Transmit Elastography and Sonography for Prediction of Liver Fibrosis in Infants With Biliary Atresia

Na-Young Shin, MD, Myung-Joon Kim, MD, Mi-Jung Lee, MD, Seok Joo Han, MD, Hong Koh, MD, Ran Namgung, MD, Young Nyun Park, MD

Objectives—The purpose of this study was to assess the diagnostic performance of transient elastography and sonography for noninvasive evaluation of liver fibrosis in infants with biliary atresia.

Methods—Forty-seven infants with biliary atresia who underwent both transient elastography and sonography before surgery were included in this study. Two types of transient elastographic probes were used: an M probe, which is used for the general adult population; and an S probe, which is specific to children. Transient elastographic measurements and sonographic findings such as triangular cord thickness and hepatic artery and portal vein diameters were compared with the METAVIR histopathologic fibrosis scoring system.

Results—Only transient elastography (\(\rho = 0.63; P < .001\)) was significantly correlated with METAVIR fibrosis stages. The areas under the receiver operating characteristic curves for transient elastography were 0.86 and 0.96 for diagnosis of severe fibrosis and cirrhosis, respectively. The cutoff value of transient elastography for diagnosis of severe fibrosis was greater than 9.6 kPa, with sensitivity of 89.5% and specificity of 75%. The cutoff value of transient elastography for diagnosis of cirrhosis was greater than 18.1 kPa, with sensitivity of 100% and specificity of 90.5%. The success rate for the S probe (100%) was significantly higher than that for the M probe (77%; \(P < .001\)).

Conclusions—Transient elastography may be a useful noninvasive method for diagnosis of severe fibrosis and cirrhosis and may help predict outcomes before surgery or invasive liver biopsy in infants with biliary atresia. The success rate of transient elastography in infants was improved by using the S probe.

Key Words—biliary atresia; elastography; fibrosis; histology; pediatric ultrasound; sonography

Liver fibrosis is a common and prominent feature of biliary atresia, and many studies have reported that age at the time of portoenterostomy is the major predicting factor for the outcome.\(^1\)\(^-\)\(^4\) Specifically, infants who undergo portoenterostomy before 60 to 90 days of age have more favorable outcomes.\(^3\) Although the reason for the effect of age at the time of portoenterostomy is not well understood, some studies have suggested that it correlates with the degree of liver fibrosis, which may be a determinant of the outcome.\(^5\)\(^,\)\(^6\) Therefore, evaluation of the degree of liver fibrosis is worth considering before surgical treatment of biliary atresia.

Liver biopsy is the reference standard for evaluating liver fibrosis. However, because of its invasive nature, repeated monitoring of liver fibrosis by biopsy is difficult.\(^7\) In addition, the accuracy of liver biopsy...
is limited by both intraobserver and interobserver variability as well as sampling errors.8 As a result of these limitations, many investigators have focused on identifying alternative noninvasive methods for assessing liver fibrosis.

Sonography is a noninvasive procedure and is usually used as a first step when a patient is suspected to have biliary atresia. Among the many sonographic predictors of biliary atresia, the triangular cord sign is very specific, as it represents congenital fibrous ductal remnants.9–12 Choi et al12 reported no correlation between portal fibrosis and triangular cord size; their study, however, was limited to 10 patients with biliary atresia.

According to a recent systematic review and meta-analysis, transient elastography (FibroScan; Echosens, Paris, France; Figure 1)13 is a promising noninvasive method for assessing liver fibrosis.14,15 It consists of a modified ultrasound device and is based on the principle that the propagation velocity of an elastic shear wave is proportional to the stiffness (elasticity) of tissue. In other words, the harder the tissue, the faster the elastic shear wave propagation. To assess liver stiffness, a transducer mounted on the vibrator is placed over the liver, and a shear wave is transmitted. As this wave propagates through the liver, its velocity, which correlates with liver stiffness, is measured by pulse-echo acquisition of the ultrasound signal. There have been a few studies focused on children with chronic liver diseases of mixed etiology16 as well as specific liver diseases such as cystic fibrosis–associated liver disease17 and nonalcoholic fatty liver disease.18 Together, the results of these studies indicate that transient elastography is a viable method for assessing liver fibrosis. However, limited data are available on the use of transient elastography in children with biliary atresia for evaluating the degree of liver fibrosis. Thus, the aim of this study was to assess the diagnostic performance of transient elastography and sonography for noninvasive evaluation of liver fibrosis in infants with biliary atresia.

Materials and Methods

Patients

This study was approved by our Institutional Review Board with a waiver of informed consent. A total of 51 infants younger than 1 year who underwent transient elastography and sonography before portoenterostomy or liver transplantation between April 2007 and July 2010 were retrospectively included in our study. The interval between transient elastography and sonography was less than 5 days. Kettaneh et al19 suggest that at least 5 valid measurements are necessary to mitigate substantial loss in transient elastographic performance for diagnosis of liver cirrhosis; thus, we excluded 4 patients who had fewer than 5 valid transient elastographic measurements. Finally, a total of 47 patients (19 boys and 28 girls; median age, 60 days) were included in the study. Among the 47 patients, 27 (11 boys and 16 girls; median age, 63 days) underwent transient elastography with an M probe, which is used for the general adult population, whereas 20 (8 boys and 12 girls; median age, 49 days) were analyzed with an S probe, which is specific to children, as it only became available after July 2009.

Routine biochemical studies, including measurement of total and direct serum bilirubin levels, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and γ-glutamyl transferase (GGT), were performed for all patients. Reference ranges for blood sample parameters used by our institution were as follows: 0.2 to 1.2 mg/dL for total bilirubin, 0.1 to 0.4 mg/dL for direct bilirubin, 13 to 34 IU/L for AST, 5 to 46 IU/L for ALT, 60 to 300 IU/L for ALP, and 12 to 54 IU/L for GGT.

Sonographic Measurements

One pediatric radiologist (M.-J.K., with >15 years of experience in pediatric sonography) performed sonographic examinations in all patients using 5–8-MHz curved linear and 5–12-MHz linear transducers (HDI 5000 and iU22, respectively; Philips Healthcare, Bothell, WA). Patients had not been fed for at least 4 hours before sonography. In a longitudinal scan, the triangular cord thickness was measured as the thickness of the echogenic anterior wall of the right portal vein just proximal to the right portal vein bifurcation site.10 We also evaluated the diameter of the proper hepatic artery, which runs parallel to the main portal vein, as well as the portal vein diameter at a level proximal to the portal vein bifurcation.

Transient Elastographic Measurements

An experienced sonographer performed transient elastography (FibroScan 502) under the supervision of a gastroenterologist (H.K.). The probe was placed between the two ribs in the intercostal position in proximity to the right lobe of the liver with the patients in the supine position with maximal abduction of the right arm. A minimum liver parenchymal thickness of 6 cm and a maximum distance of 2.5 cm between the liver and the probe were accepted as suitable probe placement. The elasticity was measured at a depth of 25 to 65 mm under the skin surface with the adult M probe, which was used until June 2009. The M probe operates at a frequency of 3.5 MHz. The measurement volume, which consisted of a diameter of 1 cm and a
length of 4 cm, was located in an area that was free of large vessels with the assistance of M- and A-mode sonograms (Figure 2). We used the pediatric S probe after July 2009. The transducer of the S probe operates at an increased frequency of 5 MHz and is smaller than the M probe, allowing access to the narrower intercostal spaces of smaller chests and enabling adapted measurements in children. Depth calculations were performed at 15 to 50 mm for the smaller livers of the children.

Transient elastographic results are expressed in kilopascals. Measurements can be invalid if the probe is placed incorrectly above the rib or lung; the elastographic instrument automatically indicates whether these measurements are valid or invalid. The manufacturer recommends that 10 valid measurements should be obtained for each patient to establish reliable measurements. The median value of the 10 valid measurements is considered representative of liver stiffness. The success rate is defined as the number of valid measurements divided by the total number of measurements. An examination is considered reliable when the success rate is greater than 60% and the interquartile range is less than one-third of the median value. As mentioned above and proposed by Kettaneh,19 however, we considered an examination acceptable if at least 5 valid measurements were obtained.

Figure 1. FibroScan instrument (A) and probes (B; top, M probe; bottom, S probe).13
Histologic Assessment
All infants (n = 47) with biliary atresia underwent portoenterostomy with liver biopsy (n = 46) or liver transplantation (n = 1). One pathologist (Y.N.P., with >10 years of experience) performed histopathologic examinations of specimens. The liver fibrosis stage was determined according to the METAVIR 5-point (F0–F4) scoring system as follows: stage F0, no fibrosis (n = 0); F1, mild fibrosis (portal fibrosis without septa; n = 1); F2, substantial fibrosis (portal fibrosis and a few septa; n = 27); F3, severe fibrosis (numerous septa without cirrhosis; n = 14); and F4, cirrhosis (n = 5).

Statistical Analysis
The Kolmogorov-Smirnov test was used to determine whether data were normally distributed. Accordingly, data that did or did not show a normal distribution were presented as mean ± standard deviation or median, and quantitative variables were compared by either an unpaired t test or a Mann-Whitney test, respectively. Correlations between transient elastographic and sonographic measurements and histologic fibrosis stages were analyzed by Spearman or Pearson correlation coefficients when appropriate. We assessed diagnostic performance by using receiver operating characteristic curves. Area under the curve (AUC) values with 95% confidence intervals were calculated by the method developed by Hanley and McNeil.20 In addition, receiver operating characteristic curves for the M and S elastographic probes were directly compared. P < .05 indicated a significant correlation or difference. A Multivariate regression test was used to evaluate whether any clinical or laboratory variables affected the diagnostic performance of transient elastography. Data management and statistical calculations were performed with SPSS version 19 software (IBM Corporation, Armonk, NY) and MedCalc Version 9.5.0.0 software (MedCalc Software, Mariakerke, Belgium).

Results
Between April 2007 and July 2010, 47 patients met the inclusion criteria for our study. Among these patients, 27 and 14 had METAVIR fibrosis stages of 2 and 3, respectively, and 1 and 5 had stages 1 and 4.

Figure 2: M-mode (left) and A-mode (center) images and elastogram (right) displayed on the transient elastographic screen during liver stiffness measurement. A steeper slope in the elastogram indicates faster shear wave propagation and increased liver stiffness.
fibrosis (F3) and cirrhosis (F4) were significantly older than the patients with substantial fibrosis (F2; Table 1).

The total and direct bilirubin, ALT, and AST levels were not significantly different between each fibrosis group. The ALP and GGT levels were significantly higher in patients with severe fibrosis (F3) compared to patients with substantial fibrosis (F2) but tended to decrease in patients with cirrhosis (F4; Table 1).

The success rates of transient elastography were significantly different between the M- and the S-probe groups. Specifically, the success rate was higher in the S-probe group (100%) than the M-probe group (77%; P < .001; Table 2).

The transient elastographic values were 10.3, 6.5, 12.0, and 34.9 kPa for F1, F2, F3, and F4, respectively (Table 3). Only the transient elastographic measurements were significantly positively correlated with METAVIR fibrosis stages (ρ = 0.63; P < .001), whereas the triangular cord thickness and hepatic artery and portal vein diameters were not (Figure 3).

The performance of transient elastography was excellent (A_z = 0.96) for diagnosis of cirrhosis (F4) and good (A_z = 0.86) for diagnosis of severe fibrosis (≥F3). The cutoff values of transient elastography were greater than 9.6 kPa (sensitivity, 89.5%; specificity, 75%) and greater than 18.1 kPa (sensitivity, 100%; specificity, 90.5%) for diagnosis of severe fibrosis (≥F3) and cirrhosis (F4), respectively. The A_z value of the S probe (0.93) was higher than that of the M probe (0.85) with respect to predicting severe fibrosis (≥F3), although this difference did not reach statistical significance. The A_z value of the S probe (0.94) was compatible with that of the M probe (0.96) in predicting cirrhosis (F4; Figures 4 and 5 and Table 4). Multivariate regression showed that with the exception of the histologic fibrosis stage (β = 8.01; P = .001), age was the only parameter that had an independent effect on the performance of transient elastography (β = 0.16; P = .001).

### Table 1. Clinical and Laboratory Features of the Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients (n = 47)</th>
<th>F1 (n = 1)</th>
<th>F2 (n = 27)</th>
<th>F3 (n = 14)</th>
<th>F4 (n = 5)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female, n</td>
<td>39/28</td>
<td>0/1</td>
<td>10/17</td>
<td>8/6</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Age, d</td>
<td>60 (9.5–179.2)</td>
<td>78</td>
<td>42</td>
<td>71.5</td>
<td>116</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>8.4 ± 2.4</td>
<td>8.3</td>
<td>8.5</td>
<td>9.0</td>
<td>9.7</td>
<td>NS</td>
</tr>
<tr>
<td>Direct bilirubin, mg/dL</td>
<td>6.75 ± 2.0</td>
<td>6.7</td>
<td>6.6</td>
<td>7.5</td>
<td>7.4</td>
<td>NS</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>185.0 (12–11.6)</td>
<td>263</td>
<td>148</td>
<td>215</td>
<td>270</td>
<td>NS</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>142.0 (40.7–908.9)</td>
<td>168</td>
<td>88</td>
<td>254.5</td>
<td>195</td>
<td>NS</td>
</tr>
<tr>
<td>ALP, IU/L</td>
<td>559.0 (241–1759.0)</td>
<td>705</td>
<td>496</td>
<td>763.5</td>
<td>479</td>
<td>0.15</td>
</tr>
<tr>
<td>GGT, IU/L</td>
<td>582 ± 390.7 (102–16270)</td>
<td>1119</td>
<td>368</td>
<td>802</td>
<td>430</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Data are presented as median (95% central range) and mean ± SD (range) where applicable. NS indicates not significant (P > .05).

### Table 2. Transient Elastographic Measurements for All Patients and M- and S-Probe Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients (n = 47)</th>
<th>M Probe (n = 27)</th>
<th>S Probe (n = 20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stiffness, kPa</td>
<td>10.2</td>
<td>10.2</td>
<td>10.0</td>
<td>NS</td>
</tr>
<tr>
<td>Valid measurements, n</td>
<td>9.2 ±2.5</td>
<td>9.2 ± 1.7</td>
<td>9.3 ±3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Success rate, %</td>
<td>85</td>
<td>77</td>
<td>100</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>2.8</td>
<td>2.8</td>
<td>2.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are presented as median and mean ± SD where applicable. NS indicates not significant (P > .05).
Table 3. Transient Elastographic and Sonographic Measurements for Each Fibrosis Stage

<table>
<thead>
<tr>
<th>Parameter</th>
<th>F1 (n = 1)</th>
<th>F2 (n = 27)</th>
<th>F3 (n = 14)</th>
<th>F4 (n = 5)</th>
<th>P</th>
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<tr>
<td>Elastography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiffness, kPa</td>
<td>10.3</td>
<td>6.5</td>
<td>12.0</td>
<td>34.9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Valid measurements, n</td>
<td>11</td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>Success rate, %</td>
<td>100</td>
<td>89</td>
<td>83</td>
<td>100</td>
<td>NS</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>3.6</td>
<td>1.8</td>
<td>5.5</td>
<td>12.3</td>
<td>0.003</td>
</tr>
<tr>
<td>Sonography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triangular cord thickness, mm</td>
<td>4.8</td>
<td>5</td>
<td>4.7</td>
<td>6.5</td>
<td>NS</td>
</tr>
<tr>
<td>Hepatic artery diameter, mm</td>
<td>1.9</td>
<td>2.4</td>
<td>2.5</td>
<td>2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Portal vein diameter, mm</td>
<td>4.3</td>
<td>4.5</td>
<td>4.3</td>
<td>4.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are presented as median where applicable. NS indicates not significant (P > .05).

Figure 3. Scatterplots for transient elastography (A), triangular cord thickness (B), hepatic artery diameter (C), and portal vein diameter (D) at each fibrosis stage. The transient elastographic measurements correlated positively with fibrosis stages (ρ = 0.63; P < .001): the stiffer the liver, the higher the fibrosis stage. None of the sonographic findings correlated with fibrosis stages.
Discussion

Liver fibrosis is a common feature in biliary atresia and the most important prognostic factor in predicting the outcome after portoenterostomy: patients with biliary atresia and severe fibrosis or cirrhosis at portoenterostomy have been shown to have poor outcomes.5,6,21 The pathogenesis of liver fibrosis in biliary atresia is still unknown. In addition to cholestasis from bile duct obliteration, several novel hypotheses have been proposed, including recurrent cholangitis or involvement of oxidative stress.22 Liver fibrosis can be progressive even after portoenterostomy and is associated with complications such as portal hypertension and esophageal and gastric varices, which can be life threatening. Patients with severe fibrosis or cirrhosis at diagnosis of biliary atresia might benefit from early liver

Figure 4. Receiver operating characteristic curves for transient elastography in all patients (A), the M-probe group (B), and the S-probe group (C) for diagnosis of severe fibrosis (≥F3). The A\textsubscript{z} value of transient elastography for predicting severe fibrosis was 0.86. The A\textsubscript{z} value of the S probe (0.93) was higher than that of the M probe (0.85) for predicting severe fibrosis, although the difference did not reach the level of statistical significance.
transplantation over portoenterostomy. Patients with milder stages of fibrosis can be candidates for new therapies such as anti-inflammatory and anti-fibrotic therapies to prevent progression of liver fibrosis after portoenterostomy. Moreover, identification of the stage of liver fibrosis can help predict the prevalence of associated complications postoperatively. Therefore, it is important to monitor the degree of liver fibrosis in biliary atresia both before and after portoenterostomy.

Liver biopsy remains the reference standard for evaluation of liver fibrosis, but it has several shortcomings, such as invasiveness, sampling errors, and interobserver variability. Therefore, when used as a monitoring tool, liver biopsy can be problematic. As a result of these limitations,
considerable efforts have focused on identifying and validating noninvasive methods for assessing liver fibrosis. One promising method is transient elastography, which was shown in a recent meta-analysis to have excellent diagnostic accuracy in predicting cirrhosis but to have less accuracy in predicting less-severe fibrosis.14 To date, only a few studies on the use of transient elastography in children have been performed, which evaluated the feasibility of transient elastography and compared it with surrogate serum fibrosis markers such as the FibroTest (BioPredictive, Paris, France) and the aspartate transaminase-to-platelet ratio index.16–18 They suggested that transient elastography is feasible in children, with the highest diagnostic accuracy of 0.88 for diagnosis of cirrhosis. However, they studied children across a wide range of ages (2 months to 20 years) that had mixed etiologies of chronic liver diseases. Menten et al17 prospectively compared transient elastography and sonography in children and adults with only cystic fibrosis–associated liver disease and suggested that transient elastography is an attractive and noninvasive method for assessing and monitoring liver disease in patients with cystic fibrosis. However, their study did not include histologic evaluation as a reference standard. Nobili et al18 also evaluated the performance of transient elastography compared with histologic fibrosis stages in pediatric patients with nonalcoholic steatohepatitis and reported that transient elastography had excellent diagnostic accuracy. Their study group also included patients from a wide age range (4–17 years). Last, Chang et al23 evaluated transient elastography as a pre-endoscopic screening tool in postoperative patients with biliary atresia, but that study did not focus on examining the degree of liver fibrosis.

In our study, transient elastography was excellent (A_{z} = 0.96) for diagnosing cirrhosis (F4) but less accurate (A_{z} = 0.86) for diagnosing severe fibrosis (≥F3), which was consistent with the findings of previous studies. The cutoff values of transient elastography for predicting severe fibrosis and cirrhosis reported in previous studies varied, ranging from 7.9 to 11 and 11.0 to 25.8 kPa, respectively.24–29 In our study, the cutoff values for diagnosis of severe fibrosis and cirrhosis were greater than 9.6 and greater than 18.1 kPa, which were comparable with values in previous studies.16,30 Because most patients with biliary atresia had stage F2 fibrosis or higher, we could not evaluate the diagnostic performance of transient elastography for predicting substantial fibrosis (≥F2).

The positive relationship between transient elastographic measurements and the degree of necroinflammatory activity, which is represented as the ALT level, has been well described mostly in adult patients with viral hepatitis.31–34 In our study, ALT levels did not show a significant difference between fibrosis groups and did not have an independent effect on transient elastographic measurements in the multivariate logistic analysis. We were unable to investigate the basis of differences between our results and those of previous studies because of a lack of available histologically based assessments of the degree of necroinflammatory activity as well as an insufficient number of patients, especially in the normal, mild fibrosis (F1), and cirrhosis (F4) groups, in our retrospective study. Thus, a larger-scale, histologically based study is needed.

Nobili et al18 reported that there was no relationship between age and liver stiffness in both control study participants and patients with cystic fibrosis. On the other hand, Roulot et al35 performed transient elastography in 429 healthy study participants with a mean age of 45.1 years, and their results showed that mean liver stiffness values tended to increase with age. To the best of our knowledge, however, there has been no related study per-

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients (n = 47)</th>
<th>M Probe (n = 27)</th>
<th>S Probe (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe fibrosis (≥F3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A_{z}</td>
<td>0.86 (0.73–0.94)</td>
<td>0.85 (0.67–0.96)</td>
<td>0.93 (0.72–0.99)</td>
</tr>
<tr>
<td>Cutoff, kPa</td>
<td>&gt;9.6</td>
<td>&gt;9.6</td>
<td>&gt;10.3</td>
</tr>
<tr>
<td>SN/SP/PPV/PPV, %</td>
<td>89.5/75/80.8/91.3</td>
<td>84.6/78.6/78.6/84.6</td>
<td>100/78.6/66/78.5</td>
</tr>
<tr>
<td>Cirrhosis (F4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A_{z}</td>
<td>0.96 (0.85–0.99)</td>
<td>0.96 (0.81–0.99)</td>
<td>0.94 (0.74–0.99)</td>
</tr>
<tr>
<td>Cutoff, kPa</td>
<td>&gt;18.1</td>
<td>&gt;18.1</td>
<td>&gt;18.1</td>
</tr>
<tr>
<td>SN/SP/PPV/PPV, %</td>
<td>100/90.5/55.6/100</td>
<td>100/92/50/100</td>
<td>100/88.2/60/100</td>
</tr>
</tbody>
</table>

Values in parentheses are 95% confidence intervals. NPV indicates negative predictive value; PPV, positive predictive value; SN, sensitivity; and SP, specificity.
formed in an infant group younger than 1 year, and this study may be the first in that age group. Our results showed that age (β = 0.16; P = .001) had a significant effect on transient elastography, even though our patients were confined to a very narrow age range. However, to confirm our results, a study with healthy controls in the same age range should be performed.

According to de Lédinghen et al., there are some limitations associated with using the M probe for transient elastography in children. Because children have smaller livers, the depth of measurement should be adapted. Likewise, because of narrow intercostal spaces, the transducer may push not only soft tissues but also the ribs, causing several shear waves. As a result, a faster band corresponding to propagation of the wave into interferences can lead to an overestimation of liver stiffness. Therefore, the S probe was developed for children, who have narrower intercostal spaces and smaller livers. The S probe operates at a higher frequency (5 MHz) and has a measurement depth of 15 to 50 mm. In our institution, the S probe became available in July 2009, and all patients in this study underwent transient elastography with the S probe from that time. The success rate of the S probe (100%) was significantly higher than that of the M probe (77%). Likewise, the diagnostic accuracy of the S probe predicting severe fibrosis tended to be higher than that of the M probe, although this difference did not reach the level of statistical significance.

The triangular cord sign on sonography is an important component for diagnosis of biliary atresia, as it represents congenital fibrous ductal remnants in the porta hepatis. Ohi and Ibrahim divided surgical morphologic findings into several types according to the pattern of hepatic radicles at the porta hepatis in patients with biliary atresia: namely, triangular cone-shaped fibrous masses (67%), fibrous hepatic ducts (15%), aplasia of hepatic ducts (6%), dilated hepatic ducts (5%), hypoplastic hepatic ducts (4%), and bile lakes (3%). The most common type, a fibrous mass, shows the triangular cord sign on sonography, whereas the others do not show that sign. In biliary atresia, because the triangular cord thickness is influenced primarily by the morphologic type of congenital fibrous ductal remnants, the degree of fibrosis is of little importance to the triangular cord thickness. Likewise, the triangular cord thickness was not significantly correlated with METAVIR fibrosis stages in our study.

Burgener et al. observed an increase in the number and diameter of hepatic arterial branches in patients with advanced hepatic fibrosis. Some authors have described hyperplastic and hypertrophied hepatic arteries in patients with biliary atresia, which may represent changes to compensate for the diminished portal vein flow in advanced liver fibrosis or a manifestation of ductal plate malformation, although its exact pathogenesis remains uncertain.

Therefore, an enlarged hepatic artery cannot be explained only by liver fibrosis, especially in patients with biliary atresia, and our results showed no significant correlation between the diameter of the hepatic artery and histologic fibrosis stages. Likewise, the portal vein diameter was not correlated with histologic fibrosis stages. The portal vein diameter may increase or decrease depending on hepatopetal or hepatofugal blood flow, respectively, which could explain our results.

There were several limitations to our study. First, the study was performed retrospectively; thus, we did not have access to data on infants without liver disease as a control group. As a consequence, we had to compare our results with those of previous studies that were performed with adult patients. As mentioned above, age can alter transient elastographic values within the same histologic fibrosis stage. A larger-scale study is necessary to establish normal values in infants. Another limitation of our study was that we did not obtain information about the degree of necroinflammatory activity or cholestasis on histologic liver analysis, which may have led to an overestimation of liver stiffness. Laboratory data such as ALT, which is a poor marker of inflammation, cannot accurately reflect factors influencing liver stiffness other than fibrosis. Therefore, a histologically based analysis is needed to clarify other potential factors affecting liver stiffness. An additional limitation was the small number of patients with no fibrosis (F0), mild fibrosis (F1), and cirrhosis (F4). As a result, we were unable to obtain reliable data from these patient groups.

In conclusion, transient elastography can be used as a noninvasive method for the diagnosis of severe fibrosis and cirrhosis in infants with biliary atresia. The degree of liver fibrosis is the major prognostic factor in predicting the outcome following portoenterostomy. Therefore, transient elastography may help predict the therapeutic outcome before invasive liver biopsy or surgical management, suggesting more effective treatment options. The S probe, which is specific to children, may increase the success rate of transient elastography in infants with biliary atresia. Further evaluation is needed to determine the effects of the S probe on the diagnostic accuracy of transient elastography for assessing the degree of liver fibrosis in infants with biliary atresia and controls. Sonographic findings, including the triangular cord thickness and hepatic artery and portal vein diameters, were not useful for predicting liver fibrosis in infants with biliary atresia.
References


Shin et al—Prediction of Liver Fibrosis in Infants With Biliary Atresia


