for non-invasive liver fibrosis assessment.

Materials and Methods: A prospective study was conducted in the Department of Radiology and Imaging Sciences at Sri Ramachandra Institute of Higher Education and Research from 2022 to 2023 for 58 patients with clinically suspected or known cases of fatty liver disease.

Results: The LSM values (measured in kilopascal) taken using USE and MRE showed a statistically significant correlation with each other, with an r value of 0.8. Patients were graded according to FIB-4, scoring into low-, intermediate-, and high-risk categories. The average (LSM) was found to be significantly higher among the high-risk category. Fat quantification (measured in db/m) also showed a positive correlation with LSM taken with USE and MRE, the r values being 0.6 and 0.5, respectively.

Conclusion: LSM taken with USE could replace MRE for non-invasive assessment of liver fibrosis in patients with fatty liver disease. It is cheaper, easier, and more comfortable for the patients. Moreover, fat quantification using ultrasound-guided attenuation parameter (UGAP) can also be used to predict LSMs.

Key words: Shear wave elastography, Magnetic resonance, Brightness mode, Young's modulus, Kilopascal, Acoustic radiation force impulse elastography, Point shear wave elastography, Two-dimensional shear wave elastography, Liver stiffness measurement, Region of interest

INTRODUCTION

Fibrosis is a dynamic process, and research indicates that treating the underlying illness (such as using antiviral therapy for viral hepatitis or immunosuppression for autoimmune hepatitis) may cause fibrosis to regress. Previously, a liver biopsy was the sole way to stage the degree of fibrosis.

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Research on non-invasive evaluation has been extensive and includes elastographic techniques utilizing magnetic resonance imaging (MRI) and ultrasonography (US).[1]

HPE's Shortcomings

While liver biopsy sample histologic assessment has been the gold standard for hepatic fibrosis staging, it is not a perfect reference standard.

Apart from being invasive, the uneven distribution of fibrosis in chronic liver disease makes sampling unavoidably variable to some extent; Obtaining biopsy samples for fibrosis staging requires a minimum of 2 cm length and a 16-gauge needle, as 94% of these biopsies have 11 or more portal tracts.

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A further disadvantage of liver biopsy is that most staging systems have only five or seven stages. Rather than falling into distinct groups, fibrosis in liver disease is essentially a continuous continuum.[2]

Two-Dimensional Shear Wave Elastography (2D-SWE)

It uses the acoustic radiation force from concentrated ultrasonic beams to create mechanical vibrations in the liver parenchyma. The liver is interrogated by the ultrasound probe as shown in Figure 1.

An "elastogram" is a color-coded map that is superimposed on a B-mode image. It provides a visual representation of the liver's elasticity. By drawing a circular region of interest (ROI) on the elastogram, the value of liver elasticity can be quantitatively determined, offering an objective assessment of the liver's elasticity as shown in Figure 2.[3]

Transient elastography has several limitations, including a lack of clinical precision, especially when combined with concomitant diseases such as ascites, and intra- and inter-observer variability. In contrast, SWE offers the added benefit of scanning the entire liver using B-mode pictures to detect hepatic steatosis or localized lesions.

One of this technique's strengths is its ability to avoid masses and huge vessels due to its real-time imaging capability. The greater measuring area allows for a more significant ROI for averaging readings.[4]

Figure 1: LOGIQ P10 XDClear ultrasound machine

Using US-based elastography techniques, the patient is scanned in the supine position with the right arm kept above the head.

The best outcomes come from holding breath. A data set is considered good if its IQR/median value is <0.30. More than 60% of the measurements should be "good" measurements.[2,5-7]

Magnetic Resonance Elastography (MRE)

MRE allows for the sampling of bigger regions of the liver than any US LSM approach. It can be used with diagnostic MRI for the most thorough liver imaging evaluation.

Fundamental MRE Principles

To examine the mechanical characteristics of tissues, MRE propagates mechanical shear waves with a frequency range of 20–200 Hz. These waves travel more quickly in more complex tissue, but in softer tissue, they move more slowly. A unique acoustic driver system produces low-frequency mechanical shear waves and transmits them throughout the body.[8]

A special pulse sequence timed with the mechanical waves is utilized to depict the micron-level displacements linked to wave propagation.

The imaging procedure produces pictures that show the pattern of waves propagating in the liver, which can be completed in one or more breath holds. After processing the wave images, specialist software – an inversion algorithm – creates quantitative cross-sectional images showing the tissue's stiffness as shown in Figures 3 and 4. Compared to tissues with shorter wavelengths, those with longer wavelengths of shear waves are depicted as having more stiffness.[9]

Equipment

A flexible 25-foot polyvinyl chloride tube connects an active pneumatic, mechanical wave driver outside the MRE

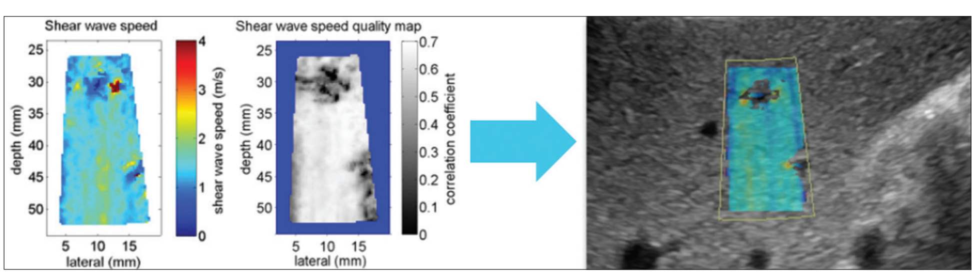

Figure 2: Elastogram in 2D-SWE with quality map

chamber to a passive driver attached to the abdominal wall above the liver in a typical liver MRE configuration. At a set frequency, usually 60 Hz, the passive driver creates a continuous acoustic vibrations that travel through the entire belly, including the liver.[10]

The patient is prepared for MRE, like a typical liver MRI examination. Patients are advised to fast for 4–6 h before the MRE examination.

The passive driver is positioned over the right lobe, which is often the most significant area of the liver.[11]

Objectives of the Study

1. To correlate ultrasound (USG) 2D-SWE and MR liver elastography in the non-invasive assessment of liver fibrosis in patients within patients with fatty liver disease
2. To correlate steatosis values with liver stiffness measurements (LSMs) taken by US and MRE.

MATERIALS AND METHODS

Cases referred from Medical Gastroenterology and general medicine to the Department of Radiology and Imaging Sciences for Liver fat quantification and Elastography at Sri Ramachandra Institute of Higher Education and Research, a prospective study was conducted from 2022 to 2023.

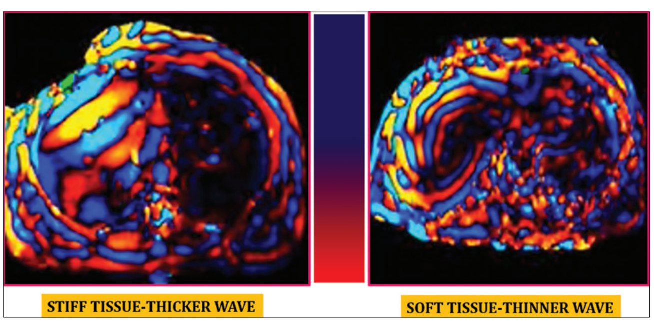

Figure 3: Wave elastograms in fibrosed (left) and normal livers (right). The waves are thicker and less parallel in the case of fibrosed liver

Inclusion Criteria

1. Known cases of fatty liver disease
2. Clinically suspected fatty liver disease
3. Family history of fatty liver disease.

Exclusion Criteria

1. Uncooperative patients
2. Severe ascites
3. Patients with hemochromatosis.

Sample Size

This was a total of 58 patients.

Study Procedure

In the USG liver elastography study, the liver stiffness (measured by kilopascal [kPa]) was calculated for each patient and graded based on F0-F4 using the normogram provided with the General Electronics (GE) LOGIQ P10 USG machine as shown in Figure 5 and Table 1.

Fat quantification was also done and graded as S1-S3 using a nomogram provided by a GE LOGIQ P10 USG machine as shown in Table 2.

Clinical details of the cases, such as age, sex, body mass index (BMI), presence of comorbids and their duration, and liver function tests (LFTs), were also collected.

Patients were also subjected to an MRE study in a GE 3.0 T Signa Architect MR machine.

Plan for Analysis

At the end of imaging investigations and data collection, we performed the following steps:

- Using the Pearson correlation coefficient, we compare the kPa values of liver stiffness calculated by US and MRE to evaluate the presence of either positive, negative, or nil correlation
- Using the Pearson correlation coefficient, we compare the steatosis values (calculated with USG-guided attenuation parameter [UGAP]) with MR and US

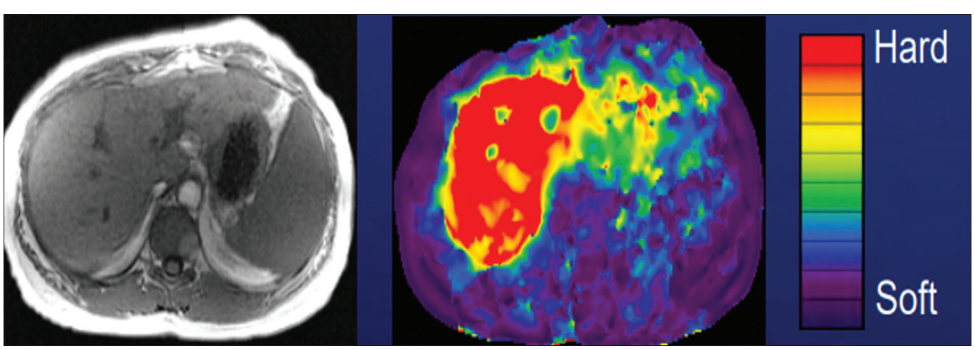

Figure 4: Gray scale and color elastogram with color scale

stiffness kPa values and evaluate the presence of either positive, negative, or nil correlation.

USG Elastography

First, all patients were explained the USG procedure and the requirement of breath hold while measuring liver stiffness values, and then, written consent was obtained.

USG Scanner (B-Mode and 2D-SWE)

GE LOGIQ P10 USG machine.

2-D SWE Protocol

- Probe used: Convex probe, Frequency range-1.5–6.0 MHz

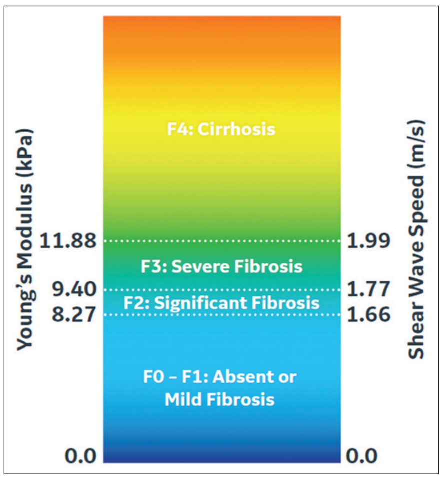

Figure 5: Grades of fibrosis in 2D-SWE (Reference: Whitepaper GE UGAP)

- Frequency: 3.0 MHz
- Size of the color box: 2.5 × 2.0 cm.

Prerequisites

Minimum 6 h of fasting and 10 min of rest (since exercise and postprandial state increases liver stiffness).

Procedure

- Patient was made to lie in a supine position with the right arm kept above the head
- After applying the gel, the curvilinear probe was used to image and scan the entire liver in B-mode before starting the elastography study to rule out focal lesions or hepatic steatosis
- The right lobe of the liver is then focused from the right intercostal position
- Then, fibrosis mode was initiated in the LOGIQ P10XD USG machine, giving a magnified view of the right lobe of the liver
- The color box is introduced over the B-mode image, and its position is adjusted to be 2 cm below the liver capsule and away from the vessels and biliary radicles
- The patient is asked to hold the breath, shear wave mode is activated, and an elastogram is obtained, uniformly blue
- An ROI of approximately 1 cm is used to measure the liver stiffness. Care was taken to put the ROI at vessel-free liver parenchyma.

Parameters Measured in 2D-SWE

A dozen measurements were taken from the right lobe, and the median value was used as the tissue's elasticity value (in kPa).

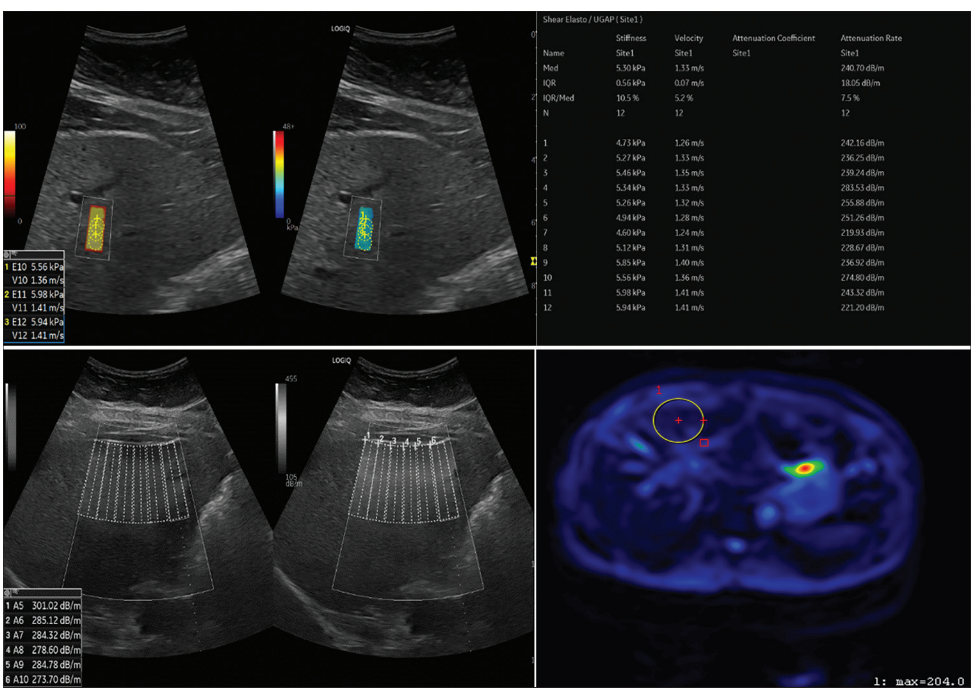

Figure 6: Representative Case 1

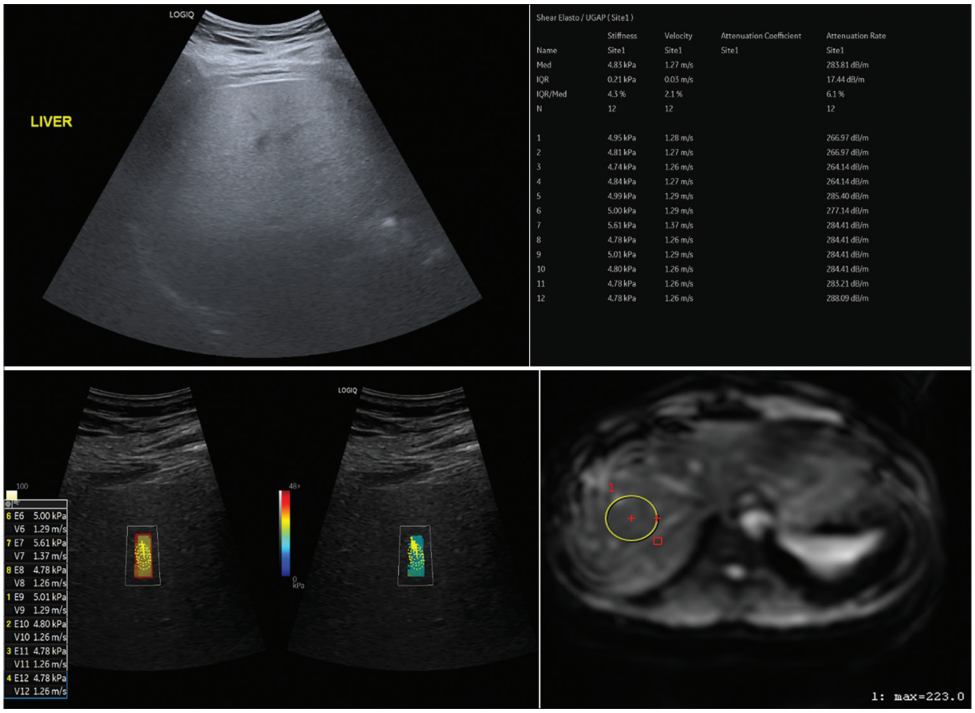

Figure 7: Representative Case 2

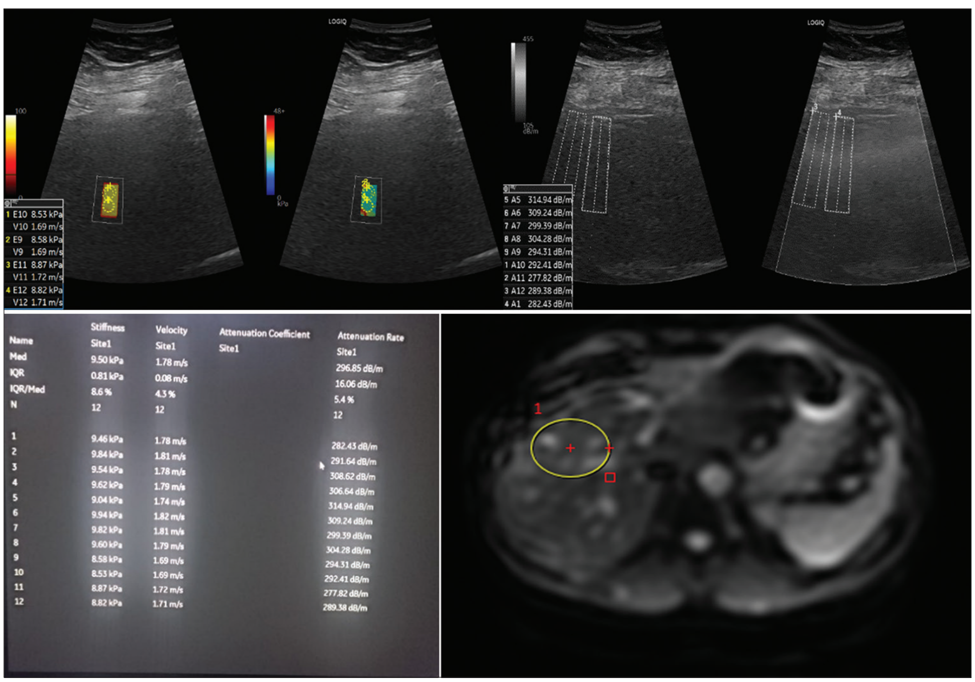

Figure 8: Representative Case 3

All the measurements in the study were taken by a single-skilled radiologist to avoid any interobserver variations in the measurements. At the end of ten readings, the IQR/median was <0.3, ensuring the data set was good.

MRE

Machine: GE Signa 3.0T Architect.

All the patients had MRE. The acquisition is performed during held breath at full expiration and takes 12–15 s. It is repeated four times, bringing the acquisition time to <1 min.

Elastograms are generated from which ROIs are taken, and the average is calculated.

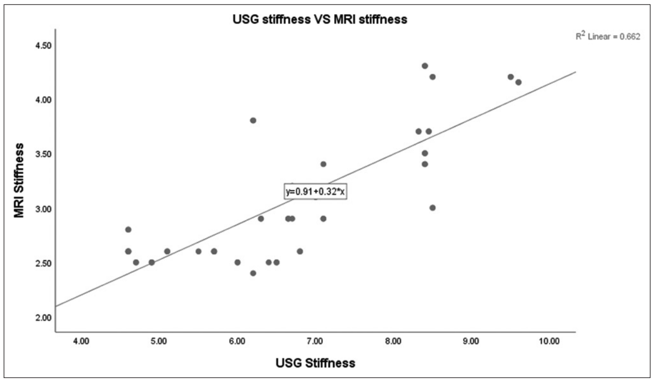

Figure 9: Correlation of ultrasound and magnetic resonance imaging stiffness

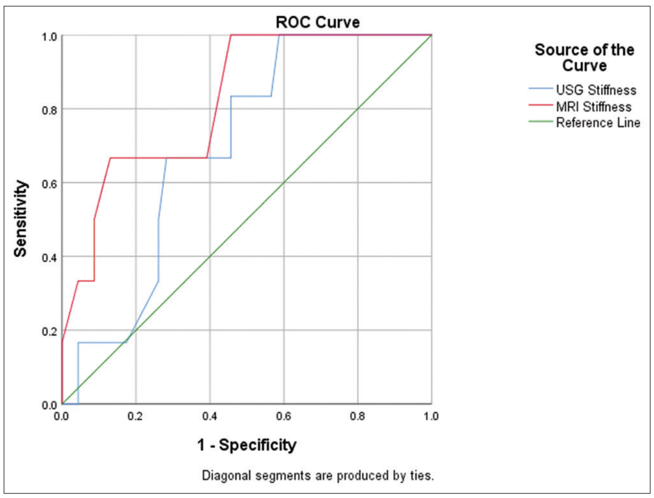

Figure 10: Receiver operating characteristic curve for FIB-4 staging 1 to 2

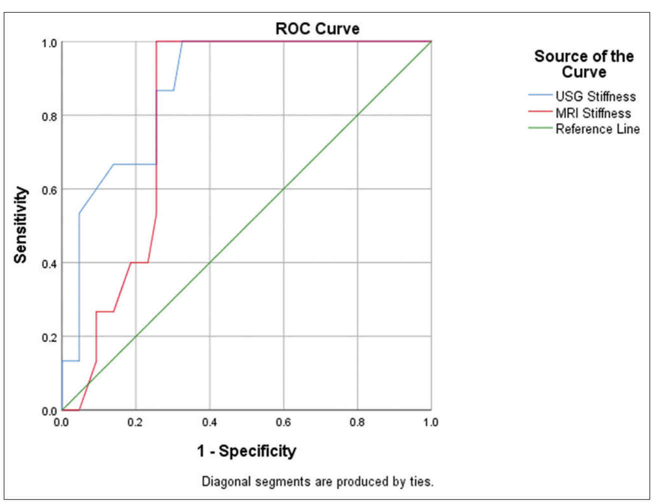

Figure 11: Receiver operating characteristic curve for FIB-4 staging 2 to 3

Representative Cases

Case 1 [Figure 6]

A 33-year-old, newly diagnosed type 2 diabetes mellitus, liver stiffness was found to be 5.3 Kpa on US elastography corresponding to F1, and 2.5 Kpa on MRE corresponding to F1.

Fat quantification using UGAP was found to be 240.7 db/m, corresponding to S1.

Case 2 [Figure 7]

A 80-year-old female presented with a known case of type 2 diabetes for over 20 years.

Liver stiffness was 4.8 Kpa on US elastography, corresponding to F0, and 2.4 Kpa on MRE, corresponding to F0.

Fat quantification using UGAP was 280.5 db/m, corresponding to S3.

Case 3 [Figure 8]

A 74-year-old male, increased BMI, known case of type 2 diabetes and hypertension, increased LFTs

Liver stiffness was 9.5 Kpa on US elastography corresponding to F3 and 3.2 Kpa on MRE corresponding to F3.

Fat quantification using UGAP was 293.5 db/m, corresponding to S3.

RESULTS AND OBSERVATIONS

This study aimed to correlate US elastography and MRE in assessing liver stiffness and quantifying fat in patients with alcoholic non-alcoholic fatty liver disease (NAFLD).

Statistical Analysis

The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe the data, descriptive statistics, frequency analysis, and percentage analysis were used for categorical variables, and the mean and SD were used for continuous variables. The unpaired sample t-test was used to find a significant difference between the bivariate samples in independent groups. The Chi-square test was used to find significance in categorical data. Pearson's correlation was used to assess the relationship between the variables. The probability value of < 0.05 ($P < 0.05$) was considered significant in all the above statistical tools.

Results

Nearly, 38 (65.5%) were between 45 and 65 years old, 14 (24.1%) were between 25 and 45, and 6 (10.3%) were older than 65.

Out of 58 participants, 42 (72.4%) were male and 16 (27.6%) were female.

Among the study participants, 27 (46.6%) were identified as Grade I, 21 (36.2%) as Grade II, and 10 (17.2%) as Grade III in USG.

Of 58 study participants, 23 (39.7%) were graded F1 (mild fibrosis), 16 (27.6%) were graded F2 (significant fibrosis), and 6 (10.3%) were graded F3 (severe fibrosis) on USG.

Among the study participants, 30 (51.7%) were graded S1, 19 (32.8%) were graded S2, and 9 (15.5%) were graded S3 on USG fat grading.

Of 58 study participants, 22 (37.9%) were graded F1 (mild fibrosis), 25 (43.1%) were graded F2 (significant fibrosis), and 8 (13.8%) were graded F3 (severe fibrosis) on MRI.

According to the FIB-4 fibrosis score, 31 (53.5%) individuals in the study population belonged to the low-risk category, 12 (20.7%) were categorized as indeterminate, and 15 (25.9%) were categorized as high-risk.

The average USG and MRI stiffness was found to be significantly higher among the high-risk category. The results were found to be statistically significant ($P < 0.001$).

USG fat measurements show a positive correlation with USG and MR LSMs (LSM) ($r = 0.625$, $P < 0.001$) and MRI stiffness ($r = 0.593$, $P < 0.001$).

Of 22 patients graded as F1 in MRI, nine were graded as F1 in USG. Out of 25 patients graded as F2 in MRI, 12 were graded as F2 in USG. Six of eight patients graded as F3 in MRI were correctly graded as F3 in USG.

Table 1: Fibrosis grading for ultrasonography and magnetic resonance elastography

STAGING OF FIBROSIS	USG(kPa)	MRI(kPa)
NORMAL	6.6(F0-F1)	<2.5
STAGE -1	6.9 (F1-F2)	2.5-2.9
STAGE -2	7.5(F2-F3)	2.9-3.5
STAGE -3	8.2(F3)	3.5-4
STAGE -4	10(F4)	>5

USG stiffness measurements correlate positively with MRI stiffness measurements ($r = 0.814$, $P < 0.001$) as shown in Figure 9 and Table 3. Figures 10 and 11 summarize the area under curve.

Tables 2 and 3 summarize the area under the curve, sensitivity, and specificity of MRI and USG stiffness in diagnosing the stages of FIB-4 staging. There were no differences in the diagnostic ability between MRI and USG stiffness in detecting liver fibrosis Stages 2 to 3. However, the diagnostic accuracy for liver fibrosis Stages 1 to 2 was significantly greater with USG stiffness than MRI.

DISCUSSION

The main aim of our study was to assess and compare the use and accuracy of USG 2D-SWE and MRE in detecting liver fibrosis and quantifying fat in patients with alcoholic and NAFLD. Both the USG and MR machines are from GE.

We also sought to assess whether the degree of steatosis correlates with the degree of liver fibrosis using 2D-SWE and MRE.

We also tried to assess whether any patient parameters, like LFTs calculated by the FIB-4 scoring, affected the severity of liver fibrosis.

Our study included 28 subjects between the ages of 21 and 82, with the majority being male (72.4%). Most of the patients were in the age group with a mean age of 50. All of the cases were either previously diagnosed or newly diagnosed cases of hypertension or type 2 diabetes.

Of the 58 study participants, 23 (39.7%) were graded F1 (mild fibrosis), 16 (27.6%) were graded as F2 (significant fibrosis), and 6 (10.3%) were graded as F3 (severe fibrosis) on USG.

Of the 58 study participants, 22 (37.9%) were graded F1 (mild fibrosis), 25 (43.1%) were graded F2 (significant fibrosis), and 8 (13.8%) were graded F3 (severe fibrosis) on MRI.

Of 22 patients graded as F1 in MRI, nine were graded as F1 in USG. Out of 25 patients graded as F2 in MRI, 12 were graded as F2 in USG. Six of eight patients graded as F3 in MRI were correctly graded as F3 in USG.

Among the study participants, 30 (51.7%) were graded S1, 19 (32.8%) were graded S2, and 9 (15.5%) were graded S3 on USG.

Table 2: AUROCs, 95% confidence interval, and cutoff values of ultrasound-guided attenuation parameter for the prediction of ≥ S1, ≥ S2, and S3 steatosis

	UGAP Steatosis Staging		
	≥ S1	≥ S2	S3
AUROC (95% CI)	0.900 (0.834-0.967)	0.912 (0.894-0.929)	0.894 (0.873 -0.916)
Attenuation Coefficient cut off value (dB/cm/MHz)	0.53	0.60	0.65
Attenuation Rate cut off value (dB/m)	186	210	228

S1: Mild, S2: Moderate, S3: Severe

Table 3: Comparison of USG and MRI stiffness among FIB-4 staging

FIB-4	*n*	Mean	Standard deviation	*P*-value
USG stiffness				
0–1	31	5.77	1.07	<0.001*
1–2	12	7.70	1.19	
2–3	15	8.09	0.97	
Total	58	6.77	1.51	
MRI stiffness				
0–1	31	2.69	0.29	<0.001*
1–2	12	3.63	0.58	
2–3	15	3.51	0.47	
Total	58	3.09	0.60	

USG: Ultrasound, MRI: Magnetic resonance imaging, FIB-4: Fibrosis index based on four factors

The patient's LFT parameters were taken, and FIB-4 scores were calculated. The average USG and MRI stiffness were significantly higher among the high-risk category.

Using Pearson's Chi-squared test, we correlated liver stiffness calculated using USG and MRE. It showed a strong positive correlation, and $P < 0.01$, which was significant. Imajo *et al*.[6] also demonstrated a positive correlation between 2D SWE and MRE in detecting fibrosis in NAFLD. There were no significant differences in diagnosing Stages 1, 2, and 3 fibrosis patients. However, MRE was found to be more accurate in Stage 4 fibrosis patients. According to the study, 2D-SWE is similar to MRE in terms of diagnostic accuracy when it comes to identifying Stage 2 and 3 fibrosis in NAFLD. Vibration-controlled transient elastography (VCTE) and 2D-SWE had poorer intraobserver and interobserver repeatability than MRE, indicating that the MRE results were consistent. It was determined that US elastography experience is required for accurate NAFLD results. Compared to VCTE and 2D-SWE, MRE seems to have advantages. It offers a more precise diagnosis of Stage 4 fibrosis, to start. It also makes it possible for LSM and histologic staging to differ from one another less. Third, in patients with little intercostal space, it might be simpler to execute. Fourth, it eliminates sampling variability brought on by the heterogeneity of liver tissue by enabling the assessment of larger hepatic area. Nevertheless, no method is obviously better than another due to variations in these modalities' pricing, availability, and level of skill.

Furlan *et al*.[12] also demonstrated similar diagnostic accuracy for liver fibrosis in MRE and 2D-SWE in NAFLD patients. For the diagnosis of severe fibrosis (F2 or greater), the AUROC values (95% CIs) of 2D SWE, TE, and MRE were 0.80 and 0.85, respectively, whereas, in our study, they were 0.69 and 0.82, respectively. In our investigation, the corresponding AUROC values (95% CIs) for 2D SWE and MRE were 0.87 and 0.80, respectively, but they were 0.89 and 0.95 for the diagnosis of advanced fibrosis (F3 or higher). In comparison to liver biopsy, LSM obtained with 2D SWE, TE, and MRE performed well for the identification of advanced fibrosis.

While there was a tendency to use MRE rather than TE to discriminate between significant and mild fibrosis, pairwise examinations of the three modalities did not reveal any differences in their effectiveness in identifying either advanced or significant fibrosis.

Song *et al*.[13] also demonstrated a similar correlation between 2D-SWE and MRE when USE values are taken at seventh and eight intercostal spaces.

For the seventh and eighth intercostal spaces, liver Segment 7 or 8, linear regression between MRE and 2D SWE revealed strong correlation and slopes approaching one, indicating good agreement between the two methods in the same patient cohort. The 7 and 8 intercostal areas showed the strongest associations between 2D SWE and MRE. A plausible explanation could be that the majority of the 2D SWE data in this investigation originated from the liver's right lobe, which is also the usual location for MRE measurements. Similar to this, in our investigation, the liver's right lobe was used for MRE, and the seventh and eighth intercostal gaps were used for 2D-SWE to obtain the LSMs.

Using Pearson's Chi-squared test, we correlated USG fat (Calculated by UGAP) with US and MR stiffness. *P*-value was found to be statistically significant with a positive correlation. According to Kumada *et al*.,[14] among patients with F1 fibrosis, LSMs were substantially higher in patients with severe steatosis compared to those without steatosis by UGAP. Other than that, liver stiffness assessments at a particular fibrosis stage did not differ substantially between steatosis grades (all $P > 0.05$).

Tahmasebi *et al*.[15] have able to demonstrate a positive correlation in 140 subjects who are clinically diagnosed or suspected NAFLD. It concluded that severe steatosis may also cause overestimation in 2D SWE whereas it did not affect LSM by MRE.

It is important to recognize some of the study's shortcomings. Due to the small sample size, it is possible that the high percentage of the Indian subpopulation with fatty liver disease is not accurately represented. The study may not be representative of the population seen in other clinical settings because it was conducted at a single institution.

Furthermore, a liver biopsy was not carried out to validate the stages of fibrosis.

CONCLUSION

- LSM taken with USE could replace MRE for non-invasive assessment of liver fibrosis in patients with alcoholic and NAFLD
- It is cheaper, easier to do, and more comfortable for patients overall
- Moreover, fat quantification using UGAP can also be used to predict LSMs.

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Author Queries???

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