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ORIGINAL ARTICLE

Retrospective Study

Magnetic resonance elastography is accurate in detecting advanced fibrosis in autoimmune hepatitis

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Abstract

AIM

To assess the value of magnetic resonance elastography (MRE) in detecting advanced fibrosis/cirrhosis in autoimmune hepatitis (AIH).

METHODS

In this retrospective study, 36 patients (19 treated and 17 untreated) with histologically confirmed AIH and liver biopsy performed within 3 mo of MRE were identified at a tertiary care referral center. Liver stiffness (LS) with MRE was calculated by a radiologist, and inflammation grade and fibrosis stage in liver biopsy was assessed by a pathologist in a blinded fashion. Two radiologists

evaluated morphological features of cirrhosis on conventional magnetic resonance imaging (MRI). Accuracy of MRE was compared to laboratory markers and MRI for detection of advanced fibrosis/cirrhosis.

RESULTS

Liver fibrosis stages of 0, 1, 2, 3 and 4 were present in 4, 6, 7, 6 and 13 patients respectively. There were no significant differences in distribution of fibrosis stage and inflammation grade between treated and untreated patient groups. LS with MRE demonstrated stronger correlation with liver fibrosis stage in comparison to laboratory markers for chronic liver disease (r = 0.88 *vs* -0.48-0.70). A trend of decreased mean LS in treated patients compared to untreated patients was observed (3.7 kPa *vs* 3.84 kPa) but was not statistically significant. MRE had an accuracy/sensitivity/specificity/positive predictive value/negative predictive value of 0.97/90%/100%/100%/90% and 0.98/92.3%/96%/92.3%/96% for detection of advanced fibrosis and cirrhosis, respectively. The performance of MRE was significantly better than laboratory tests for detection of advanced fibrosis (0.97 *vs* 0.53-0.80, P < 0.01), and cirrhosis (0.98 *vs* 0.58-0.80, P < 0.01) and better than conventional MRI for diagnosis of cirrhosis (0.98 *vs* 0.78, P = 0.002).

CONCLUSION

MRE is a promising modality for detection of advanced fibrosis and cirrhosis in patients with AIH with superior diagnostic accuracy compared to laboratory assessment and MRI.

Key words: Autoimmune hepatitis; Advanced fibrosis; Magnetic resonance elastography; Liver stiffness; Cirrhosis

Core tip: Magnetic resonance elastography (MRE) provides a non-invasive imaging-based biomarker with excellent diagnostic accuracy for detecting advanced fibrosis and cirrhosis in patients with autoimmune hepatitis (AIH). The diagnostic performance of MRE is superior compared to conventional laboratory tests and morphology assessment with conventional magnetic resonance imaging. MRE may have utility in assessing disease progression during therapy, anticipating complications of cirrhosis, and evaluation of the risk of hepatocellular carcinoma in patients with AIH.

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INTRODUCTION

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease which can progress to advanced fibrosis and cirrhosis[1,2]. Hepatic fibrosis scores increase in 25% of patients despite corticosteroid therapy[3]. Cirrhosis develops in 3% of treated patients per year[4], and 1%-6% of individuals with cirrhosis develop hepatocellular carcinoma (HCC)[5,6]. The prevention and reversal of hepatic fibrosis are key objectives in AIH, and the safe and reliable assessment of hepatic fibrosis is essential[7].

Histological evaluation is the gold standard for assessing hepatic fibrosis, but is suboptimal for monitoring disease progression due to its invasiveness, sampling error, and inter-observer variation[8-10]. Noninvasive tests of hepatic fibrosis include laboratory and radiological tests, which have been validated in chronic viral hepatitis, but have not been rigorously assessed in AIH. Laboratory-based methods for staging liver fibrosis include the FibroTest®[11], the serum aspartate aminotransferase/platelet ratio index (APRI)[12], the Fibrosis 4 (FIB-4) test[13], and the enhanced liver fibrosis test[14]. These tests may detect cirrhosis, but their ability to reflect the stages of fibrosis in AIH is uncertain[15,16].

The radiological tests of hepatic fibrosis include transient elastography by ultrasonography (TE), acoustic radiation force impulse (ARFI) imaging, and magnetic resonance elastography (MRE). TE has had high sensitivity and specificity for advanced stages of fibrosis and cirrhosis in chronic viral hepatitis, but its performance may differ in AIH[17,18]. Serum alanine aminotransferase (ALT) levels greater than twice the normal limit have reduced the accuracy of TE in detecting early stages of fibrosis in chronic hepatitis B, and AIH is characterized by chronic inflammation of fluctuating intensity[19,20]. Acute liver damage, as may occur in AIH, can also increase liver stiffness (LS) to levels suggestive of cirrhosis, only to resolve spontaneously with recovery[21]. Obesity can reduce the accuracy of TE and can be an important consequence of corticosteroid-treated AIH[22,23]. The technical specifications of TE may also limit its utility in patients with ascites[24]. The correlation between LS and acute liver inflammation has expanded the clinical applications of TE to include the diagnosis of acute cellular rejection after liver transplantation[25].

Early studies with TE in AIH have reported that TE is an accurate and reliable non-invasive tool in assessing liver fibrosis in AIH[26,27]. However one study by Hartl *et al*[26] and another case series by Romanque *et al*[28] demonstrated that inflammation impacts the accuracy of TE in evaluation of fibrosis. The same confounding factors that limit TE also affect the performance of ARFI. Although ARFI can differentiate normal from fibrosis secondary to chronic immune-mediated liver

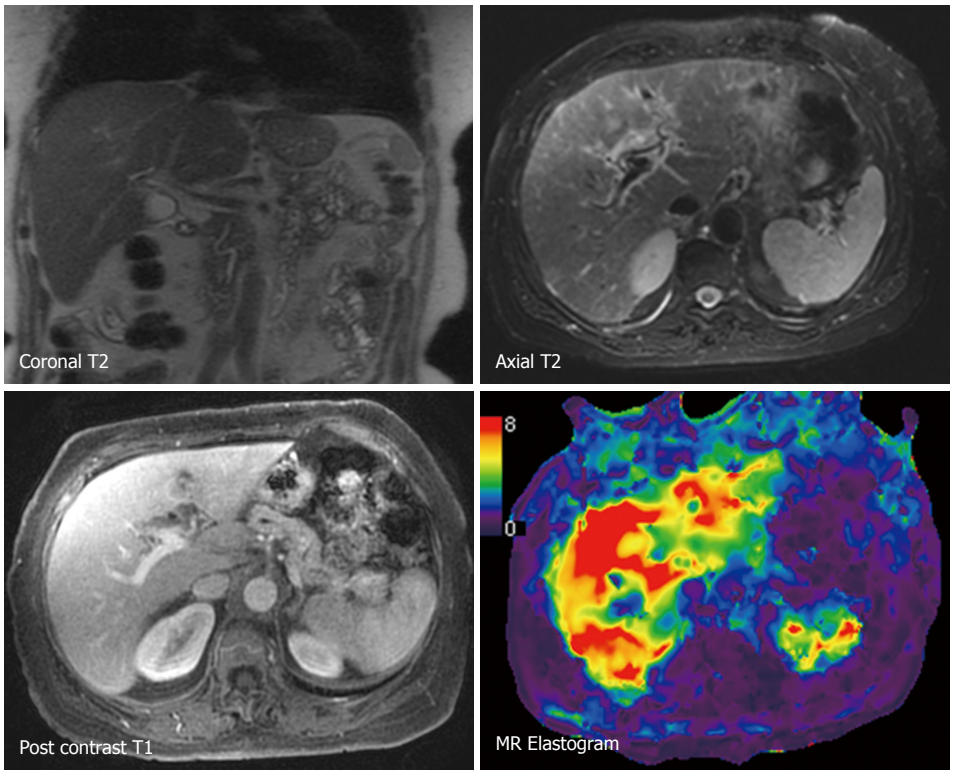

Figure 1 Magnetic resonance elastography in untreated autoimmune hepatitis. An 84-year-old female with grade 4 inflammation and cirrhosis. The liver has normal contour with no morphological features of cirrhosis. Lab tests were: AST 473, ALT 406, APRI 6.26 and FIB-4 10.31. LS was 6.4 kPa consistent with cirrhosis. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; APRI: AST to platelet ratio index; FIB-4: Fibrosis 4 test; LS: Liver stiffness.

disease[29], it has been outperformed by TE in diagnosing early fibrosis and distinguishing normal from fibrosis stage 1[30-32]. The attributes that could support current diagnostic, prognostic, and therapeutic efforts to improve outcomes in AIH may reside in MRE.

MRE (Figure 1) has had excellent performance parameters for all stages of fibrosis in diverse liver diseases[33-37], and it has outperformed TE for staging liver fibrosis in patients with diverse chronic liver diseases[38]. Furthermore, MRE is unaffected by body habitus or hepatic steatosis[39,40] and it can distinguish early from late stages of fibrosis and late stages of fibrosis from cirrhosis in liver diseases outside of AIH. It also may have prognostic implications *via* the assessment of splenic stiffness and the prediction of portal hypertension and esophageal varices[41].

Our goals were to determine the accuracy of MRE in the diagnosis of advanced hepatic fibrosis or cirrhosis in patients with AIH and to compare the findings to those of APRI, FIB-4, and magnetic resonance imaging (MRI).

MATERIALS AND METHODS

Patient selection

This retrospective study was approved by the Institution Review Board and informed consent was waived. We performed a search in the hospital database for patients who underwent MRE between 2007-2015 and had a diagnosis of AIH based on histology and by International AIH Group criteria[42-45]. One hundred and thirty-eight patients met these criteria, of whom 62 were excluded as the interval between liver biopsy and MRE exceeded 3 mo. Another 40 patients were excluded due to overlapping features of another chronic liver disease. The final study group comprised of 36 patients. Of these, 17 patients were treatment-naïve and 19 patients had received immunosuppression treatment either at our institution or elsewhere. The treatment naïve patients had MRE performed within 3 mo of liver biopsy (mean 5 d; range 0 to 42 d). The treated patients had diagnosis of AIH and received treatment for variable period ranging from 1 mo to 25 years with a mean duration of 5.5 years. The time interval between liver biopsy and MRE in this group was 8.2 d (range 0 to 85 d).

Laboratory parameters

Laboratory tests performed within two weeks of MRE were recorded for each patient, and included international normalized ratio (INR), platelet count, serum aspartate amino transferase (AST) and ALT levels, AST/ALT ratio, AST to Platelet Ratio Index (APRI), and FIB-4 score. The APRI was calculated using the equation (AST × 100)/platelet count (10^9/L)[46]. The FIB-4 score as calculated using the equation patient age [(years) × AST (U/L)]/[platelet count (10^9/L) × ALT (U/L)][7,47,48].

Histological assessment

Liver biopsy specimens were reviewed and scored by an experienced hepatopathologist who was blinded to patient data and MRE results. Portal-periportal and lobular inflammation activity grade and fibrosis stage were scored according to Batts *et al*[49]. Fibrosis was staged on a 0-4 scale on Masson Trichome stain. Interface hepatitis was defined as a portal-periportal inflammation score of ⩾ 2. Liver fibrosis stage was scored on a 5-point ordinal scale (0, 1, 2, 3, and 4). All patients with liver biopsy evidence of stage 3 (bridging fibrosis) or stage 4 (cirrhosis) were classified as having advanced fibrosis.

MRE

MRE of the liver was performed according to technique described previously[37]. A pneumatic passive driver was placed overlying the liver which transmitted acoustic vibrations generated at 60 Hz to produce propagating shear waves in the liver which were imaged using a standard MRE sequence as described previously[50]. Four slices were obtained through the largest cross section of the liver in each patient. Total acquisition time was approximately 2 min.

MRE data were processed by an inversion algorithm installed on the scanner to produce stiffness maps and wave images. Regions of interest were drawn by a single experienced abdominal radiologist over the liver and excluded artifacts, vessels > 3 mm in size, liver edges and fissures. LS levels above 2.5 kPa were interpreted as elevated[33].

MRI morphologic features

Two radiologists in consensus evaluated the liver on T2-weighted, T1-weighted, diffusion weighted and post gadolinium enhanced MRI images, and the results required consensus. The following features were assessed: (1) liver parenchyma signal: homogeneous, heterogeneous, patchy/segmental; (2) fatty change; (3) parenchymal enhancement: homogeneous, heterogeneous; (4) surface nodularity: absent, equivocal, present; (5) narrowed hepatic veins: yes/no; (6) presence/absence of the following signs: expanded gall bladder fossa sign, increased hilar periportal space (> 10 mm), hepatic notch sign, creeping mesenteric fat sign; (7) splenomegaly; (8) collaterals; (9) caudate-to-right lobe liver ratio; (10) modified caudate-to-right lobe liver ratio; and (11) ascites. An overall impression of the presence of cirrhosis was entered as absent, equivocal, or present.

Statistical analyses

Statistical analyses were performed using MedCalc for Windows, version 15.0 (MedCalc Software, Ostend, Belgium). Statistical analysis was performed by one author (Venkatesh SK) experienced in using MedCalc statistical software. Summary statistics are presented as mean ± SD for continuous variables and as numbers and percentages for categorical variables. The relationship between MRE and serum tests was evaluated using Pearson's correlation coefficient test. The relationships between serum tests, MRE, inflammation grade, and fibrosis stage were assessed using Spearman's correlation coefficient. Partial correlation analysis was used to evaluate the correlation between fibrosis stage and MRE correcting for inflammation grade. Kruskal-Wallis test was performed on serum tests and MRE to determine significant differences between fibrosis stages.

The overall performance of MRE for the diagnosis of advanced fibrosis and cirrhosis was determined by analyzing the area under the receiver operating characteristic (ROC) curve. Optimal cut-off values with accuracies, sensitivities, specificities, positive and negative predictive values were reported for predicting advanced fibrosis and cirrhosis. The performance parameters of all variables were compared by analyzing ROC curves. A two-tailed *P* value of < 0.05 was considered statistically significant for all analyses.

RESULTS

Clinical features

The study population had mean age of 51.6 ± 20.6 years and mean body mass index (BMI) of 27.8 ± 6.4 kg/m^2. The mean FIB-4 score was significantly lower in the treated group compared to the untreated group (2.72 *vs* 5.99, *P* = 0.025). A trend of higher levels of serum AST and ALT levels at the time of MRE and liver biopsy was found in the untreated group but was not statistically significant. There were no significant differences in BMI, mean LS, APRI, platelet and INR values between two groups (Table 1).

Histology findings

Liver biopsy was performed within 3 mo of MRE study with a mean interval of 11.7 d (95%CI: 2-76 d). Histological evaluation revealed fibrosis stages of 0, 1, 2, 3 and 4 in 4, 6, 7, 6 and 13 patients, respectively. Fibrosis (⩾ F1) was present in 32 patients (88.9%); significant fibrosis (⩾ F2) in 27 patients (75%); advanced fibrosis (⩾ F3) in 19 patients (52.8%) and cirrhosis (F4) in 13 patients (36.1%). Inflammation grade 0, 1, 2, 3, and 4 in 2, 7, 15, 9 and 3 patients respectively. The distribution of fibrosis stage and inflammation grade between treated and untreated patients was similar

Correlations between histological findings and laboratory tests

Spearman rank correlation analysis showed significant correlation between fibrosis stage and all serum tests except AST and ALT levels (Table 2). Both APRI and INR showed significant correlations with inflammation grade. No significant differences in ALT (*P* = 0.68), AST (*P* = 0.25), AST/ALT ratio (*P* = 0.07), and APRI

Table 1 Comparison of untreated and treated patients with autoimmune hepatitis

Characteristic	Untreated group (n = 17)		Treated group (n = 19)		P value
	mean ± SD	95%CI	mean ± SD	95%CI	
Age (yr)	62.9 ± 18.6	53.4-72.5	41.4 ± 16.8	33.30-49.5	0.001
BMI (kg/m^2)	27.2 ± 6.3	24.0-30.5	28.2 ± 6.8	24.9-31.5	0.65
Serum albumin	3.81 ± 0.8	3.39-4.23	4.0 ± 0.43	3.78-4.2	0.4
Serum ALP	117.6 ± 74.7	76.3-159.0	109.4 ± 45.6	85.9-132.9	0.19
Serum ALT	298.8 ± 459.9	62.3-535.3	144.5 ± 217.8	39.5-249.4	0.22
Serum AST	238.2 ± 313.1	77.2-399.1	110.0 ± 144.4	42.6-178.0	0.12
AST/ALT	1.0 ± 0.4	0.8-1.27	0.9 ± 0.41	0.8-1.0	0.38
APRI	2.9 ± 3.47	1.1-4.67	3.2 ± 5.8	0.36-6.0	0.85
FIB-4	5.99 ± 4.94	3.4-8.53	2.7 ± 3.3	1.1-4.3	0.025
Platelet	178.9 ± 78.0	138.8-219	193.3 ± 99.0	145.6-241.0	0.63
INR	1.1 ± 0.2	1.0-1.24	1.14 ± 0.3	1.0-1.3	0.96
Total bilirubin	1.5 ± 2.3	0.3-2.69	1.5 ± 1.9	0.5-2.5	0.96
Gamma globulin	2.3 ± 0.9	1.9-2.9	2.2 ± 0.9	1.6-2.8	0.61
Mean LS (kPa)	4.1 ± 1.6	3.2-4.9	4.5 ± 2.0	3.5-5.4	0.51

ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; APRI: AST to platelet ratio index; BMI: Body mass index; FIB-4: Fibrosis 4 test; INR: International normalization ratio; LS: Liver stiffness.

Table 2 Spearman rank correlation analysis results between variables and histological fibrosis stage and inflammation grade

Test	Fibrosis stage			Inflammation grade		
	Correlation	95%CI	P value	Correlation	95%CI	P value
AST	0.21	-0.13-0.50	0.2236	0.29	-0.043-0.56	0.0870
ALT	0.02	-0.31-0.35	0.8916	0.31	-0.02-0.58	0.0660
APRI	0.44	0.14-0.68	0.0064	0.39	0.07-0.64	0.0184
AST/ALT	0.40	0.08-0.65	0.0143	0.01	-0.32-0.34	0.9432
FIB-4	0.52	0.23-0.72	0.0012	0.24	-0.09-0.53	0.1497
Platelet	-0.48	-0.69--0.18	0.0032	-0.04	-0.37-0.29	0.7972
INR	0.49	0.19-0.71	0.0022	0.36	0.04-0.62	0.0294
Total Bil	0.36	0.030-0.63	0.0338	0.31	-0.03-0.58	0.0784
LS	0.83	0.69-0.91	< 0.0001	0.19	-0.14-0.49	0.2465

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; APRI: AST to platelet ratio index; FIB-4: Fibrosis 4 test; INR: International normalization ratio; LS: Liver stiffness.

(P = 0.09) were found between different stages of fibrosis by the Kruskal-Wallis test. INR values for stage 4 fibrosis were significantly higher than for stage 1 and 2 fibrosis (1.2 *vs* 1.0, P < 0.05). Total bilirubin levels were different between fibrosis stage 2 and 4 (P = 0.049), and platelet counts were significantly higher in fibrosis stage 0 and 2 than in stage 4 and between fibrosis stage 2 and 3. Fib-4 scores were significantly higher for fibrosis stage 4 than stages 0-2.

Correlations between histological findings and radiological tests

MRE correlated closely with fibrosis stage (r = 0.83, P < 0.001), and it performed better than MRI. The correlation between LS and fibrosis stages remained significant after correction for age and BMI (r = 0.75, P < 0.001), inflammation grade (r = 0.76, P < 0.001), and all laboratory tests (r = 0.68, P < 0.0001). LS was significantly higher in fibrosis stage 4 than stage 0-3; similarly stage 3 had significantly higher stiffness than stages 0-2. There were no significant differences in LS between stages 0-2 (Figure 2).

Untreated patients had a slightly higher mean LS as compared to treated patients (3.83 kPa *vs* 3.7 kPa), but this was not statistically significant. This trend was seen at each fibrosis stage (stage 0, 3.1 kPa *vs* 2.61 kPa; stage 1, 2.94 kPa *vs* 2.74 kPa; stage 2, 3.2 kPa *vs* 2.63 kPa; stage 3, 4.1 kPa *vs* 3.99 kPa). The only exception was cirrhotic patients where the treated patients had a higher LS compared to the untreated group (6.5 kPa *vs* 5.9 kPa).

ROC analysis showed that MRE (cut off, 4.1 kPa) predicted advanced fibrosis (≥ stage 3) with 0.97 accuracy (95%CI: 0.85-0.99), 89.5% sensitivity (95%CI: 67%-99%), 100% specificity (95%CI: 80.5%-100%), 100% positive predictive value (PPV, 95%CI: 80.5%-100%), and 89.5% negative predictive value (NPV, 95%CI: 67%-99%) NPV. Similarly, a cut-off of 4.5 kPa predicted cirrhosis with 0.98 accuracy (95%CI: 0.87-1.00), 92.31% sensitivity (95%CI: 85%-99%) and 96% specificity (95%CI: 78%-99.9%), 92.3% PPV (95%CI: 64%-99.8%) and 88% NPV (95%CI: 68.8%-97.5%).

Comparison between radiological tests and laboratory tests

Comparison of ROC curves for MRE and laboratory tests showed that MRE performed significantly better

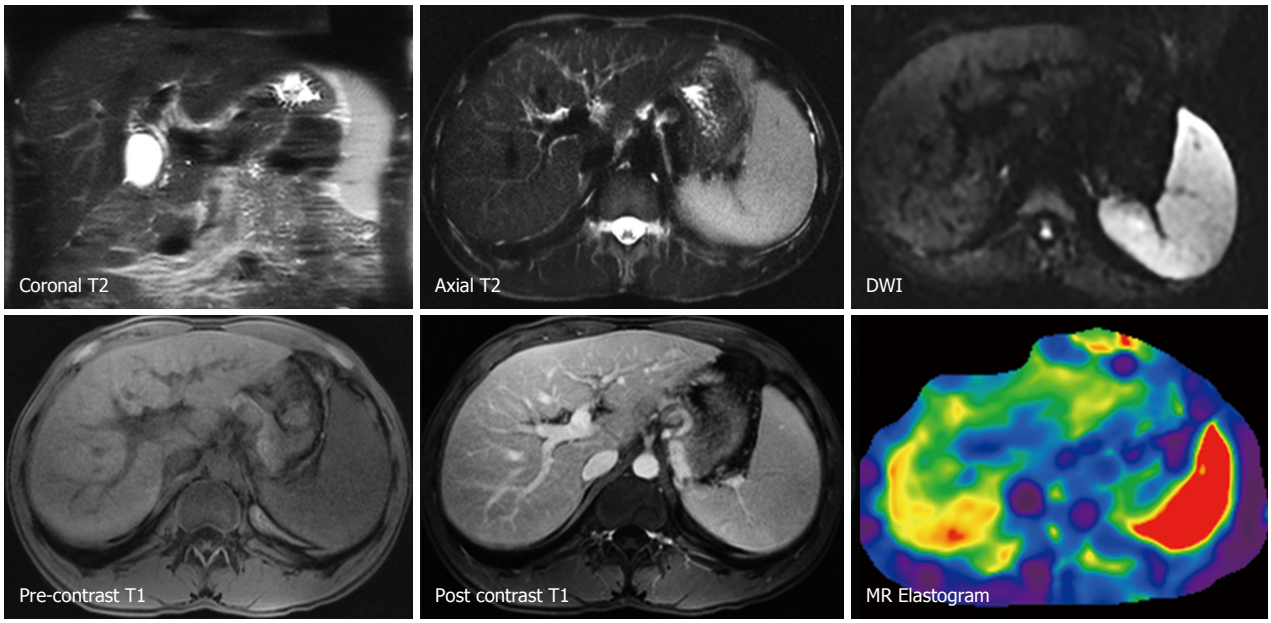

Figure 2 Magnetic resonance elastography in treated autoimmune hepatitis. A 43-year-old male with grade 2 inflammation and advanced fibrosis. MRI images show no features to suggest advanced fibrosis. Note prominent spleen. Lab tests were AST 81, ALT 147, FIB-4 2.95 and APRI 1.98. LS was 5.1 kPa consistent with advanced fibrosis. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; APRI: AST to platelet ratio index; FIB-4: Fibrosis 4 test; LS: Liver stiffness.

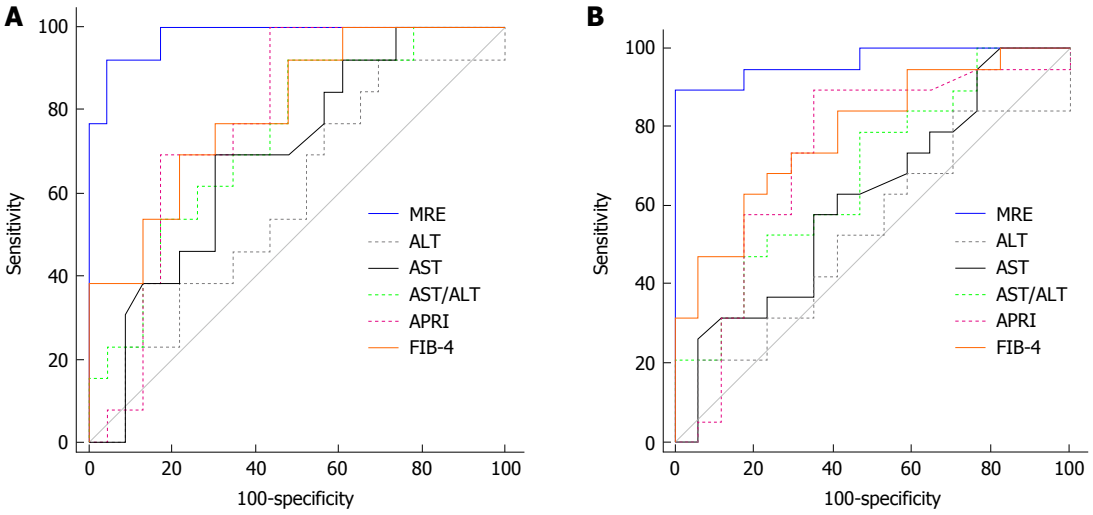

Figure 3 Graph showing area under the receiver operating characteristic curves of magnetic resonance elastography and lab tests for prediction of advanced fibrosis (A) and cirrhosis (B) in autoimmune hepatitis.

than ALT, AST, AST/ALT, APRI, FIB-4, INR and platelet counts for the detection of advanced fibrosis (Table 3, Figure 3A). FIB-4 performed better than AST, ALT and APRI for detecting advanced fibrosis, and all the laboratory tests performed better than the serum ALT level in making this distinction. Similarly for cirrhosis, MRE performed significantly better than all laboratory tests (Table 3, Figure 3B). FIB-4 only performed better than the serum ALT level in detecting cirrhosis, and the serum ALT level was worse than all other laboratory tests in making this distinction. We also analyzed diagnostic performance of MRE and laboratory tests for two study groups. In the untreated group of 17 patients MRE performance was better than laboratory tests for both advanced fibrosis (0.93 *vs* 0.51-0.86) and cirrhosis (0.95 *vs* 0.57-0.95). In the treated group of 19 patients, MRE performance was also better than serum tests for advanced fibrosis (0.98 *vs* 0.59-0.87) and cirrhosis (1.0 *vs* 0.64-0.89).

DISCUSSION

A non-invasive, accurate method of detecting advanced fibrosis and cirrhosis in patients with AIH is required to assess disease progression during therapy, anticipate complications of cirrhosis, and evaluate the risk of HCC. Our study demonstrates high accuracy of MRE in detecting advanced fibrosis and cirrhosis in patients with

Table 3 Area under the receiver operating characteristic curves of magnetic resonance elastography and laboratory tests for prediction of advanced fibrosis and cirrhosis in autoimmune hepatitis

	Advanced fibrosis			Cirrhosis		
	AUC	SE	95%CI	AUC	SE	95%CI
LS	0.966	0.0278	0.845-0.998	0.980	0.0175	0.867-1.000
ALT	0.526	0.0998	0.354-0.695	0.582	0.1010	0.406-0.744
AST	0.618	0.0964	0.441-0.774	0.691	0.0909	0.515-0.834
AST/ALT	0.681	0.0904	0.505-0.826	0.736	0.0860	0.563-0.868
APRI	0.728	0.0932	0.554-0.862	0.776	0.0789	0.606-0.898
FIB_4	0.786	0.0760	0.618-0.905	0.803	0.0750	0.636-0.916
INR	0.770	0.0770	0.596-0.891	0.800	0.0880	0.635-0.915
Platelet	0.802	0.0780	0.636-0.916	0.763	0.0904	0.592-0.888

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; APRI: AST to platelet ratio index; FIB-4: Fibrosis 4 test; INR: International normalization ratio; LS: Liver stiffness.

AIH, and its superiority to laboratory assessment and conventional MRI. Our findings are consistent with other studies that demonstrate greater diagnostic accuracy of MRE over laboratory assessment in detecting advanced fibrosis and cirrhosis in patients with diverse chronic liver diseases[34,38,40,50,51]. Furthermore, our study indicates that the laboratory and histological indices of liver inflammation do not compromise the accuracy of MRE in assessing hepatic fibrosis in AIH.

Untreated patients showed mildly higher LS as compared to treated patients which was not statistically significant, likely related to the presence of inflammation in the untreated group, and the subset of untreated AIH patients did have higher inflammation grades. This finding suggests that hepatic inflammation could have an impact on determinations of LS by MRE, and it was similar to that in patients with chronic viral hepatitis in whom the presence of chronic inflammation has been shown to increase LS by MRE[52]. In our study, there was no significant difference in the distribution of inflammation grades between the treated and untreated groups, and fibrosis stages were detected with similar accuracy in the treated and untreated patients. Our study also showed that cirrhotic livers in treated patients had higher mean stiffness as compared to cirrhotic livers in untreated patients. The exact reason is not known, however it is possible that the fibrosis content in treated patients is likely to be more as the duration of disease was longer in these patients. This needs to be confirmed in studies with a larger number of participants.

Recent studies performed with TE and ARFI in AIH have shown that both techniques are useful in assessment of significant fibrosis and cirrhosis in AIH. In one study with nearly 100 patients, Hartl *et al*[26] showed excellent diagnostic performance of TE for diagnosis of cirrhosis. They also showed that liver inflammation has a major impact on LS in first few months of AIH treatment and its diagnostic performance improves after 6 mo of immunosuppression treatment. In our study we also showed that untreated patients had higher stiffness compared to treated patients. In addition the diagnostic performance of MRE in treated patients was slightly better than that in untreated patients, however the numbers of patients in our study groups are too small to draw conclusions. In another study of only 15 patients, Efe *et al*[53] showed that ARFI is able to accurately differentiate significant fibrosis from non-significant fibrosis. There are no comparison studies between MRE, TE and ARFI and future studies combining all three modalities may be useful for determining their utility in different clinical scenarios.

Our study has limitations. First, the study was retrospective. This was unavoidable as patients frequently received treatment at outside medical centers. This also precludes assessment of the time interval between initial diagnosis and treatment to liver biopsy and MRE. Second, our sample size is small because the timing of liver tissue examinations and the performance of MRE was variable, and overlap syndromes were excluded. Third, the reference standard was histological assessment, which is limited by sampling error and inter-observer variability[8-10]. This was mitigated by applying a standardized scoring system for fibrosis and inflammation, requiring all specimens to be stained for fibrosis, and having each tissue sample re-reviewed by a pathologist specialized in autoimmune liver diseases[54]. Fourth, our study group comprised treated and untreated patients, which was unavoidable due to the rarity of AIH and retrospective nature of the study. Fifth, patients were assessed at varying intervals during the course of their disease, and were not studied sequentially to assess for detection of small gradations of change.

MRE is a non-invasive imaging-based biomarker with superior diagnostic accuracy for detecting advanced fibrosis and cirrhosis in patients with AIH compared to conventional laboratory and MRI assessment. MRE may become useful as a non-invasive tool for staging fibrosis in AIH, evaluating response to treatment, and decision-making regarding drug administration, dose adjustment, and duration of therapy. Our study provides a foundation for future prospective studies that evaluate the role of MRE to detect changes in LS that can be used safely and repeatedly in patients with AIH of all ages, habitus, and disease severity.

COMMENTS

Background

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease which can progress to advanced fibrosis and cirrhosis. Histological evaluation is the gold standard for assessing hepatic fibrosis, but is suboptimal for monitoring disease progression due to its invasiveness, sampling error, and inter-observer variation. A non-invasive, accurate method of detecting advanced fibrosis and cirrhosis in patients with AIH is required to assess disease progression during therapy, anticipate complications of cirrhosis, and evaluate the risk of hepatocellular carcinoma. Magnetic resonance elastography (MRE) has the potential to fulfill this function.

Research frontiers

MRE is a non-invasive imaging-based biomarker that has far reaching applications in the diagnosis, management, and treatment of patients with AIH.

Innovations and breakthroughs

This study provides a foundation for future prospective studies that evaluate the role of MRE to detect changes in liver stiffness that can be used safely and repeatedly in patients with AIH of all ages, habitus, and disease severity.

Applications

MRE may become useful as a non-invasive tool for staging fibrosis in AIH, evaluating response to treatment, and decision-making regarding drug administration, dose adjustment, and duration of therapy.

Terminology

MRE is a magnetic resonance imaging based technique that non-invasively assesses tissue stiffness.

Peer-review

These findings represent a first effort at defining the role of MRE in the evaluation of AIH. There is robust information supporting the usefulness of this technique in accurately assessing liver fibrosis in other liver diseases, such as hepatitis C, hepatitis B and non-alcoholic fatty liver disease.

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