Magnetic Resonance Elastography of Liver: Utility in Autoimmune Hepatitis

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Target Audience: Radiologists and research scientists interested in liver imaging

Background: Autoimmune hepatitis (AIH) is a chronic relapsing disease of unknown etiology and characterized by immune mediated injury to the liver resulting in hepatocellular inflammation and necrosis. Chronic AIH results in liver fibrosis that may progress to cirrhosis, which when left untreated can lead to hepatic failure and associated complications. Overlap syndromes with AIH have been reported in up to 40% of patients and may mask the underlying liver disease [1]. AIH promptly responds to immunosuppression but nearly 80% relapse after drug withdrawal. AIH may progress or regress depending on therapeutic response. Due to the chronic relapsing nature of the disease, progression of fibrosis is likely [2, 3]. AIH patients with cirrhosis are candidates for liver transplantation and are under routine surveillance for development of HCC and other complications. Treatment of established cirrhosis without any increased serum enzymes is not well established. Therefore it is important to differentiate patients without cirrhosis from patients with cirrhosis. Liver biopsy, although current gold standard is not a preferred technique by both patients and attending physicians due to its invasive nature, sampling error and low interobserver agreement for staging fibrosis. Magnetic resonance elastography, a MRI based method for assessment of liver stiffness, correlates with fibrosis/ cirrhosis in patients with chronic liver disease [4, 5]. MRE may be useful to detect fibrosis and assess treatment response. The aim of this study is to retrospectively assess the diagnostic accuracy of 2D-MRE for predicting cirrhosis (fibrosis stage 4) in patients with biopsy-proven AIH.

Methods: The study population consisted of 40 patients with biopsy proven AIH and a MRE of liver performed within 3 months. There were two groups of patients- a pre-treatment group (19 patients) who received no prior treatment for AIH and a treatment group (21 patients) who were on treatment or completed treatment (2 months to 12 years duration) and had a follow up liver MRI study to assess response. MRE of the liver was performed for diagnosis and assessment of severity of fibrosis. MRE was performed on a 1.5T clinical scanner with breath hold 2D GRE MRE sequence at 60Hz (TR/TE: 50/22ms; slice thickness: 10 mm). Four slices were obtained through the largest cross section of the liver in each patient. Stiffness maps were automatically generated by the software at the workstation and displayed. Regions of interest were drawn on the right lobe of the liver and copied on to the stiffness maps avoiding major vessels, liver edge and wave interference and any other artifacts seen on the magnitude and phase images. Mean liver stiffness values in kilopascals (kPa) were calculated. The fibrosis staging was performed by experienced pathologists in our institution. Diagnostic accuracy of MRE for the detection of cirrhosis was evaluated with receiver operating characteristics (ROC) in both pretreatment and post treatment groups. The mean stiffness was also correlated with standard liver function tests (serum ALP, serum AST, serum ALT, serum GGT, total bilirubin, direct bilirubin) in the two groups.

Results: In the pretreatment group, the distribution of fibrosis stages 0, 1, 2, 3, and 4 were 1, 2, 5, 4 and 7 respectively. MRE accurately differentiated cirrhotic patients from lesser degree of fibrosis (stage 0-3) with an accuracy of 0.90 (95%CI, 0.68-0.99). A cut-off stiffness value of 6.1kPa had 71.4% sensitivity, 100%specificity, 100%positive predictive value and 86% negative predictive value for cirrhosis. In the treatment group, the distribution of fibrosis stages 0,1,2,3, and 4 were 3,1,5,3 and 9 respectively. MRE accurately differentiated cirrhotic patients from lesser degree of fibrosis (stage 0-3) with an accuracy of 0.95 (95%CI, 0.76-0.99). A cut-off stiffness value of 4.2kPa had 100% sensitivity, 83.3%specificity, 82% positive predictive value and 100% negative predictive value for cirrhosis. No significant correlations were observed between liver stiffness value and standard liver function tests (correlation, r ranging from 0.04 to 0.4). Seven patients also had MRE performed twice during their follow up. Six patients showed a decrease in liver stiffness in the follow up MRE suggestive of a response to treatment with reduction in fibrosis and inflammation. One patient showed no change in liver stiffness in follow up MRE suggesting a stable disease.

Discussion and conclusion: Our study demonstrates that 2D-MRE of liver accurately detects cirrhosis in AIH. Interestingly, the cut-off value for distinguishing cirrhosis in treatment group was much lower than that of pretreatment group (4.2 kPa vs. 6.1 kPa). This may be attributed to the presence of inflammation in the untreated patients with AIH. Our preliminary data suggests a role for MRE in assessing treatment response in AIH; and identifying patients who progress to cirrhosis even on treatment as shown in our results.
MRE is an accurate, noninvasive imaging-based biomarker, useful for diagnosis of cirrhosis in AIH, and has a potential role in evaluation of treatment response. Prospective studies are required for evaluating its utility in AIH for assessing response to treatment and longitudinal clinical follow up.

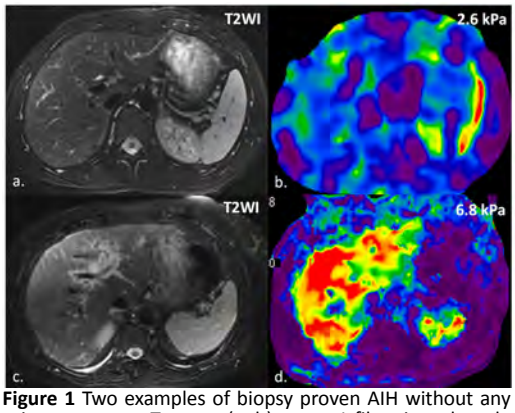

Figure 1 Two examples of biopsy proven AIH without any prior treatment. Top row (a, b)- stage 1 fibrosis and grade 1 inflammation, the mean liver stiffness is 2.6kPa; Bottom row (c, d)- stage 4 fibrosis and stage 4 inflammation, the mean liver stiffness is 6.8kPa.

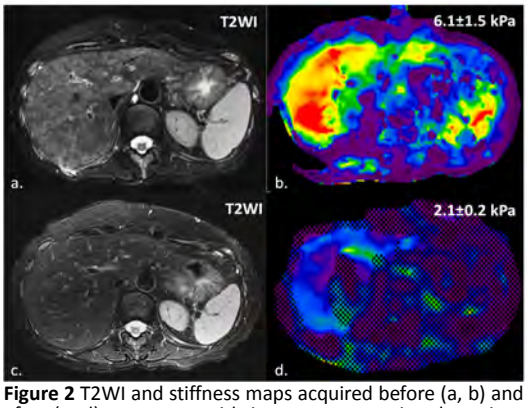

Figure 2 T2WI and stiffness maps acquired before (a, b) and after (c, d) treatment with immunosuppressive drugs in a 76-year-old female. The mean liver stiffness before treatment was 6.1kPa consistent with advanced fibrosis at biopsy. Liver stiffness improved significantly to 2.1kPa after 4 years of treatment.

References:

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