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Pre- and Immediate Post-Kasai Portoenterostomy Shear Wave Elastography for Predicting Hepatic Fibrosis and Native Liver Outcomes in Patients With Biliary Atresia

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Objective: To evaluate the feasibility of ultrasound shear wave elastography (SWE) for predicting hepatic fibrosis and native liver outcomes in patients with biliary atresia.

Materials and Methods: This prospective study included 33 consecutive patients with biliary atresia (median age, 8 weeks [interquartile range, 6–10 weeks]; male:female ratio, 15:18) from Severance Children's Hospital between May 2019 and February 2022. Preoperative (within 1 week from surgery) and immediate postoperative (on postoperative days [PODs] 3, 5, and 7) ultrasonographic findings were obtained and analyzed, including the SWE of the liver and spleen. Hepatic fibrosis, according to the METAVIR score at the time of Kasai portoenterostomy and native liver outcomes during postsurgical follow-up, were compared and correlated with imaging and laboratory findings. Poor outcomes were defined as intractable cholangitis or liver transplantation. The diagnostic performance of SWE in predicting METAVIR F3–F4 and poor hepatic outcomes was analyzed using receiver operating characteristic (ROC) analyses.

Results: All patients were analyzed without exclusion. Perioperative advanced hepatic fibrosis (F3–F4) was associated with older age and higher preoperative direct bilirubin and SWE values in the liver and spleen. Preoperative liver SWE showed a ROC area of 0.806 and 63.6% (7/11) sensitivity and 86.4% (19/22) specificity at a cutoff of 17.5 kPa for diagnosing F3–F4. The poor outcome group included five patients with intractable cholangitis and three undergoing liver transplantation who showed high postoperative liver SWE values. Liver SWE on PODs 3–7 showed ROC areas of 0.783–0.891 for predicting poor outcomes, and a cutoff value of 10.3 kPa for SWE on POD 3 had 100% (8/8) sensitivity and 73.9% (17/23) specificity.

Conclusion: Preoperative liver SWE can predict advanced hepatic fibrosis, and immediate postoperative liver SWE can predict poor native liver outcomes in patients with biliary atresia.

Keywords: Biliary atresia; Children; Liver; Ultrasound; Elastography

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INTRODUCTION

Biliary atresia is a rare but severe fibroinflammatory disease of the bile duct. Even with Kasai portoenterostomy (KPE), which is available as a treatment option for the long-term survival of the native liver, biliary atresia can progress to liver cirrhosis and is the most common indicator of pediatric liver transplantation. Therefore, early diagnosis, proper management, and regular follow-up with appropriate monitoring are crucial for the treatment of this rare disease.

Ultrasonography is the primary imaging modality used to evaluate neonatal cholestasis, including biliary atresia. Well-known imaging findings of biliary atresia include triangular cord sign, abnormal gallbladder morphology, non-visualization of the common bile duct, presence of hepatic subcapsular flow, presence of microcysts or macrocysts near the porta hepatis, and increased hepatic artery diameter [1-3]. However, ultrasonography may not show extrahepatic bile ducts well in normal newborns, and some extrahepatic bile ducts may be visible depending on the subtype of biliary atresia [4]. After KPE, follow-up imaging studies are performed to track the progression of hepatic fibrosis and the development of complications such as cholangitis.

Recent advances in ultrasound-based technology, especially shear wave elastography (SWE), have provided a noninvasive and easy-to-use approach for measuring liver stiffness. A few small cohort studies have assessed liver SWE in children with neonatal jaundice and found SWE to have potential value in differentiating biliary atresia from neonatal hepatitis [5-7]. However, liver SWE alone is less predictive than grayscale imaging. Adding liver SWE can help diagnose patients when grayscale images are equivocal to biliary atresia [8]. However, liver SWE can diagnose liver cirrhosis before KPE [9] and is thought to be another promising indicator of prognosis during postoperative surveillance of biliary atresia [10,11]. Spleen SWE has also been used as a potential marker of liver fibrosis and esophageal varices after KPE. Spleen SWE is reportedly the most accurate predictor of high-risk esophagogastric varices in children with biliary atresia [12]. However, studies on the diagnostic value of liver and spleen SWE in predicting fibrosis grade and the clinical impact of immediate postoperative findings are limited.

Traditionally, the early outcomes of KPE are best estimated by a postoperative decrease in serum total bilirubin within 3 months postoperatively [13-15]. However, various clinical parameters, such as perioperative age and degree of hepatic fibrosis and repeated or intractable cholangitis, enable a more accurate prediction of long-term native liver survival [16]. Moreover, several noninvasive combinations of serum markers, such as the aspartate aminotransferase-to-platelet ratio index (APRI), have been utilized to predict the timeframe of end-stage liver disease in subsets of pediatric patients with chronic liver disease, even with inconsistent results [14,17-19].

Better management and treatment of biliary atresia requires noninvasive means of diagnosing hepatic fibrosis preoperatively and during follow-up to predict outcomes as early as possible. However, no study has predicted the prognosis by analyzing the changes in liver SWE as soon as possible after surgery. Therefore, this study aimed to evaluate the feasibility of ultrasonographic imaging studies with liver and spleen SWE and laboratory findings for predicting hepatic fibrosis and the outcomes of the native liver in patients with biliary atresia.

MATERIALS AND METHODS

Patients

The ethics committee of Severance Children's Hospital approved this prospective study, and written informed consent was obtained from the guardians of all participants. Between May 2019 and February 2022, all consecutive patients who were diagnosed with biliary atresia under 6 months of age were prospectively enrolled in this study. The exclusion criteria were as follows: 1) neonatal cholestasis other than biliary atresia and 2) other recent diseases, such as acute febrile illness, which could affect biochemical parameters other than biliary atresia.

Examination Protocol

All patients underwent routine laboratory and ultrasonographic examinations to diagnose biliary atresia. Sex and age at the time of surgery were documented. Among the laboratory results, gamma-glutamyl transferase (GGT) and direct bilirubin levels were recorded. In our hospital, the imaging protocol after KPE is abdominal ultrasonography 1 week and 6 months postoperatively. In this study, SWE imaging at 3 and 5 days after surgery were added to evaluate liver and spleen elasticity changes immediately after surgery. Preoperative SWE was performed within 1 week postoperatively, and we used the laboratory results from the day of preoperative SWE for preoperative analyses. The grade of pathologic hepatic fibrosis at the time of KPE was

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recorded based on the METAVIR scoring system as follows: F0, no portal fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with rare septa; F3, numerous septa or lobular distortion without cirrhosis; and F4, cirrhosis. Advanced hepatic fibrosis was defined when the liver was classified as F3 or F4. All patients also underwent repeated postoperative abdominal ultrasonography on the third, fifth, and seventh postoperative days (PODs 3, 5, and 7, respectively) to record immediate postoperative findings. Follow-up ultrasonography was also performed 6 months after KPE.

During follow-up, liver-related events, such as prolonged jaundice, cholangitis, ascites, gastrointestinal bleeding, hepatic encephalopathy, liver transplantation, and death, were also recorded. Since recurrent cholangitis is associated with the accelerated development of liver fibrosis and other severe complications [20,21], a poor outcome for the native liver was defined when a patient developed intractable cholangitis or underwent liver transplantation during follow-up. Intractable cholangitis was defined as recurrent cholangitis with 1) hospitalization of 1 month or longer required to treat the cholangitis and 2) three consecutive hospitalizations for cholangitis at intervals of less than 1 month between the previous discharge and readmission [22].

Ultrasonography Including SWE

Infants were fasted for at least 4 hours before imaging with an Aixplorer scanner (Supersonic Imagine). On grayscale ultrasonography, spleen size and any structural abnormalities, such as intrahepatic cystic lesions or masses, were recorded. Liver and spleen SWE was performed with a linear array transducer (SL10–2) in free-breathing status by three dedicated pediatric radiologists with more than 3 years of experience in elastography. SWE was performed in dual mode (i.e., elastograms displayed alongside grayscale sonograms in real-time). For liver SWE, the probe was placed using a right intercostal approach and the operator chose the best static SWE display images and a fixed circular region of interest (ROI) (diameter 4 mm) within the center of the rectangular ROI, at least 2 cm deep to the liver capsule, avoiding vessels and areas of artifacts (Fig. 1). For spleen SWE, the same fixed circular ROI was used and positioned at least 0.5 cm away from the spleen capsule. A successful SWE was defined as an ROI box that could be filled with over 90% color of the box. Seven measurements were performed [23], and the mean value of each organ was used in the analysis. Temporary bottle feeding was performed to soothe patients who were too irritable for SWE acquisition.

Statistical Analyses

Descriptive statistics were obtained for the demographic, clinical, and laboratory findings. Quantitative variables were expressed as medians and interquartile ranges (25th–75th percentile). Qualitative variables were summarized as counts and percentages.

The Mann-Whitney U test or Kruskal-Wallis test was used for non-parametric group comparison. Kendall's Tau correlation was performed to evaluate the correlation between hepatic fibrosis grade and other parameters. Spearman's rank coefficient was used to test the correlation between two study variables, and partial correlation analyses were performed to remove the effects of other variables. The diagnostic performance and cutoff values for advanced

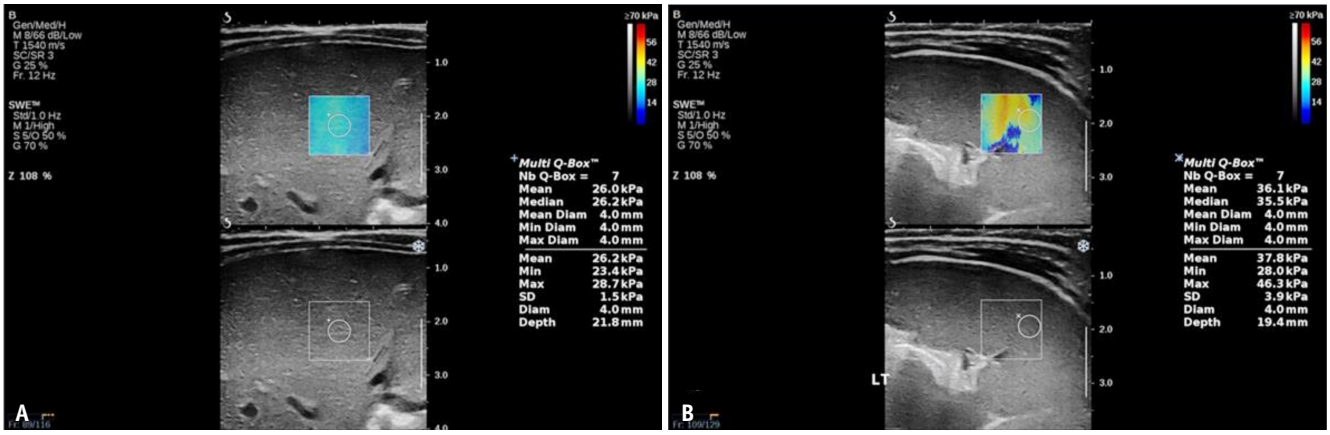

Fig. 1. Two-dimensional shear wave elastography (SWE) images of an 11-week male infant with biliary atresia before operation. Ultrasound images of **(A)** liver and **(B)** spleen SWE. **A:** The stiffness color map (top) was relatively homogenous, and the mean SWE value of the region of interest (bottom) was 26.0 kPa. **B:** For the spleen, the stiffness color map (top) was rather heterogeneous, and the mean SWE was 36.1 kPa. The histological stage of liver fibrosis in infants was F3. SD = standard deviation

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hepatic fibrosis (F3–F4) and poor outcomes were assessed using receiver operating characteristic (ROC) curves and the Youden index. The area under the ROC curve (AUROC) was compared pairwise.

A linear mixed model was used to compare changes in the liver and spleen SWE measurement over time between the poor and good outcome groups. Liver and spleen SWE between each time point were compared by pairwise comparison of time using post-hoc analyses with estimated means. Due to the exploratory nature of this study, *P*-values were not adjusted for a potential increase in type 1 error when performing post hoc analyses. The trends of liver and spleen SWE were also analyzed over time using a regression equation.

Data analyses were performed using SPSS version 26 (IBM Corp.), MedCalc Statistical Software version 19.3.1 (MedCalc Software Ltd.), and R version 4.1.1. (R Foundation for Statistical Computing, Vienna, Austria). *P*-values < 0.05 were considered statistically significant.

RESULTS

Patient Characteristics

Thirty-three patients were enrolled and analyzed. The clinical characteristics of the patients are summarized in Table 1. The study included 15 boys and 18 girls. The mean perioperative age was 2–13 weeks. For the fibrosis stage, no (0%) patients with F0, 2 (6.1%) with F1, 20 (60.6%) with F2, 10 (30.3%) with F3, and 1 (3.0%) with F4 were identified. Patients were followed-up for 2–35 months postoperatively, with a median duration of 13 months.

Four patients were followed-up for less than 6 months. Therefore, all 33 patients underwent immediate postoperative SWE examinations, and only 29 patients underwent SWE examinations 6 months postoperatively (Table 1). Follow-up SWE was performed in all patients without measurement failure. During follow-up, 14 patients (42.4%) developed cholangitis, including five patients with intractable cholangitis. Three additional patients underwent liver transplantation at the ages of 6, 9, and 11 months, one of whom expired within a month of liver transplantation.

Predicting Hepatic Fibrosis

In the correlation analyses, the stage of hepatic fibrosis positively correlated with the age at the time of surgery (tau = 0.331, *P* = 0.025), preoperative direct bilirubin (tau = 0.341, *P* = 0.017), and preoperative liver SWE (tau = 0.369, *P* = 0.010). However, these parameters did not correlate significantly with the fibrosis stage after adjusting for age at the time of surgery. The advanced hepatic fibrosis group also showed higher values for age at the time of surgery, preoperative direct bilirubin, and liver and spleen SWE (Table 1).

On ROC analyses, age at the time of surgery, direct bilirubin level, and preoperative liver and spleen SWE showed good diagnostic performance for advanced hepatic fibrosis (Table 2). The AUROC was 0.762 (95% confidence interval [CI]: 0.583–0.893) for age at the time of surgery with a cutoff value of 7 weeks, 0.798 (95% CI: 0.622–0.917) for direct bilirubin, 0.806 (95% CI: 0.631–0.922) for preoperative liver SWE with a cutoff value of 17.5, and 0.756 (95% CI: 0.554–0.899) for preoperative spleen SWE (Fig. 2). The diagnostic performance for advanced hepatic fibrosis did not differ among the parameters. All *P*-values were > 0.05 (0.253–0.951).

Predicting Poor Liver Outcomes

The poor outcome group included five patients with intractable cholangitis and three patients who underwent liver transplantation. Only the values for liver SWE on the immediate postoperative days differed between the two outcome groups (Table 1). Perioperative age and hepatic fibrosis grade, preoperative liver SWE, preoperative and immediate postoperative spleen SWE, and laboratory values, including direct bilirubin, were not different between patients with poor and good outcomes. The SWE of the liver and spleen and laboratory values 6 months postoperatively also did not differ between the two outcome groups.

On ROC analyses, liver SWE on POD 3, 5, and 7 showed good diagnostic performance for predicting poor outcomes (Table 3, Fig. 3 and 4). The AUROC was 0.891 (95% CI: 0.727–0.974) for liver SWE on POD 3, 0.783 (95% CI: 0.598–0.910) on POD 5, and 0.881 (95% CI: 0.718–0.968) on POD 7 (Fig. 5). A cutoff value of 10.3 kPa for liver SWE on POD 3 showed 100% sensitivity and 73.9% specificity. A cutoff value of 11.4 kPa for liver SWE on POD 5 showed 75% sensitivity and 73.9% specificity. The predictive performance for poor outcomes did not differ between parameters. All *P*-values were > 0.05 (0.214–0.671) (Fig. 5).

Comparison of Liver and Spleen SWE Measurements Over Time between Poor and Good Outcomes

Liver SWE showed a significant decrease from the preoperative value to POD 3 in the good outcome group (estimated mean, 13.8–9.6 kPa, *P* = 0.025) (Supplementary Fig. 1). However,

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Table 1. A Comparison of Demographics, Laboratory and Imaging Findings between Patients with Hepatic Fibrosis of Low Grade (F0–F2) and High Grade (F3–F4) at the Time of Operation and between Patients with Good Outcome and Poor Outcome during Follow-up

	All Patients	Fibrosis Group			Outcome Group		
		F0–F2	F3–F4	*P*	Good	Poor	*P*
Number of patients	33	22	11		25	8	
Sex (boy:girl)	15:18	11:11	4:7	0.534	14:11	1:7	0.067
Age at the time of operation, wk	8.0 (6.0–10.0)	7.0 (5.8–10.0)	9.0 (8.0–11.0)	0.014*	7.0 (6.0–10.0)	9.5 (8.0–10.8)	0.107
Direct bilirubin at diagnosis, μmol/L	5.7 (4.4–7.2)	5.1 (4.0–6.5)	6.9 (5.7–8.3)	0.005*	5.2 (4.4–6.8)	7.1 (5.5–7.8)	0.117
Gamma-glutamyl transferase at diagnosis, U/L	428.0 (209.5–686.5)	422.5 (228.3–640.8)	511.0 (128.0–698.0)	0.807	421.0 (192.5–653.5)	511.0 (235.3–729.5)	0.420
METAVIR fibrosis stage (F1, F2, F3, F4)	2, 20, 10, 1				2, 17, 5, 1	0, 3, 5, 0	0.138
Follow-up length, month	11.0 (5.0–17.5)	10.5 (3.0–16.8)	14.0 (10.0–21.0)	0.418	10.0 (3.0–20.0)	14.0 (10.0–15.5)	0.522
Liver SWE, kPa							
Preoperative	13.9 (10.1–19.4)	11.6 (8.3–16.2)	18.4 (13.9–26.0)	0.004*	12.9 (8.5–17.9)	17.5 (12.9–23.7)	0.081
POD 3	10.2 (6.5–17.4)				7.5 (6.3–12.0)	18.0 (12.5–19.8)	0.001*
POD 5	10.7 (8.5–15.9)				9.4 (8.0–12.5)	15.3 (11.1–21.4)	0.018*
POD 7	11.5 (8.9–17.9)				9.9 (7.8–13.5)	17.0 (12.3–23.7)	0.013*
POD 180 (n = 29)	22.9 (11.4–26.4)				17.9 (9.6–25.6)	25.6 (18.6–37.7)	0.135
Spleen SWE, kPa							
Preoperative	24.3 (19.5–29.0)	22.0 (19.3–26.3)	27.1 (23.4–34.4)	0.031*	24.2 (19.4–30.4)	24.5 (21.7–26.6)	0.755
POD 3	24.4 (20.4–27.4)				24.4 (19.0–26.8)	25.3 (22.1–27.4)	0.674
POD 5	23.7 (20.3–30.6)				22.7 (18.6–29.1)	24.7 (22.5–31.3)	0.200
POD 7	24.3 (19.5–30.8)				23.3 (19.3–30.0)	30.7 (21.5–31.1)	0.144
POD 180 (n = 29)	20.8 (21.2–39.8)				30.2 (20.0–36.0)	36.5 (26.9–43.5)	0.154
Direct bilirubin, μmol/L							
POD 3	5.5 (4.3–6.9)				5.8 (4.4–6.9)	5.6 (4.5–8.7)	0.550
POD 5	6.0 (4.4–7.9)				5.8 (4.6–7.7)	6.6 (4.1–10.4)	0.374
POD 7	5.4 (4.2–6.9)				5.0 (4.3–6.8)	6.1 (3.3–10.5)	0.606
POD 180 (n = 29)	0.4 (0.1–1.0)				0.3 (0.1–0.7)	1.0 (0.1–5.0)	0.115

Data are presented as patient number or median (interquartile ranges) as appropriate. Unless specified otherwise, the data are for 33 patients. *Statistically significant results. SWE = shear wave elastography, POD = postoperative day

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Table 2. Diagnostic Performance for Predicting Advanced Hepatic Fibrosis (F3–F4)

	Area Under the ROC Curve*	Cutoff Value	Sensitivity†	Specificity†
Age at the time of operation	0.762 (0.583–0.893)	7.0 wk	90.9 (10/11)	59.1 (13/22)
Direct bilirubin at diagnosis	0.798 (0.622–0.917)	4.9 μmol/L	100.0 (11/11)	50.0 (11/22)
Preoperative liver SWE	0.806 (0.631–0.922)	17.5 kPa	63.6 (7/11)	86.4 (19/22)
Preoperative spleen SWE	0.756 (0.554–0.899)	24.3 kPa	77.8 (7/9)	66.7 (12/18)

*Data in parentheses are 95% confidence intervals, †Data are % with the raw numbers in parentheses. ROC = receiver operating characteristic, SWE = shear wave elastography

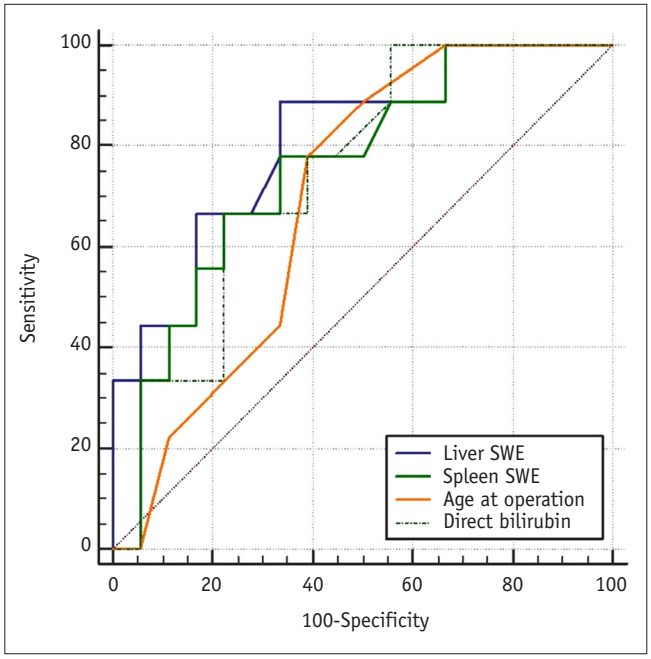

Fig. 2. Receiver-operating characteristics curves for preoperative liver shear wave elastography (SWE), spleen SWE, age at the time of operation (weeks), and direct bilirubin for the diagnosis of significant hepatic fibrosis (F3–F4). The area under the receiver-operating characteristics curve was 0.806 (95% confidence interval [CI]: 0.631–0.922) for liver SWE and 0.756 (95% CI: 0.554–0.899) for spleen SWE, 0.762 (95% CI: 0.583–0.893) for age, and 0.798 (95% CI: 0.622–0.917) for direct bilirubin. No significant differences were observed between parameters (*P*-values: 0.253–0.951).

the other values of immediate postoperative liver and spleen SWE did not differ significantly in the amount of change in measurement over time, depending on the outcome (Supplementary Tables 1 and 2). The liver and spleen SWE increased significantly from POD 0 to 180 in both the poor and good outcome groups. However, this difference was not significant between the good and poor outcome groups.

DISCUSSION

This study demonstrated the value of liver SWE before and immediately after KPE in predicting hepatic fibrosis and native liver outcomes in biliary atresia patients. The preoperative cutoff value was 17.5 kPa for predicting advanced hepatic fibrosis (F3–F4). After surgery, the cutoff value was 10.3 kPa for POD 3 and 11.4 kPa for POD 5 for predicting poor outcomes for the native liver. However, the perioperative hepatic fibrosis stage, preoperative or immediate postoperative laboratory findings, and spleen SWE values did not help predict native liver outcomes.

Liver cirrhosis in KPE suggests a poor prognosis and may require patients to undergo early liver transplantation. Precise preoperative detection of liver cirrhosis in biliary atresia patients is significant for surgical success and for judging the prognosis of the native liver. SWE has been used to accurately assess liver fibrosis in children with jaundice [24,25]. However, only one study has analyzed the relationship between preoperative SWE values and hepatic fibrosis grade in biliary atresia patients, and for liver stiffness measurements, it suggested a cutoff value of 13.0 kPa for F3 and 15.7 kPa for F4 METAVIR scores [26]. In that study, SWE showed the greatest diagnostic performance for predicting the stage of liver fibrosis compared to those of APRI and other serum fibrosis markers. In our study, perioperative age, direct bilirubin level, and preoperative liver and spleen SWE showed good diagnostic performance for predicting advanced hepatic fibrosis in biliary atresia patients. Our cutoff value for liver SWE was 17.5 kPa for predicting advanced hepatic fibrosis. This cutoff value is slightly higher than other reported values, which may be due to the relatively small number of cases with F4 scores and the differences in age distributions between studies. The previously discussed parameters did not correlate significantly with the hepatic fibrosis stage when adjustments were made for age at the time of surgery. This also implies that age is an important determining factor for hepatic fibrosis in biliary atresia patients.

The predictive value of liver stiffness after KPE for biliary atresia was investigated using transient elastography. Patients with high liver stiffness 3 months after KPE also had a higher incidence of chronic liver disease [27]. Moreover,

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Table 3. Diagnostic Performance of Postoperative Liver SWE for Predicting Poor Native Liver Outcome

	Area Under the ROC Curve*	Cutoff Value	Sensitivity†	Specificity†
POD 3	0.891 (0.727–0.974)	10.3 kPa	100.0 (8/8)	73.9 (17/23)
POD 5	0.783 (0.598–0.910)	11.4 kPa	75.0 (6/8)	73.9 (17/23)
POD 7	0.881 (0.718–0.968)	13.7 kPa	100.0 (8/8)	78.2 (18/23)

*Data in parentheses are 95% confidence intervals, †Data are % with the raw numbers in parentheses. ROC = receiver operating characteristic, SWE = shear wave elastography, POD = postoperative day

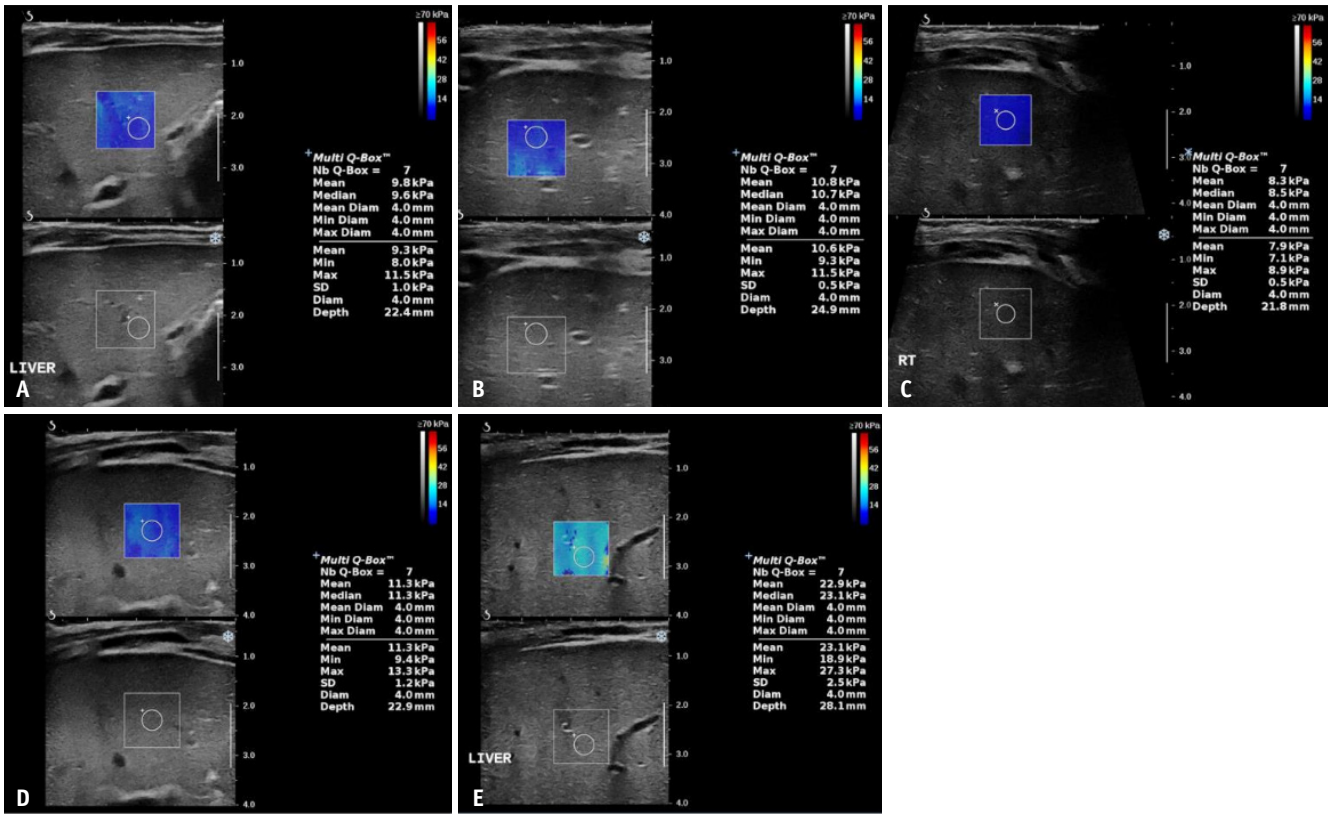

Fig. 3. Serial two-dimensional shear wave elastography (SWE) images of a 7-week female infant with biliary atresia in the poor outcome group. **(A)** Preoperative liver SWE measurements in the regions of interest have a mean of 9.8 kPa. The histological stage of liver fibrosis in the infant was F3. Serial liver SWE measurements showed the mean values as **(B)** 10.8 kPa on postoperative day (POD) 3, **(C)** 8.3 kPa on POD 5, **(D)** 11.3 kPa on POD 7, and **(E)** 22.9 kPa on POD 180. This patient underwent liver transplantation at 8 months. SD = standard deviation

liver stiffness measured 1 week after KPE was associated with thrombocytopenia, splenomegaly, and esophageal varices 6 months after KPE [28]. The risk of earlier liver transplantation was associated with a TE value of > 16 kPa measured 1 week after KPE. This suggests that very early serial liver stiffness measurements after the Kasai operation can be a predictive indicator of clinical outcomes. However, no study has demonstrated immediate postoperative changes in liver stiffness within a week after KPE. Therefore, in our study, we attempted to measure the immediate postoperative values for liver SWE on POD 3, 5, and 7. Although our study used a different modality, it yielded similar results. Liver SWE on immediate POD showed good diagnostic performance for predicting poor outcomes.

Contrary to prior knowledge, perioperative age and hepatic fibrosis grade did not show significant predictive value for poor outcomes in this study. This may be because the Kasai operation was performed relatively early in our patients. All patients underwent surgery before 11 weeks, and only one METAVIR fibrosis stage 4 was identified perioperatively in our study group. Second, the number of patients in the poor-outcome group was small (8/33); therefore, a statistical significance might not have been identifiable. This may explain why the median age (7 vs. 9 years) of the

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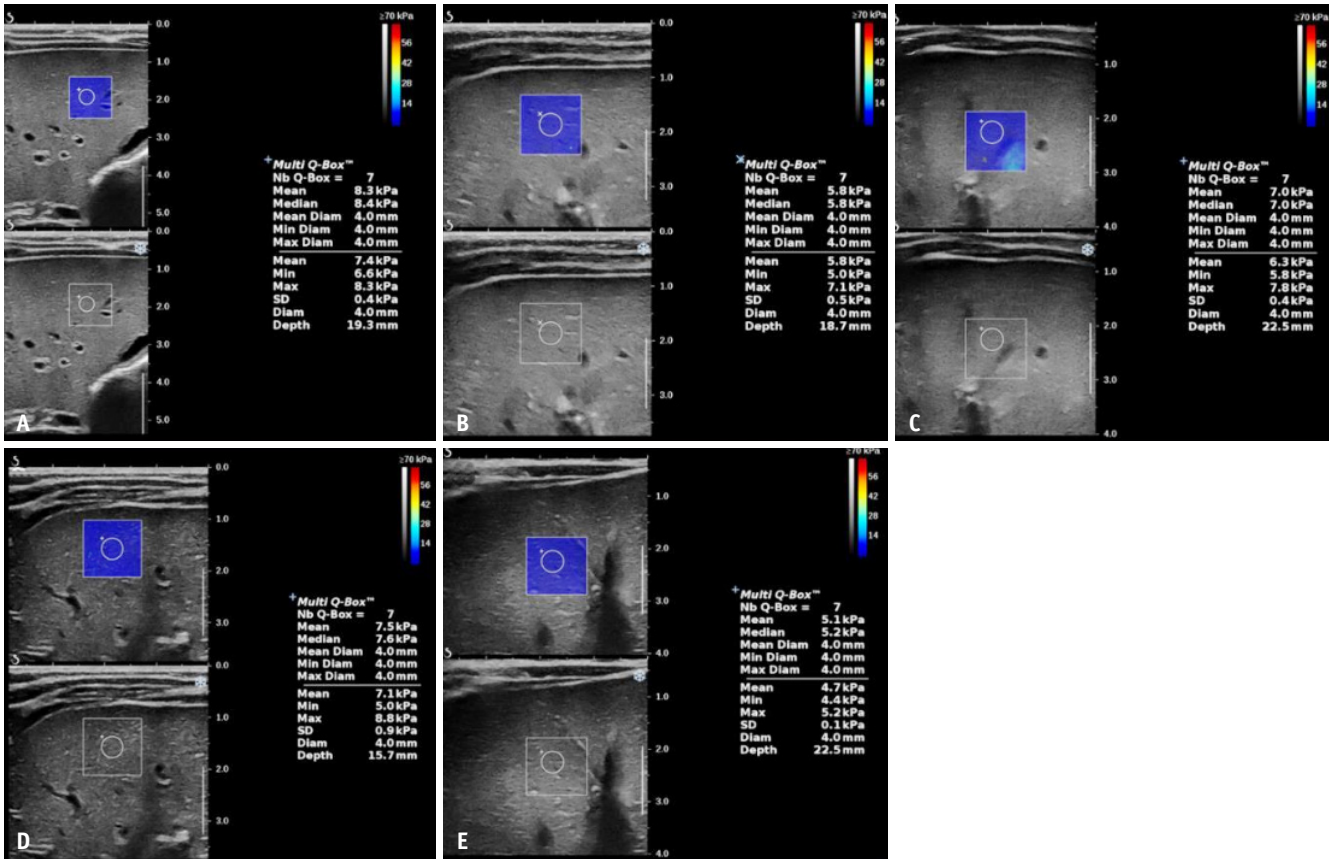

Fig. 4. Serial two-dimensional shear wave elastography (SWE) images of a 9-week male infant with biliary atresia in the good outcome group. **(A)** Preoperative liver SWE measurements in the regions of interest have a mean of 8.3 kPa. The histological stage of liver fibrosis in the infant was F2. Serial liver SWE measurements showed the mean values as **(B)** 5.8 kPa on postoperative day (POD) 3, **(C)** 7.0 kPa on POD 5, **(D)** 7.5 kPa on POD 7, and **(E)** 5.1 kPa on POD 180. Except for the history of hospitalization for simple cholangitis during follow-up, he is doing well without esophageal varices. SD = standard deviation

low-grade (F0–F2) and high-grade (F3–F4) hepatic fibrosis groups was significantly different, but that (7 vs. 9.5 years) of the good vs. poor outcome groups was not significantly different, even though the median age was similar. In addition, although the number of F3–F4 was higher in the poor outcome group (5/8, 62.5%) than in the good outcome group (6/25, 24.0%), this difference was not statistically significant, which might have been due to the small number of patients in the poor outcome group. Further studies with a larger number of patients are required.

Despite the small number of patients with poor outcomes, the immediately postoperative value of liver elasticity differed significantly depending on the prognosis group. Therefore, the results of this study are meaningful. Our study focused on immediately postoperative elasticity changes. Liver SWE showed a significant decrease from the preoperative value to POD 3 in the good-outcome group. Although the statistical significance could not be confirmed due to the small sample size, the SWE values in the good outcome group tended to decrease significantly immediately postoperatively, especially on POD 3, where it was consistently lower and then increased slowly over time than those in the poor outcome group. SWE values may reflect inflammation, edema, and elevated intracellular pressure, which can be caused by cholestasis due to increased serum bilirubin levels [29]. This inflammation is another reason for poor outcomes after KPE. Thus, higher SWE values might indicate not only severe fibrosis but also inflammation which reduces the native liver survival. Early liver SWE on POD 3 may suggest successful bile drainage. The median values of liver SWE at POD 180 between the good (17.9 kPa, range 9.6–25.6) and poor (25.6 kPa, range 18.6–37.7) outcome groups were not statistically different, which might have been due to the small number of patients in the poor outcome group. Future research with a larger sample size is needed to confirm our results.

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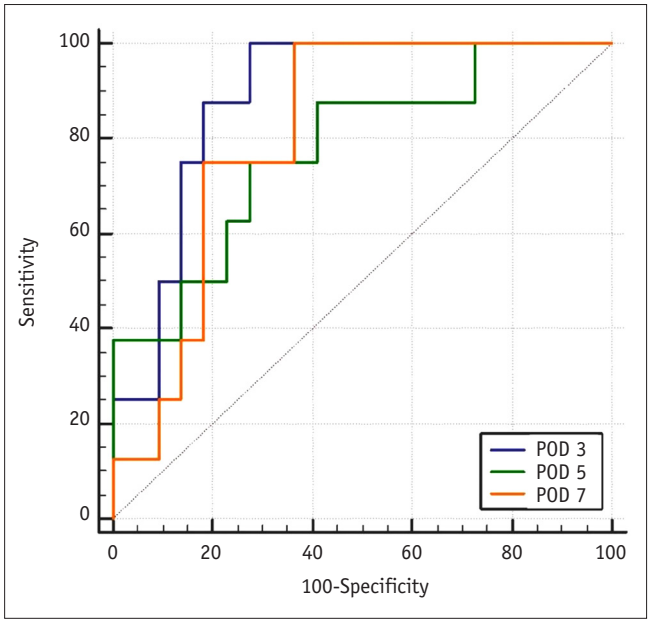

Fig. 5. Receiver-operating characteristics curves for liver shear wave elastography on postoperative days (PODs) 3, 5, and 7 for predicting poor outcomes. The area under the receiver-operating characteristics curve was 0.891 (95% confidence interval [CI]: 0.727–0.974) on POD 3, 0.783 (95% CI: 0.598–0.910) on POD 5, and 0.881 (95% CI: 0.718–0.968) on POD 7. No significant differences were observed between the parameters (*P*-values: 0.214–0.671).

Histological analysis of liver biopsies has great value as its findings allow us to predict the survival of the native liver after KPE by enabling and specifically documenting hepatic injury grade based on multiple parameters, such as portal fibrosis and inflammatory infiltration. However, approximately 5% of children may develop infection or hemorrhage after liver biopsies [30-32]. The longitudinal assessment of fibrosis using novel noninvasive investigations may reduce or eliminate the need for serial liver biopsies. As our research shows, SWE can be a promising noninvasive diagnostic tool after KPE for biliary atresia patients that can help predict liver fibrosis.

The rapid clearance of serum total and direct bilirubin, which leads to levels below the normal range 3 months after KPE, accurately reflects favorable outcomes in biliary atresia. Other traditional markers, such as GGT, serum albumin, and AST, have shown weaker associations with survival and native liver rates [33-35]. However, known serum indices or markers are not representative prognostic factors for biliary atresia, and their clinical significance is somewhat uncertain; therefore, the goal of this study was to determine a cutoff point or threshold using noninvasive SWE so that patients would not have to undergo liver biopsies [19,36].

This study had several limitations. First, it was performed at a single institution within a limited period. The short-term follow-up might have been a cause of bias. We could not analyze only patients who underwent liver transplantation separately for the poor outcome group from a limited number. Second, we included no control group for comparison, although such a comparison was not considered effective for the study purposes. Due to the small number of patients, a validation test could not be performed using our results. Third, we did not perform a comparative analysis with laboratory fibrosis index markers, such as APRI. Fourth, there may be intersegmental variability in both SWE measurements and pathology. Fifth, each patient underwent SWE by a single radiologist; therefore, interobserver and intraobserver variations could not be analyzed. In addition, we could not use the measurement reliability index when measuring the SWE. Liver SWE has been used for a long time, and its reliability and reproducibility have been verified even in children. However, the results of spleen SWE can be relatively inhomogeneous compared to those of liver SWE and can be affected by free breathing during measurement in small children. Sixth, there were no intermediate measurements on the first 180 postoperative days because we tried to focus on immediately postoperative changes. Further studies that incorporate multicenter data and intermediate- and long-term follow-ups with variable laboratory fibrosis index markers are needed.

In conclusion, age, direct bilirubin level, and liver and spleen SWE can predict the degree of hepatic fibrosis before KPE. Immediate postoperative values of liver SWE measured on PODs 3 and 5 can also predict native liver outcomes in patients with biliary atresia. Cutoff values of 10.3 and 11.4 kPa on PODs 3 and 5, respectively, result in high diagnostic performance for predicting poor outcomes.

Supplement

The Supplement is available with this article at https://doi.org/10.3348/kjr.2022.0586.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

Kyunghwa Han and Mi-Jung Lee, contributing editors of the *Korean Journal of Radiology*, were not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Haesung Yoon, Kyong Ihn, Hong Koh, Mi-Jung Lee. Data curation: Haesung Yoon, Kyong Ihn, Jisoo Kim, Hyun Ji Lim, Sowon Park, Seok Joo Han, Hong Koh, Mi-Jung Lee. Formal analysis: Haesung Yoon, Kyong Ihn, Kyunghwa Han, Hong Koh, Mi-Jung Lee. Funding acquisition: Hong Koh. Investigation: Haesung Yoon, Kyong Ihn, Hong Koh, Mi-Jung Lee. Methodology: Haesung Yoon, Kyong Ihn, Kyunghwa Han, Hong Koh, Mi-Jung Lee. Project administration: Hong Koh, Mi-Jung Lee. Resources: Hong Koh, Mi-Jung Lee. Software: Haesung Yoon, Kyong Ihn, Jisoo Kim, Hyun Ji Lim, Kyunghwa Han. Supervision: Hong Koh, Mi-Jung Lee. Validation: Haesung Yoon, Kyong Ihn, Hong Koh, Mi-Jung Lee. Visualization: Haesung Yoon, Kyong Ihn, Hong Koh, Mi-Jung Lee. Writing—original draft: Haesung Yoon, Kyong Ihn, Hong Koh, Mi-Jung Lee. Writing—review & editing: all authors.

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