Assessment of Liver Fibrosis: Comparison of Magnetic Resonance Elastography (MRE) and Diffusion-weighted Imaging (DWI)

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INTRODUCTION: Hepatic fibrosis is a wound-healing response to multiple types of chronic liver disease or injury. Cirrhosis, the end-stage of liver fibrosis, is a major cause of death due to its association with hepatocellular carcinoma and complicated portal hypertension. Accurate discrimination of advanced fibrosis and cirrhosis from mild fibrosis in patients with chronic liver disease is essential for diagnostic and therapeutic management. Liver biopsy is considered the gold standard for diagnosis of hepatic fibrosis; however, sampling errors, cost, and low acceptance by patients are inherent problems. Therefore, a more accurate, reproducible and well-tolerated technique is required for clinical practice. Recently, magnetic resonance elastography (MRE) [1,2,3] and diffusion-weighted imaging (DWI) [4] have been used as non-invasive imaging tools to evaluate liver fibrosis. The purpose of our study was to compare the discriminatory capabilities of MRE and DWI in detecting and staging hepatic fibrosis in patients with suspected chronic liver disease using histopathologic analysis as the reference standard.

MATERIALS AND METHODS: The prospective study was approved by our institutional review board (IRB). All patients gave written informed consent. Forty patients with chronic liver disease and 9 normal volunteers underwent clinical routine MRI, MRE and DWI using 1.5-T MR system (Magnetom Espree, Siemens Healthcare, Erlangen, Germany). Stages of liver fibrosis were confirmed by histopathologic analyses according to the METAVIR system and the Brunt system. The liver shear stiffness and apparent diffusion coefficient (ADC) values were measured on elastogram and DW images, respectively. The shear stiffness and ADC values of liver tissue at different stages of fibrosis were compared using the Kruskal-Wallis H test. The correlation of liver stiffness and ADC values with stage of fibrosis was analyzed by non-parametric method of Spearman's coefficient of rank correlation coefficient. Based on the METAVIR system and Brunt system, the overall predictive power of MRE and DWI in detecting and staging fibrosis was determined and compared by constructing a receiver operating characteristic curve (ROC) and calculating the area under the curve (AUC) based on the histopathologic reference standard. Optimal cutoff values of liver stiffness and ADC values were chosen to maximize the sum of the sensitivity and specificity, and the positive and negative predictive values were computed for these cutoff values.

RESULTS: Liver stiffness values increased as the stage of fibrosis increased and a positive linear correlation between shear stiffness values and stage of fibrosis was observed (roh=0.87; P<0.0001). Furthermore, liver tissue without fibrosis (F0), with mild fibrosis (F1), moderate fibrosis (F2) and advanced fibrosis to cirrhosis (F3-4) were distinguishable from one another by shear stiffness values (P<0.001) (Fig1). A negative linear correlation between stage of fibrosis and ADCs was also observed (roh=-0.58; P<0.0001). However, a significant difference in ADC values was only seen between tissue without fibrosis (F0) and tissue with advanced fibrosis to cirrhosis (F3-4) (P<0.0001) (Fig 2). Comparison of overall predictive power of MRE and DWI in characterizing and staging fibrosis is shown in Table 1. When identifying mild fibrosis to cirrhosis (≥F1), the difference in AUC between MRE and DWI was 0.102 (95% confidence interval CI, -0.031 to 0.235) and a significant difference was not seen (P=0.132). MRE showed significantly greater predictive power for identifying moderate fibrosis to cirrhosis (≥F2) and advanced fibrosis to cirrhosis (≥F3) compared to DWI and the differences in AUC between them were shown to be 0.172 (95% CI, 0.053 to 0.291; P=0.005) and 0.156 (95% CI, 0.042 to 0.270; P=0.007), respectively.

Table 1.

	F0/ F1-4	F0-1/ F2-4	F0-2/ F3-4
Stiffness value (kPa)			
Cut-off value	3.60	5.37	5.97
AUC	0.93	0.99	0.99
Sensitivity	86.7 %	95.7 %	94.4 %
Specificity	83.3 %	96.2 %	93.3 %
PPV	89.7 %	95.7 %	89.5 %
NPV	78.9 %	96.2 %	96.6 %
ADC value ($\times 10^{-3}$mm^2/sec)			
Cut-off value	1.12	1.12	1.12
AUC	0.83	0.82	0.83
Sensitivity	66.7 %	68.2 %	77.8 %
Specificity	94.4 %	88.5 %	86.7 %
PPV	95.2 %	83.3 %	77.8 %
NPV	63.0 %	76.7 %	86.7 %

CONCLUSIONS: In conclusion, our study demonstrated that shear stiffness value measured on MRE had a positive linear correlation with degree of liver fibrosis and had greater capability for discriminating the severity of liver fibrosis compared to ADC values on DWI. Furthermore, the absence of fibrosis (F0), mild fibrosis (F1), moderate fibrosis (F2) and late-stage fibrosis (F3-4) can be distinguished from one to another by shear stiffness values on MRE. In contrast, the individual stages of fibrosis could not be differentiated by ADC values. Although DWI showed lower discriminatory capability in staging fibrosis compared to MRE, it showed relatively high predictive power in identifying advanced fibrosis to cirrhosis (F3-4), as shown by its sensitivity of 77.8% and specificity of 86.7%. Both MRE and DWI can be valuable in the diagnosis of advanced fibrosis and cirrhosis, which is essential for management of chronic liver disease.

References:
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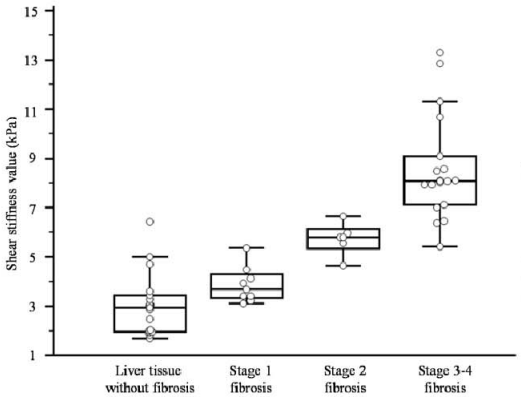

Figure 1. Box plot of shear stiffness value shows the median and distribution of various stages of fibrosis. A significant difference in liver stiffness values was seen among the various stages of fibrosis, P<0.001.

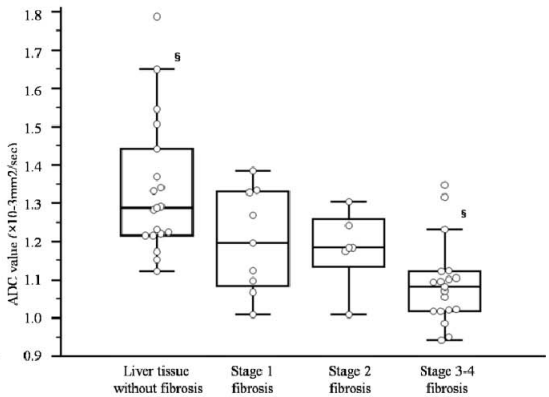

Figure 2. Box plot of ADC value shows the median and distribution of various stages of fibrosis. § = median ADC value of liver tissue without fibrosis (F0) is higher than that of advanced fibrosis to cirrhosis (F3-4), P<0.0001.

The circles represent the distribution of the data ranging from minimum to maximum. The line through each box represents median value and lines extend from the box to the range with the 10th to 90th percentile. The horizontal line through each box represents median value and box represents data from the 25th to the 75th percentile (middle 50% of observations). (Kruskal-Wallis H test and Mann-Whitney U test).