Clinical Feasibility of MR Elastography in Patients With Biliary Obstruction

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OBJECTIVE. The purpose of this study is to evaluate the clinical effect of liver stiffness measured using MR elastography (MRE) in patients with cholestasis due to biliary obstruction.

MATERIALS AND METHODS. In this retrospective study, 69 consecutive patients with no history of diffuse liver disease who underwent pancreaticobiliary imaging with MRE were included. Quantitative MRI parameters (i.e., liver stiffness, apparent diffusion coefficient, R²*, and proton density fat fraction) and laboratory results (i.e., aspartate aminotransferase, alanine aminotransferase, and total bilirubin levels) were measured. Patients were classified as having either normal bilirubin (group A; n = 49) or hyperbilirubinemia (group B; n = 20). Continuous variables were compared using the independent t test or Mann-Whitney U test. Correlation between parameters was analyzed using the Pearson correlation coefficient. The ROC curve analysis was used to evaluate the diagnostic performance and clinical effect of MRE.

RESULTS. Liver stiffness was significantly higher in group B (mean ± SD, 3.8 ± 0.7 kPa) than in group A (2.8 ± 0.5 kPa) (p < 0.001); there were no differences in other MRI parameters. There were positive correlations between liver stiffness and total bilirubin (r = 0.609; p < 0.001), aspartate aminotransferase (r = 0.376; p = 0.001), and alanine aminotransferase (r = 0.285; p = 0.017) levels. There was a negative correlation between the degree of biliary decompression 1 week after bile drainage and liver stiffness (r = −0.71; p = 0.003). The sensitivity and specificity for predicting biliary decompression were 83.3% and 100%, respectively, at a liver stiffness cutoff of 4.0 kPa.

CONCLUSION. Liver stiffness measured by MRE increases as cholestasis increases and can be a predictive factor for the sufficiency of biliary decompression after biliary drainage.

MR elastography (MRE) is a quantitative imaging method based on MRI that directly measures liver stiffness. It generates and transfers mechanical waves through the liver and obtains images of wave propagation in tissues. From this, the shear stiffness of tissue can be measured by calculating the shear-wave speed and the density of tissue using the equation μ = ρc², where μ = shear modulus, ρ = density of tissue, and c = shear-wave speed. Compared with transient elastography, MRE permits 2D or 3D imaging of propagating waves within the liver, resulting in the assessment of a large volume of liver and, ultimately, more accurate diagnostic performance [1, 2]. According to previous studies, the diagnostic accuracy of MRE for differentiating fibrosis stages has been reported to have a sensitivity of up to 98% and a specificity of 99% [3, 4].

Despite the higher accuracy of MRE for the diagnosis of liver fibrosis, there are confounding factors that may affect liver stiffness measurement. According to previous studies, liver stiffness measured using MRE could be overestimated in patients with acute hepatitis [5–7], whereas age, sex, race, and isolated fatty liver have not shown any significant association with liver stiffness [5, 6, 8]. Furthermore, it has been reported that massive ascites, iron deposition, and high body mass index are associated with failure of MRE measurements in the liver [4, 9].

Transient elastography is a modality widely used to assess liver fibrosis by measuring liver stiffness [10]. Liver stiffness measured by transient elastography has been strongly associated with the degree of liver fibrosis, and for acute biliary obstruction, a significant positive correlation has been reported between liver stiffness measured using transient elastography and bilirubin levels [10–12]. In addition, liver stiffness decreased in patients after successful biliary drainage. It was believed...
that the reason for the increase in liver stiffness in cases of acute biliary obstruction may be the increased hydrostatic pressure due to impaired bile flow and accompanying tissue swelling, inflammation, and edema [10, 12]. On the basis of this information, we hypothesized that liver stiffness measured using MRE could also be affected by biliary obstruction. Hence, the purpose of this study was to investigate the effect of liver stiffness measured using MRE in patients with cholestasis due to biliary obstruction. The effect of other quantitative MRI parameters, including apparent diffusion coefficient (ADC), T2* relaxation time, and proton density fat fraction (PDFF), on cholestasis were also evaluated. Furthermore, we investigated the clinical effect of liver stiffness measured using MRE in patients with cholestasis due to biliary obstruction.

Materials and Methods

Study Population

This retrospective study was approved by our institutional review board. Given the retrospective nature of the investigation and the use of anonymized patient data, requirements for informed consent were waived. Patients who underwent pancreaticobiliary MRI including MRE between September 2015 and August 2016 were eligible for inclusion in this study. Among them, patients who underwent blood chemistry examination, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum total bilirubin (TB) levels, at least 1 week before MRI were included. However, patients with any history of diffuse liver disease (e.g., chronic viral hepatitis B or C or liver cirrhosis due to any cause), those who underwent previous liver surgery, or those who consumed more than 14 units of alcohol per week (or 20 g/day) were excluded [13]. Patients enrolled in the study were divided into one of two groups: those with a TB level within normal limits (≤ 1.8 mg/dL; group A) and those with hyperbilirubinemia (> 1.8 mg/dL; group B). Data on age, sex, and AST, ALT, and TB levels were collected from all patients. In patients with hyperbilirubinemia who underwent biliary decompression for biliary obstruction, TB levels 1 day and 1 week after biliary drainage were analyzed to assess the effectiveness of the procedure. The percentage of TB change before and after biliary decompression was calculated using the following formula: percentage bilirubin change = [(1 − TB level after procedure) / TB level before procedure] × 100.

MR Image Acquisition

MRI examinations were performed using a 3-T MRI scanner (Discovery 750w 3 T, GE Healthcare) equipped with a 32-channel torso coil. MRE was included in the routine pancreaticobiliary MRI protocol for the upper abdomen to determine the possibility of surgery or to evaluate the liver stiffness of patients, if necessary. The routine pancreaticobiliary MRI protocol also included iterative decomposition of water and fat with echo asymmetry and the least squares estimation, as well as DWI. MRE and iterative decomposition of water and fat with echo asymmetry and the least squares estimation were performed before the injection of contrast media. DW images were acquired after contrast-enhanced dynamic MRI because the gadolinium-based contrast agent does not significantly alter the ADC [14]. MRE was performed according to previously established methods [15]. In brief, axial slices were acquired using a 2D spin-echo MRE technique. Mechanical waves with a frequency of 60 Hz were generated in the active driver, which was located outside the MRI room and transferred to a passive pneumatic driver via a plastic duct. The passive pneumatic driver was placed at the anterior wall of the right upper abdomen adjacent to the liver, and mechanical waves were transferred to the liver during MRE. The MR elastograms, quantitative images displaying shear stiffness, were generated by processing the sequence to collect axial wave images sensitized along the through-plane motion direction, which was previously described as a local frequency estimation inversion algorithm [16]. Patients held their breath at the end of expiration at each section, and four slices of MR elastograms were obtained for each patient. Iterative decomposition of water and fat with echo asymmetry and the least squares estimation is a noninvasive 3D volumetric imaging sequence for creating R2* (1/T2*) and PDFF maps from a single breath-hold acquisition in the liver. Six different echoes were applied to separate water and triglyceride fat, and PDFF and R2* maps were automatically reconstructed in the console [17, 18]. The DWI sequence was performed using three b values (50, 400, 800 s/mm²), and the ADC was generated in the MRI console. Detailed MRI parameters are summarized in Table 1.

Image Analysis

Quantitative measurements were performed by one radiologist by drawing an ROI (mean ± SD) = 339 ± 39.1 mm² (range, 300–400 mm²) on the right lobe of the liver on three contiguous images on the MR elastogram, R2* map, PDFF map, and ADC map. The ROIs were oval or circular and excluded the liver boundary, fissures, gallbladder fossa, artifacts, and large blood vessels. In terms of liver stiffness measurement, a confidence map, which indicated areas of high confidence and acceptable signal-to-noise ratio, was initially reviewed, and an ROI was drawn within the high-confidence area [19]. Finally, the mean value of three measurements in each sequence was calculated.

Furthermore, to exclude causes of hyperbilirubinemia other than biliary obstruction (e.g., hemolysis, drug-induced liver disease, and genetic disorders, including Gilbert syndrome), the diameter of the bile duct was measured where the biliary dilatation was the greatest, including the intrahepatic duct and common bile duct, on axial CT images taken before the procedure, and the degree of diameter change in the bile duct (percentage) was measured on axial CT images taken after the procedure. The percentage difference in the degree of diameter change in the bile duct was investigated between the group with sufficient biliary decompression and the group without sufficient biliary decompression, calculated as follows: percentage of bile duct diameter change = [(1 − bile

### Table 1: Parameters of MRI Sequences Used in This Study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sequence</th>
<th>TR/TE</th>
<th>Matrix</th>
<th>Slice Thickness (mm)</th>
<th>Slice Spacing (mm)</th>
<th>Sensitivity Encoding</th>
<th>Flip Angle (°)</th>
<th>Scan Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iterative decomposition of water and fat with echo asymmetry and least squares estimation</td>
<td>Proton density fat fraction and R2*</td>
<td>6.3/2.9</td>
<td>160 × 160</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Axial MRI Touch 1</td>
<td>MR elastography</td>
<td>1000.3/63.1</td>
<td>64 × 64</td>
<td>8</td>
<td>10</td>
<td>2</td>
<td>90</td>
<td>24</td>
</tr>
<tr>
<td>Axial DWI (b = 50, 400, 800 s/mm²)</td>
<td>Apparent diffusion coefficient</td>
<td>0,000/50.1</td>
<td>128 × 256</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>90</td>
<td>Variant (mean = 300)</td>
</tr>
</tbody>
</table>

Note—Touch 1 is an MR elastography protocol developed by GE Healthcare with the Mayo Clinic.

*Total scan time of 24 seconds for two 12-second scans to obtain the final MR elastogram.
Clinical Feasibility of MR Elastography

Eligible patients for assessing the quantitative parameters of pancreaticobiliary MRI (n = 165)

Excluded patients (n = 96)
- Without blood chemistry examination including AST, ALT, and TB level at least 1 week before MRI (n = 44)
- Underlying diffuse liver disease (n = 49)
- Prior liver surgery (n = 3)

Evaluation of quantitative MRI parameters including PDFF, R2* value, ADC, and liver stiffness (n = 69)

Group A with normal TB level (n = 49)

Group B with cholestasis (n = 20)

duct diameter after procedure) / bile duct diameter before procedure) × 100.

Statistical Analysis

Continuous variables are expressed as mean ± SD. Continuous variables with normal distribution, including quantitative MRI parameters and laboratory results, were compared between the two groups using the independent samples t test, and continuous variables without normal distribution, such as changes in the bile duct diameter (percentage), were compared between the two groups using the Mann-Whitney U test. Correlations between liver stiffness and age and liver stiffness and other quantitative parameters were evaluated using the Pearson correlation coefficient. ROC analysis was conducted to assess the performance of MRE for predicting the efficiency of biliary decompression over a range of sensitivity and specificity values. The optimal cutoff value was chosen to maximize the sum of sensitivity and specificity. A p < 0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS (version 21, IBM).

Results

Patients

Between September 2015 and August 2016, 165 patients underwent pancreaticobiliary MRI including MRE; 44 patients were excluded because they did not undergo blood chemistry examination including AST, ALT, and serum TB levels at least 1 week before the MRI. An additional 49 patients with underlying diffuse liver disease and three with a history of liver surgery were also excluded. Finally, a total of 69 patients (mean age, 61.8 ± 12.7 years; 41 men and 28 women) were included in this study. Of these 69 patients, 49 were assigned to group A (mean age, 61.2 ± 12.5 years; 26 men and 23 women) and 20 were assigned to group B (mean age, 63.4 ± 13.6 years; 15 men and 5 women) (Fig. 1). Three patients in group A (one with a

![Table 2: Demographics and Diagnoses of Patients Included in the Study](https://www.ajronline.org/download/210/Jun/2018/1275/Table2_Demographics_and_Diagnoses_of_Patients_Included_in_the_Study.png)

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Liver stiffness measured using MRE was significantly higher in group B (3.8 ± 0.7 kPa) than in group A (2.8 ± 0.5 kPa) \( p < 0.001 \). There was no significant difference between the two groups in terms of the other quantitative MRI parameters, including PDFF (3.7 ± 3.4 vs 2.7 ± 0.6; \( p = 0.257 \)), R2* value (54.4 ± 6.7 vs 50.8 ± 10.9 Hz; \( p = 0.106 \)), or ADC (1.3 ± 0.2 × 10⁻³ vs 1.2 ± 0.2 × 10⁻³ mm²/s; \( p = 0.080 \)) (Fig. 2). There were significant positive correlations between liver stiffness and TB level (\( r = 0.609; p < 0.001 \)), as well as AST (\( r = 0.376; p = 0.001 \)) and ALT (\( r = 0.285; p = 0.017 \)) levels (Fig. 3). In contrast, no significant correlation was found between liver stiffness and R2* (\( p = 0.127; r = -0.19 \)), or between liver stiffness and PDFF (\( p = 0.925; r = -0.01 \)). Also, there was no significant difference in liver stiffness according to sex (\( p = 0.073 \)) and no significant correlation between liver stiffness and age (\( p = 0.907 \)).

**Predicting Biliary Decompression**

Seventeen of 20 patients in group B underwent biliary drainage procedures for decompression, including endoscopic retrograde biliary drainage (\( n = 8 \)) and percutaneous transhepatic biliary drainage without (\( n = 7 \)) and with (\( n = 2 \)) biliary stent insertion. There was a significant negative correlation between liver stiffness and the percentage change in TB level at 1 day (\( r = -0.55; p = 0.02 \)) and 1 week (\( r = -0.71; p = 0.003 \)) after bile drainage (Fig. 4). Previous studies have defined successful biliary decompression as the development of pneumobilia or improvement of intra- or extrahepatic dilatation on follow-up CT or MRI, with a decrease in TB level to less than 20% of the pretreatment value within 7 days after the procedure [20, 21]. According to these criteria, 11 patients underwent successful biliary decompression, whereas four did not. TB was not evaluated 1 week after the procedure for two patients. The degree of diameter change in the bile duct (percentage) was not significantly different between the group with sufficient biliary decompression and the group without sufficient biliary decompression in the intrahepatic bile duct (46.1% ± 15.0% vs 28.7% ± 16.3%; \( p = 0.138 \)) and common bile duct (53.1% ± 20.3% vs 51.5% ± 4.7%; \( p = 0.376 \)). At ROC analysis, a mean liver stiffness of less than 4.0 kPa represented a possible cutoff value for predicting sufficient biliary compression, with a sensitivity of 83.3% and a specificity of 100% at 1 week after the procedure (standard error, 0.117; 95% CI, 0.638–0.896).

**Discussion**

Our results show that liver stiffness measured using MRE was significantly higher in patients with biliary obstruction compared with patients without biliary obstruction; positive correlations were found between liver stiffness and the levels of TB, AST, and ALT. Furthermore, using 4.0 kPa as the liver stiffness cutoff value, MRE may be used to predict successful biliary decompression, with a sensitivity of 83.3% and specificity of 100%.

Previous studies have reported a significant positive correlation between liver stiffness and TB level [10, 22], which is consistent with our results. The exact reasons for high liver stiffness in patients with cholestasis are unknown, but it may be associated with edema, inflammation, tissue swelling, and increased intracellular pressure caused by impaired bile flow [10, 12]. Moreover, there was a negative correlation between the degree of biliary decompression and liver stiffness in this study. Considering that biliary drainage quickly decreases hydrostatic pressure, as well as cellular edema or inflammation, we believe that patients with cholestasis showed increased liver stiffness because of multiple factors associated with biliary obstruction.
Clinical Feasibility of MR Elastography

Previous studies reported a low albumin level (< 3 g/100 mL), thrombocytopenia, high urea nitrogen level (> 20 mmol/L), and high creatinine level (> 1.2 mg/dL) as predictive factors for negative outcome of biliary decompression [23, 24]. On the basis of our results, high liver stiffness measured using MRE may represent an additional noninvasive imaging biomarker to predict the effectiveness of biliary decompression. If liver stiffness is less than 4.0 kPa before biliary drainage, successful biliary decompression could be expected in 83.3% of patients.

Although some studies have found that liver stiffness is affected by hepatic steatosis [25, 26], more recent investigations have reported no significant relationship between hepatic steatosis and liver stiffness [2, 5, 6, 8]. Our results were comparable with recent studies that have reported no significant correlation between liver stiffness and PDFF. In terms of R2*, which is usually used to evaluate iron deposition in the liver [27, 28], there was no significant difference, regardless of the presence of biliary obstruction, suggesting that R2* cannot be used to evaluate biliary obstruction or to predict the sufficiency of biliary decompression.

There were some limitations to our study, the first of which was its retrospective design and inherent selection bias, which may have affected the results. Second, the number of patients who underwent bile drainage was relatively small and the methods of decompression were variable. Third, we could not directly confirm the other causes of hyperbilirubinemia, in addition to biliary obstruction, because liver biopsies were not performed on the patients. Fourth, although the cause of impaired bile drainage was malignancy in most cases, the exact tumor burden in each patient was not considered; moreover, the exact range of liver segments in which bile drainage was accessible was not considered.

In conclusion, liver stiffness measured using MRE was increased in patients with cholestasis; therefore, our results showed that liver stiffness should be interpreted with caution to avoid overdiagnosis of liver fibrosis stage. Furthermore, liver stiffness can be used as a noninvasive imaging biomarker for predicting successful biliary decompression after bile drainage.

References
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Kim et al.