Role of ultrasound shear wave Elastography in diagnosis of liver fibrosis and its correlation with histopathology results

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Abstract
Introduction: Elastography of liver is a technique to measure tissue elasticity or stiffness using ultrasound in the staging of liver fibrosis. In Ultrasound SWE we choose a liver parenchyma preferring from the right lobe within the depth range of 2 to 8 cm from liver capsule. Present study aimed to evaluate the correlation of the SWE findings for liver fibrosis with their corresponding findings on histopathology.
Materials and methods: This was a hospital based prospective study conducted in the department of the Radio diagnosis, Saraswathi institute of medical sciences, Hapur, UP during the period of Jan 2021 to dec 2021. A sample size of 35 patients with clinical suspicion of chronic liver disease on the basis of clinical, laboratory and radiological studies were used for analysis.
Results: The overall positive predictive value for patients with non-significant fibrosis was 84.61 %, 77.8 % for patients with significant fibrosis and 75 % in patients with extensive fibrosis. There was a gradual increase of the mean values of SWE with increasing fibrosis and the difference in measurements obtained from consecutive groups of liver fibrosis (i.e. F0 to F4) were statistically significant.
Conclusion: In present study there was high positive correlation between Ultrasound SWE and METAVIR fibrosis score on liver biopsy.

Keywords: Ultrasonography (USG), shear wave elastography (SWE), kPa- kilopascals, NAFLD-, Non-alcoholic fatty liver disease

Introduction

Liver fibrosis is a progressive condition that is commonly caused by alcoholic hepatitis, NAFLD and chronic viral hepatitis. Fibrosis is defined as an abnormal increase in collagen deposition and other components of extracellular matrix in response to chronic injury.

NAFLD in India is emerging as an important cause of liver disease. Epidemiological studies suggest the prevalence of NAFLD is 9% to 32% of general population in India with higher prevalence in those with obesity and diabetes or prediabetes [1].

There are multiple causes of chronic liver disease that share a common pathway of progressive liver fibrosis ultimately culminating in liver cirrhosis [2].Early and accurate diagnosis prompts early clinical intervention that may arrest or diminish progression to end stage decompensated cirrhosis [3, 4].

Liver biopsy is the gold standard in the diagnosis and staging of liver fibrosis. It is invasive and is subject to intra and inter-observer variability. However, this procedure is painful and has many complications as hemorrhage (0.3%) or death (0.01%). Also, biopsy analysis depends on the size of the biopsy sample, the site of sampling, and the experience of the pathologist [5, 6]. Because of the imperfect nature of liver biopsies, there has been a growing trend to validate non-invasive tools to diagnose staging of liver fibrosis [7].

Elastography of liver is a technique to measure tissue elasticity or stiffness and can be done using ultrasound as well as MRI in the staging of liver fibrosis or detection of cirrhosis [8]. Ultrasound SWE has been validated in many studies to have close sensitivity and specificity to liver biopsies.

SWE and ARFI are newer techniques which measure the liver stiffness/elasticity with use of ultrasonography and assessing at least 100 times the sample volume of the liver parenchyma compared to biopsy [9]. With Ultrasound SWE it is possible to evaluate other variables like echotexture, surface, status of spleno-portal axis, assessment of spleen and ascites.
SWE imaging is guided using B-mode images with a higher frame rate. This method can provide more accurate assessment of liver tissue stiffness due to the advantages of SWE and B-mode image guidance [10]. SWE can also be done in patient with ascites unlike fibroscan [11]. The principle behind the interpretation of SWE is that shear waves produced by a focused ultrasound beam are directly related to the stiffness of the liver from where they are generated.

Materials and Methods

This was a hospital based prospective study conducted in the department of the Radio diagnosis, SIMS, Hapur, UP during the duration of Jan 2021 to dec 2021. A sample size of 35 patients with clinical suspicion of chronic liver disease on the basis of clinical, laboratory and imaging studies was used for analysis and the protocol was approved by ethical committee.

Inclusion criteria

1. All the patients referred for an Ultrasound Elastography with a clinical diagnosis of suspected liver fibrosis.
2. Patients with clinical diagnosis of chronic Hepatitis B or C (Based on HBsAG or Anti HCV positivity)and Fatty liver disease attending medicine OPD.
3. Patients from age group of 25 to 65 were included in study.

Exclusion criteria

1. Patients previously diagnosed with hepatocellular carcinoma on imaging or pathological basis.
2. Presence of hepatic encephalopathy grade 3 or grade 4.
3. Critically ill patient unable to hold breath.

Ultrasound and histopathological analyses

Logiq GE- E 10 with curvilinear transducer.
Ultrasound Shear Wave Elastography findings has been correlated with clinical, biochemical and histopathology findings. Relevant clinical details and biochemical investigation were recorded. Patient underwent an USG examination for findings like liver and spleen size, liver surface and echotexture, status of portal vein and splenic vein. In each patient 8 to 10 valid SWE measurements were obtained from the right lobe of liver. Liver biopsy were obtained in all the patients.

Statistical analysis

Collected data were compiled, managed, analysed and presented using SPSS software and MS Excel. Sensitivity, Specificity, PPV, NPV and accuracy were computed. A p-value < 0.05 is considered statistically significant.

Protocol followed for ultrasound elastography

1. Patient preparation: Patient is made to fast overnight.
2. Patient position: Supine and left lateral position.
3. Scan protocol: Patient lies in the supine position, with the right arm in maximum abduction. This makes the right hypochondrium accessible. Normal breathing is recommended unless patient is instructed to hold breath during measurement for few seconds. Choose the curved probe "Liver elasto" preset in the "Abdominal" application. Scan in the intercostal space with little pressure on probe to avoid shadowing by the ribs. Slow or even no movement of the probe is recommended to avoid motion artifact and to allow the stabilization of the map. After a perfect B-Mode image SWE Mode is acquired by placing the SWE box in right lobe region. Ensure the best possible contact between the probe and the skin. The SWE default settings have been optimized to image a wide range of fibrosis levels. Run the first exam with the default settings. Adjust them only if it is necessary. Place it within a zone of uniform vessel-free parenchyma as defined by B-Mode image. The most robust acquisition is performed from 2 to 7 cm in depth. Avoid placing the SWE Box close to the liver capsule. The patient is asked to hold breath for at least 4 seconds during expiration. This delay allows sufficient filling of the SWE box and stabilization of the image in a no-movement context. Reliability measurement index (RMI) is shown for each value of elastography on the machine and varies from 0 to 1 (Preferably in the range of 0.5 – 1.0.) Interquartile range (IQR) is preferably to be kept below 30 % for reliable measurements. This indicates variation among the various elastography measurements in a given patient.

Protocol followed for liver biopsy

Informed consent for the liver biopsy was taken and patient explained about the procedure details. Patient was required to have overnight fasting. Patient was made to lie in Supine and left lateral decubitus. Biopsy was done under the guidance of ultrasonography. After local anesthesia a needle (18 G) was passed through the skin into the liver, where a specimen was obtained and transported to the pathology lab. Slides were prepared using mainly by H & E stain and Reticulin, Masson's trichrome stain, Orcein, PAS and IHC - CK7 were used.

Results

Based on **SWE** findings, grading of patients were done in grade 0,1,2,3,4. Patients in grade 0, 1 (14 patients) were found to have non-significant fibrosis and in grade 2,3 (18 patients) were found to have significant fibrosis and grade 4 (3 patients) were included in extensive fibrosis.
Positive predictive value of elastography for detection of fibrosis was 84.61% in non-significant fibrosis, 77.8% in significant fibrosis and 75% in extensive fibrosis cases.

Table 1: Grading of patients based on ultrasound elastography

Stage by elastography	Number of patients	Percentage of patients
Grade 0	7	20%
Grade 1	7	20%
Grade 2	8	22.8%
Grade 3	10	28.5 %
Grade 4	3	8.5%

Table 2: Shows distribution of number of patients with various stages of fibrosis by elastography

Staging	Number of patients	Percentage of patients
Non-significant fibrosis F0-F1	14	40 %
Early and late significant fibrosis F2-F3	18	51.4%
Extensive fibrosis F4	3	8.5%

The MetavirScore was calculated to assess the extent of inflammation and fibrosis by histopathological evaluation of liver biopsy of patients.

Table 3: Shows distribution of patients as per scoring on Metavir Score on histopathology

Metavir score	Number of patients	Percentage of patients
F0	6	17.14 %
F1	7	20 %
F2	9	25.7 %
F3	9	25.7%
F4	4	11.42 %

Table 4: Staging of patients as per severity of fibrosis on METAVIR scoring system

Fibrosis staging	Number of patients	Percentage of patients
Non-significant fibrosis F0-F1	13	37.14 %
Early and late significant fibrosis F2-F3	18	51.4 %
Extensive fibrosis F4	4	11.4 %

Table 5: Correlation of non-significant (F0-F1) Significant (F2-F3) and extensive fibrosis (F4) on ultrasound shearwave elastography with liver biopsy

Metavir score → Elastography stage ↓	Non-significant F0-F1	Significant F2-F3	Extensive F4	Total
Non-significant	11	2	0	13
Significant	3	14	1	18
Extensive	0	1	3	4
Total	14	18	3	35

Table 5: Positive predictive value of SWE calculated after histopathological results

Elastography stage → Metavir score ↓	Positive predictive value
Non-significant Fibrosis	84. 61 %
Significant Fibrosis	77.8 %
Extensive Fibrosis	75 %

Discussion

Ultrasound SWE can map the elastic property of liver and along with grayscale ultrasonography is one of the most advanced imaging technique to assess the status of liver fibrosis in the patient with chronic liver disease noninvasively.

Present study consisted of 12 females and 23 males in ratio of approximately 1:2. All the patients were between 25 to 65 years of age with mean age of 45 years. Majority of patients (31.4 %) are from the age group 45-55 years followed by 28.5 % of patients in the age group of 35 to 45 years and 20% of patients in the age group 55-65 years. Approximately 31.5 % of cases were hepatitis C positive and 8.6 % of cases were hepatitis B positive.

Liver elastography measurements were taken from the right lobe as previous studies shows that the values from right lobe shows highest correlation with the biopsy [12].

In present study the SWE values for liver stiffness measurement were found in the range between 4.8 to 28.3 kPa. The values were analyzed with grades of fibrosis based on **Metavir** fibrosis score; patients with F0 fibrosis had SWE ranging from 4.3 to 8.8 kPa with mean value of 6.15 kPa (n = 7, 20 %). Similarly patients with F1 fibrosis had a range between 5.1 to 9.9 kPa with mean value of 7.5 kPa (n = 7, 20 %). F2 fibrosis patients had a range between 6.7 to 14.5 kPa with mean value of 10.5 kPa (n = 8, 22.8 %). F3 fibrosis patients had a range between 11 to 24 kPa with mean value of 17.5 kPa (n = 10, 28.5 %) whereas F4 fibrosis patients had a range between 19 to 27 kPa with mean value of 23 kPa (n = 3, 8.5 %). Thus there was an overlap in the ranges of SWE but a gradual increase in mean SW values was noted from F0 to F4. The SWE and fibrosis scores show good positive correlation (p-value < 0.001).

In a large multicenter study by Joyce Anyona Sande et al., using Ultrasound Shear Wave Elastography on 128 patients, good correlation was observed between elastography median score and histology fibrosis score [13]. In a meta-analysis of 40 studies Lin ZH et al. concluded that the APRI score greater than 0.7 had sensitivity of 77 % and specificity of 72% for predicting significant hepatic fibrosis [14].

Conclusion

In present study there was high positive correlation between Ultrasound Shear Wave Elastography and METAVIR fibrosis score on liver biopsy. There was a gradual increase of the mean values of SWE with increasing fibrosis and the difference in measurements obtained from consecutive groups of liver fibrosis (i.e. F0 to F4) were statistically significant. For detection of significant (77.8%) and non-significant fibrosis (84.61%) SWE shows high positive predictive value with (p value =< 0.001).

References

1. Ajay Duseja, Nonalcoholic fatty liver disease in India- a lot done, yet more required, Indian J Gastroenterol. 2010; 29:217-225.
2. Anthony E, Samir MD, MPH Manish Dhyani. Shear-Wave Elastography for the Estimation of Liver Fibrosis in Chronic Liver Disease: Determining Accuracy and Ideal Site for Measurement, radiology.rsna.org n Radiology. 2015; 274(3); 888-896.
3. Saim Dayan, Tuba Dal, Recep Tekin, Ozcan Deveci, *et al*. Non-invasive parameters in the assessment of liver fibrosis; Biomedical Research. 2017, 28(5).
4. Snyder N, Gajula L, Xiao SY, Grady J, *et al*. APRI: an easy and validated predictor of hepatic fibrosis in chronic hepatitis C; J Clin Gastroenterol. 2006; 40(6):535-42.
5. Dohan A, Guerrache Y, Boudiaf M, Gavini JP, Kaci R, Soyer P, *et al*. Transjugular liver biopsy: indications, technique and results. DiagnInterv Imaging. 2014; 95:11-15.
6. Guibal A, Renosia G, Rodec A, *et al*. Shear wave elastography: an accurate technique to stage liver fibrosis in chronic liver diseases. Diagnostic and Interventional Imaging. 2016; 97:91-99.
7. Ferraioli G, Tinelli C, Dal Bello B Brunetti E, *et al*. Performance of liver stiffness measurements by transient elastography in chronic hepatitis. World J Gastroenterol. 2013; 19:49-56.
8. Mona H. Ismail and Massimo Pinzani, Reversal of Liver Fibrosis, Saudi J Gastroenterol. 2009; 15(1):72-79.
9. Frulio N, Trillaud H. Ultrasound elastography in liver. Diagn Interv Imaging. 2013; 94:515-534.
10. Eva herrnamm, de Ledinghen V, Chu WC, *et al*. Assessment of biopsy-proven liver fibrosis by two-dimensional Shear Wave Elastography: An individual patient data-based meta-analysis: doi: 10.1002/ hep.29179. Epub 2017 Nov 15; 2018 Jan; 67(1):260-272.

11. Ferraioli G, Tinelli C, Dal Bello B, Filice C. Accuracy of real-time Shear Wave Elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study. Hepatology. 2012; 56:2125-2133.
12. Ferraioli G, Tinelli C, Lissandrin R, Zicchetti M, Dal Bello B, Filice G, *et al*. Point Shear Wave Elastography method for assessing liver stiffness. World J Gastroenterol. 2014; 20:4787-4796.
13. Joyce Anyona Sande, Suleman Verjee, Sudhir Vinayak, *et al*. Ultrasound Shear Wave Elastography and liver fibrosis: A prospective Multicenter study. World J Hepatol. 2017; 9(1):38-47.
14. Giannini E, Botta F, Fasoli A, Ceppa P, Risso D, Testa R. Progressive liver functional impairment is associated with an increase in AST/ALT ratio. Dig Dis Sci. 1999; 44:1249-1253.