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A hospital-based assessment of patients diagnosed within liver fibrosis using ultrasound elastography and MR Elastography

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Abstract
Aim: The objective of the present study was to assess ultrasound elastography and MR Elastography in liver fibrosis.
Methods: The present study was conducted and 100 patients who underwent liver biopsy were enrolled. The study protocol was approved by the ethics review committee, and all patients provided written informed consent.
Results: There were 70 males and 30 females in the study. 55% of patients were in < 2 foci per x 200 field and according to fibrosis stage, 25 were Bridging fibrosis followed by 50 Perisinusoidal or periportal. 50 patients were Steatosis grade 5%-33%. No significant differences were found in demographic or serologic profiles between patients with and without discordance.
Conclusion: Ultrasound elastography techniques are relatively inexpensive, portable, and increasingly available while providing good diagnostic accuracy but may be unreliable in obese patients and those with narrow intercostal spaces. MR Elastography offers excellent diagnostic accuracy that probably slightly exceeds that of ultrasound-based techniques, but the quality may be degraded in patients with marked iron deposition, and availability remains comparatively limited.

Keywords: Elastography, liver fibrosis, MR Elastography (MRE), MRI, ultrasound

Introduction
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 [1-4]. 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) [5].
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 [6]. 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 [7, 8]. Hence, there is a need for noninvasive techniques to assess liver fibrosis, especially in its early stages before the advent of complications. Several imaging techniques, implemented on ultrasound, computed tomography, and magnetic resonance imaging (MRI), have been proposed in recent years for quantitative assessment of liver fibrosis. Worldwide, ultrasound-based elastography techniques are arguably the most widely used.
Ultrasound elastography techniques track shear waves by using ultrasound-tracking beams. Some ultrasound-based techniques display parametric maps called “Elastograms” that display the spatial distribution of the stiffness-related parameter of interest; others provide only numeric results. MR Elastography tracks shear waves by acquiring images with wave motion-sensitized phase-contrast sequences. Tissue motion caused by the shear waves during the scan are encoded into the phase of the MR signal. This phase information is further processed to generate wave images depicting shear wave displacements within the liver. Subsequent processing of the wave images produces elastograms.

Dynamic elastography techniques, also known as shear-wave imaging, assess stiffness and stiffness-related parameters by tracking shear waves propagating through media. Shear-wave speed is related to tissue stiffness; for instance, shear waves travel faster in stiff (inflamed, fibrotic, or cirrhotic) liver and slower in soft (normal or fatty) liver [9]. By measuring shear-wave speed, the stiffness may be inferred. For most biologic tissues, the shear-wave speed and, hence, the inferred stiffness are frequency dependent: All other things being equal, shear-wave speed and inferred stiffness are greater if the shear waves are applied at higher frequency. Because the shear-wave frequencies used by different techniques differ, the stiffness-related values obtained with various techniques are not directly comparable.

The objective of the present study was to assess ultrasound elastography and MR Elastography in liver fibrosis.

Materials and Methods

The present study was conducted and 100 patients who underwent liver biopsy were enrolled. The study protocol was approved by the ethics review committee, and all patients provided written informed consent.

Histopathologic and Immuno Histochemical 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 [10]. Liver fibrosis stage was classified according to the report by Brunt [11].

Magnetic Resonance Elastography

All measurements were performed by a hepatologist with 4 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)	58.0 (52.0-72.0)
M/F	70/30
Body mass index (kg/m2)	26.4 (25.5-30.5)
Platelets (/104 mL)	18.2 (15.2-23.6)
AST (IU/L)	40.0 (32.0-60.0)
ALT (IU/L)	46.0 (33.0-75.5)
GGT (IU/L)	54.0 (37.0-96.0)
CRP (mg/L)	0.10 (0.07-0.3)
Cr (mg/dL)	0.66 (0.56-1.15)
FBS (mg/dL)	120 (102-133.3)
Fasting insulin (mU/mL)	15.0 (11.3-24.4)
HbA1c (%)	6.5 (5.7-7.0)
DM (%)	50 (50)
HT (%)	45 (45)
DLP (%)	70 (70)
Steatosis grade (n) 5%-33% 33%-66% > 66%	 50 30 20
Lobular inflammation (n) None < 2 foci per x 200 field 2-4 foci per x 200 field > 4 foci per x 200 field	 3 55 35 7
Fibrosis stage (N) None Perisinusoidal or periportal Perisinusoidal and portal/periportal Bridging fibrosis Cirrhosis	 5 40 15 25 15

There were 70 males and 30 females in the study. 55% patients were in < 2 foci per x 200 field and according to fibrosis stage, 25 were Bridging fibrosis followed by 50 Perisinusoidal or periportal. 50 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 = 80)	Discordance (N = 20)	P Value	Concordance (N = 80)	Discordance (n =20)	P Value
Age, y	63.5±13.7	62.8±8.52	.310	62.0±11.9	58.0±13.0	.390
Sex	70/10	12/8	.20	60/20	6/4	.330
BMI (kg/m2)	26.4 ±4.16	26.6±1.99	.380	28.2±3.77	26.4±4.06	.049
SCD	23.0 ±3.37	20.2±3.28	.480	22.8±4.26	24.2±4.82	.099
AST (IU/L)	47.3 ±26.2	52.4±23.7	.897	48.0±26.2	44.6±19.2	.866
ALT (IU/L)	59.1 ±40.4	54.6±24.6	.789	57.3±39.1	66.4±33.3	.501

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

Table 3: Multiple regression analysis of histologic parameters associated with LSM for US and MRE

Parameters	US Elastography		MRE	
	Coefficients	P Value	Coefficients	P Value
Fibrosis	1.07 0.09	< .001	5.15 0.32	< .001
Steatosis	–0.15 0.05	.045	0.55 0.50	.310
Inflammation	0.06 0.14	0.655	–1.20 0.80	.120
Ballooning	0.05 0.10	0.700	0.00 0.69	0.560

On multivariate regression analysis, the relationship between histologic parameters and LSM values obtained by the 2 elastography modalities was evaluated. We found that only liver fibrosis stage was significantly associated with LSM.

Discussion

Liver biopsy is the gold standard for assessing liver fibrosis stage in patients with NAFLD [12]. However, because of high costs, potential risks, and use of medical resources, it is not a suitable diagnostic modality [13]. Liver stiffness measurement (LSM) is a promising alternative surrogate marker for the severity of liver fibrosis using elastography such as magnetic resonance elastography (MRE), vibration-controlled transient elastography (VCTE), and two-dimensional shear wave elastography (2D-SWE) [14].

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 WE), and two-dimensional shear wave elastography (2D-SWE). Liver biopsy is the reference standard for diagnosis and staging of liver fibrosis [8]. The amount and distribution of fibrous tissue in the hepatic lobule are assessed visually on histopathology slides. Different liver fibrosis staging systems are used depending on the cause of underlying chronic liver disease. Some of the most frequently used staging systems include the METAVIR [15], Ishak [16, 17] and Laennec systems [18] for hepatitis B and C, and Brunt system for NAFLD and nonalcoholic steatohepatitis [19].

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. Liver cirrhosis regardless of the cause of chronic liver disease constitutes the most important risk factor for development of HCC. Patients with chronic viral hepatitis C and liver fibrosis stage 3 are also at increased risk of developing HCC. A study has found that MRE-determined liver stiffness constitutes an independent risk factor for HCC in patients with chronic liver disease [20]. If validated, liver stiffness measured by MRE may be taken into consideration for stratifying the risk of HCC development in chronic liver disease.

Conclusion

Ultrasound elastography techniques are relatively inexpensive, portable, and increasingly available while providing good diagnostic accuracy but may be unreliable in obese patients and those with narrow intercostal spaces. MR Elastography offers excellent diagnostic accuracy that probably slightly exceeds that of ultrasound-based techniques, but quality may be degraded in patients with marked iron deposition, and availability remains comparatively limited. In a research setting, MR elastography may become a surrogate reference standard when liver biopsy is either not feasible or acceptable.

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