

A Hospital-Based Assessment of the Role of Ultrasound Elastography and MR Elastography for Assessing Liver Fibrosis

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Abstract

Aim: The aim of the present study was to evaluate the role of Ultrasound elastography and MR elastography for assessing liver fibrosis.

Methods: The present study was conducted at Department of Radio Diagnosis, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India for 12 months and 200 patients who underwent liver biopsy were enrolled.

Results: There were 120 males and 80 females in the study. 60% patients were in <2 foci per x 200 field and according to fibrosis stage, 69 were Bridging fibrosis followed by 50 Perisinusoidal or periportal. 100 patients were Steatosis grade 5%–33%. No significant differences were found in demographic or serologic profiles between patients with and without discordance.

Conclusion: Several MRI-based techniques have been developed for quantitative assessment of liver fibrosis. These techniques include MRE, DWI, texture analysis, perfusion imaging, hepatocellular function imaging, strain imaging, and T1ρ quantification. Of the many suggested techniques, MRE stands out as the most standardized and the one that has been most widely adopted in clinical practice.

Keywords: Elastography, Liver Fibrosis, Magnetic Resonance, Ultrasound.

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Introduction

Liver fibrosis is a hallmark of chronic liver disease, characterized by the excessive accumulation of extracellular matrix proteins. If the underlying cause of chronic liver disease is untreated, liver fibrosis may progress to cirrhosis which constitutes the most important risk factor for hepatocellular carcinoma (HCC). [1] Liver fibrosis must be diagnosed and staged

accurately as it informs treatment decision and prioritization of intervention by clinicians. Some treatments have shown to slow down or reverse the progression of fibrosis in its early stages. [2] Although liver biopsy is the reference standard for the diagnosis and staging of liver fibrosis, it is associated with pitfalls such as its

invasiveness, high sampling variability, and low patient acceptance. [3,4]

Liver fibrosis is a wound healing response to acute or chronic liver diseases. [5] Liver injury induces inflammation, which transforms hepatic stellate cells from their quiescent state to proliferative, fibrogenic, and contractile myofibroblasts. [6] These activated hepatic stellate cells produce extracellular matrix proteins (such as collagen, laminin, elastin, and fibronectin) which lead to fibrosis deposition. [7] Liver fibrosis is characterized by an excessive accumulation of these proteins (fibrogenesis) not balanced by matrix degradation by enzymes over time. Liver fibrosis may progress to cirrhosis, the end stage, which constitutes the most important risk factor for developing HCC. [8]

Imaging-based elastography is an emerging technology that uses imaging to noninvasively assess mechanical tissue properties. Elastography techniques have evolved significantly over the last 2 decades and have now been implemented on clinical ultrasound and MR systems. [9,10] Conventional ultrasonography (US), computed tomography, and magnetic resonance imaging (MRI) are useful for the diagnosis of chronic liver disease and cirrhosis and the detection of hepatocellular carcinoma. However, these imaging methods cannot accurately differentiate the various stages of liver fibrosis. Conversely, elastography techniques using US or MRI are performed to measure liver stiffness, which increases in the presence of fibrosis. Therefore, during the last two decades, elastography techniques have been developed as quantitative noninvasive methods for the assessment of liver fibrosis that can be used in place of liver biopsy. Several US-based elastography techniques have been developed, the most important of which is shear wave elastography, which can be divided into vibration-controlled transient elastography

(VCTE), point shear wave elastography (pSWE), and two (pSWE), and two-dimensional shear wave elastography (2D-SWE).

The aim of the present study was to evaluate the role of Ultrasound elastography and MR elastography for assessing liver fibrosis.

Materials and Methods

The present study was conducted at Department of Radio Diagnosis, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India for 12 months and 200 patients who underwent liver biopsy were enrolled.

Histopathologic and Immunohistochemical Evaluations

Biopsy samples were assessed by an experienced pathologist who specialized in liver pathology. Steatosis, lobular inflammation, ballooning, and fibrosis were histologically scored. Patients with steatosis, lobular inflammation, ballooned hepatocytes, and perisinusoidal/pericellular fibrosis were diagnosed with NASH.¹¹ Liver fibrosis stage was classified according to the report by Brunt.¹²

Magnetic Resonance Elastography

All measurements were performed by a hepatologist with 6 years of experience in interpreting MRE (K.I.).

Two-Dimensional Shear Wave Elastography

2D-SWE was performed by using Logic S8 system (GE Healthcare). This new technique uses comb-push and time-aligned sequential tracking for the generation of large elasticity maps superimposed on the grayscale image obtained by using conventional ultrasound (US).

Statistical Analysis

Continuous and categorical variables are summarized as median and interquartile

ranges and frequencies and percentages, respectively. Analysis of variance with Scheffe multiple testing correction was used for univariate comparisons between groups. Kruskal–Wallis test was used for

comparisons of nonparametric data of more than 2 independent groups.

Results

Table 1: Patient details

Variables	N
Age (y)	61.0 (51.0–71.0)
M/F	120/80
Body mass index (kg/m ²)	27.1 (25.2–30.8)
Platelets (/104 mL)	19.4 (15.2–23.6)
AST (IU/L)	42.0 (32.0–60.0)
ALT (IU/L)	48.0 (33.0–75.5)
GGT (IU/L)	55.0 (37.0–96.0)
CRP (mg/L)	0.12 (0.07–0.3)
Cr (mg/dL)	0.79 (0.56–1.15)
FBS (mg/dL)	115 (102–133.3)
Fasting insulin (mU/mL)	16.0 (11.3–24.4)
HbA1c (%)	6.2 (5.7–7.0)
DM (%)	120 (60)
HT (%)	96 (48)
DLP (%)	150 (75)
Steatosis grade (n)	
5%–33%	100
33%–66%	65
>66%	35
Lobular inflammation (n)	
None	2
<2 foci per x 200 field	120
2–4 foci per x 200 field	70
>4 foci per x 200 field	8
Fibrosis stage (n)	
None	9
Perisinusoidal or periportal	50
Perisinusoidal and portal/periportal	36
Bridging fibrosis	69
Cirrhosis	36

There were 120 males and 80 females in the study. 60% patients were in <2 foci per x 200 field and according to fibrosis stage, 69 were Bridging fibrosis followed by 50 Perisinusoidal or periportal. 100 patients were Steatosis grade 5%–33%.

Table 2: Factors Associated With Discordance Between LSM and Fibrosis Staging

	US (fibrosis stage < stiffness; upstaged group)			MRE (fibrosis stage < stiffness; upstaged group)		
	Concordance (n = 190)	Discordance (n = 10)	P Value	Concordance (n = 190)	Discordance (n = 10)	P Value
Age, y	60.7 ± 12.6	64.8 ± 9.53	0.426	61.0 ± 12.3	56.0 ± 16.0	0.238
Sex	100/90	7/3	0.426	110/80	6/4	0.230

BMI (kg/m ²)	27.9 ±4.16	26.6 ±1.99	0.436	30.2 ±3.87	27.8 ±4.09	0.049
SCD	22.0 ±4.34	20.8± 3.28	0.503	21.9±4.20	24.1± 4.85	0.099
AST (IU/L)	49.9 ±28.2	50.2 ±24.6	0.978	49.0 ±26.1	47.6 ±19.2	0.866
ALT (IU/L)	58.9 ±40.8	55.8±24.1	0.854	57.7 ±39.1	66.7 ±36.3	0.501

No significant differences were found in demographic or serologic profiles between patients with and without discordance.

Discussion

Liver cirrhosis is associated with additional complications such as portal hypertension, bleeding of esophageal varices, ascites, hepatic encephalopathy, and thrombosis in the portal venous system. Early detection and treatment of the underlying cause of liver disease is critical because liver transplantation constitutes the only curative therapy for decompensated liver cirrhosis.

The study comparing MRE and VCTE (only M probe) indicated no significant difference in AUROC of the 2 modalities in distinguishing between stages 0 and 1–4 fibrosis and stages 0–2 and 3–4 fibrosis. However, the diagnostic accuracy was better with MRE than with VCTE for stage >2 (AUROC, 0.91 vs 0.82; P =.001) and stage 4 fibrosis (AUROC, 0.97 vs 0.92; P =.049). [13] In another study, MRE was more accurate than VCTE (M and XL probe) for the diagnosis of stage 2 (AUROC, 0.82 vs 0.67; P = .01) and stage 4 fibrosis (AUROC value, 0.87 vs 0.69; P =.05). [14]

However, there was no significant difference between the 2 elastography methods in diagnosing any other dichotomized stage of fibrosis. Consistent with the results of these studies, we found that MRE was more accurate than VCTE (M and XL probe) in diagnosing stage 4 fibrosis. However, in contrast to these studies, the present study demonstrated no difference in the diagnostic ability between MRE and VCTE in distinguishing stages 0–1 from stages 2–4 fibrosis. It is possible that our findings may have been affected by the ordinary use of XL probe and the

larger sample size and smaller number of patients with fibrosis stages 0–1 than the respective numbers in previous reports. Although prior studies have compared the diagnostic ability of MRE and VCTE, there are limited studies on the diagnostic ability of 2D-SWE in NAFLD. A previous study reported that 2D-SWE demonstrates good diagnostic accuracy in the detection of stage 2 and 3 fibrosis in NAFLD, but it was not different from MRE or VCTE. [15] In contrast, our findings indicated that MRE is more accurate than 2D-SWE in diagnosing stage 4 despite no differences for stages 1, 2, and 3. It is possible that our findings may have been affected by the larger sample size than that in previous reports.

A previous report using pairwise comparisons also revealed similar diagnostic accuracy between VCTE and 2D-SWE in liver fibrosis staging in patients with NAFLD. [15] Although VCTE and 2D-SWE are very useful in diagnosing the severity of liver fibrosis in NAFLD, their success rate depends on the operator's experience and other factors such as age, ascites, width of the intercostal space, BMI, and visceral fat. Sporea et al [16] reported a rate of reliable measurements of 81.6% in VCTE, which is similar to that reported by Castéra et al. [17]

Sex was a significant predictor of discordance between histology and VCTE for at least 2 fibrosis stages, whereas SCD was a significant predictor of discordance between histology and 2D-SWE. Because intercostal space tends to be narrower in women than men with NAFLD, the discordance between VCTE and histologic staging may be higher in women. Severe obesity is associated with higher SCD, which is the main reason for unreliable

LSM using standard VCTE M probes. However, XL probe reduces the failure rate of LSM in obese patients.^{26,27} No discordance associated with BMI and SCD between VCTE and liver biopsy-proven fibrosis stage may be due to the use of XL probe. [18-20]

Conclusion

Several MRI-based techniques have been developed for quantitative assessment of liver fibrosis. These techniques include MRE, DWI, texture analysis, perfusion imaging, hepatocellular function imaging, strain imaging, and T1ρ quantification. Of the many suggested techniques, MRE stands out as the most standardized and the one that has been most widely adopted in clinical practice. It also has the highest diagnostic performance compared to other MRI based techniques and other popular methods such as ultrasound elastography. By combining quantitative techniques into multiparametric examinations, MRI offers the unique opportunity to assess the concomitant pathological changes that occur in chronic liver disease, such as fat, iron, biliary disease, and inflammation. Once validated and integrated into a comprehensive examination, these quantitative techniques may reduce the need for liver biopsy in clinical practice and in the setting of clinical trials.

References

1. Forner A, Llovet JM, Bruix J. Hepatocellular carcinoma. *Lancet*. 2012; 379:1245–1255.
2. Brancatelli G, Federle MP, Ambrosini R, Lagalla R, Carriero A, Midiri M, Vilgrain V. Cirrhosis: CT and MR imaging evaluation. *European journal of radiology*. 2007 Jan 1;61(1):57-69.
3. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. Liver biopsy. *Hepatology*. 2009 Mar 1;49(3): 1017-44.
4. Bedossa P, Carrat F. Liver biopsy: the best, not the gold standard. *Journal of hepatology*. 2009 Jan 1;50(1):1-3.
5. Sebastiani G, Gkouvatsos K, Pantopoulos K. Chronic hepatitis C and liver fibrosis. *World journal of gastroenterology: WJG*. 2014 Aug 8;20 (32):11033.
6. Friedman SL. Liver fibrosis—from bench to bedside. *Journal of hepatology*. 2003 Jan 1; 38:38-53.
7. Lee UE, Friedman SL. Mechanisms of hepatic fibrogenesis. *Best practice & research Clinical gastroenterology*. 2011 Apr 1;25(2):195-206.
8. El-Serag HB. Current concepts hepatocellular carcinoma. *New England Journal of Medicine*. 2011 Sep 22;365(12):1118-27.
9. Sarvazyan AP, Rudenko OV, Swanson SD, Fowlkes JB, Emelianov SY. Shear wave elasticity imaging: a new ultrasonic technology of medical diagnostics. *Ultrasound in medicine & biology*. 1998 Dec 1;24(9):1419-35.
10. Sarvazyan AP, Rudenko OV, Swanson SD, Fowlkes JB, Emelianov SY. Shear wave elasticity imaging: a new ultrasonic technology of medical diagnostics. *Ultrasound in medicine & biology*. 1998 Dec 1;24(9):1419-35.
11. Younossi ZM, Stepanova M, Rafiq N, Makhlof H, Younoszai Z, Agrawal R, Goodman Z. Pathologic criteria for nonalcoholic steatohepatitis: interprotocol agreement and ability to predict liver-related mortality. *Hepatology*. 2011 Jun;53(6):1874-82.
12. Brunt EM. Nonalcoholic steatohepatitis: definition and pathology. In *Seminars in liver disease*. Copyright© 2001 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel.: 1 (212) 584-4662. 2001; 21(01):003-016.
13. Imajo K, Kessoku T, Honda Y, Tomeno W, Ogawa Y, Mawatari H, Fujita K, Yoneda M, Taguri M, Hyogo H, Sumida Y. Magnetic resonance imaging more accurately classifies steatosis and fibrosis in patients with nonalcoholic fatty liver disease than

- transient elastography. *Gastroenterology*. 2016 Mar 1;150(3): 626-37.
14. Park CC, Nguyen P, Hernandez C, Bettencourt R, Ramirez K, Fortney L, Hooker J, Sy E, Savides MT, Alqiraish MH, Valasek MA. Magnetic resonance elastography vs transient elastography in detection of fibrosis and noninvasive measurement of steatosis in patients with biopsy-proven nonalcoholic fatty liver disease. *Gastroenterology*. 2017 Feb 1;152(3): 598-607.
 15. Furlan A, Tublin ME, Yu L, Chopra KB, Lippello A, Behari J. Comparison of 2D shear wave elastography, transient elastography, and MR elastography for the diagnosis of fibrosis in patients with nonalcoholic fatty liver disease. *American Journal of Roentgenology*. 2020 Jan;214(1): W20-6.
 16. Sporea I, Jurchis A, Sirli R, Bota S, Sendroiu M. Can Transient Elastography be a reliable method for assessing liver fibrosis in Non-Alcoholic Steatohepatitis (NASH)? *Medical Ultrasonography*. 2013 Jun 1; 15(2):106-10.
 17. Castéra L, Foucher J, Bernard PH, Carvalho F, Allaix D, Merrouche W, Couzigou P, de Lédinghen V. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. *Hepatology*. 2010 Mar; 51(3):828-35.
 18. Wong VW, Vergniol J, Wong GL, Foucher J, Chan AW, Chermak F, Choi PC, Merrouche W, Chu SH, Pesque S, Chan HL. Liver stiffness measurement using XL probe in patients with nonalcoholic fatty liver disease. *Official journal of the American College of Gastroenterology|ACG*. 2012 Dec 1;107(12):1862-71.
 19. Myers RP, Pomier-Layrargues G, Kirsch R, et al. Feasibility and diagnostic performance of the FibroScan XL probe for liver stiffness measurement in overweight and obese patients. *Hepatology* 2012; 55:199–208
 20. Suarayasa K., Wandira B. A., & P. Study on the Development Needs of the Tadulako General Hospital as Class B State University Hospital for Education (After the Palu City Earthquake). *Journal of Medical Research and Health Sciences*. 2022; 5(8): 2190–2196.