ORIGINAL ARTICLE



Diagnosing native liver fibrosis and esophageal varices using liver and spleen stiffness measurements in biliary atresia: a pilot study

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Abstract

Background Biliary atresia commonly leads to liver fibrosis and cirrhotic complications, including esophageal varices. *Objective* To evaluate liver and spleen stiffness measurements using acoustic radiation force impulse (ARFI) imaging for diagnosing grade of liver fibrosis and predicting the presence of esophageal varices in patients treated for biliary atresia.

Materials and methods ARFI imaging of the spleen and native liver was performed in 28 patients with biliary atresia. We studied the relation between ARFI imaging values and liver histology findings (n=22), upper gastrointestinal endoscopy findings (n=16) and several noninvasive test results.

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Diagnostic accuracy was assessed using receiver operating characteristic curve analyses.

Results Liver stiffness measurements exhibited a significant difference among the different grades of liver fibrosis (P=0.009), and showed higher values in patients with highrisk esophageal varices than in the other patients (P=0.04). The areas under the receiver operating characteristic curves of liver stiffness measurements for liver fibrosis grades \geq F2, \geq F3 and = F4 were 0.83, 0.93 and 0.94, respectively. Patients with high-risk esophageal varices were preferentially diagnosed by the combined liver and spleen stiffness measurements (area under the curve, 0.92).

Conclusion Liver and spleen stiffness measurements using ARFI imaging are potential noninvasive markers for liver fibrosis and esophageal varices in patients treated for biliary atresia.

Keywords Acoustic radiation force impulse imaging \cdot Biliary atresia \cdot Liver \cdot Esophageal varices \cdot Liver fibrosis \cdot Liver stiffness \cdot Spleen stiffness

Introduction

Biliary atresia is a destructive, inflammatory, obliterative cholangiopathy that develops in 1/5,000 to 1/19,000 newborn [1]. Early referrals and timely surgeries, including Kasai portoenterostomies, to drain the bile can achieve good outcomes in 50–60% of affected infants [1]. However, liver fibrosis, a prominent feature of biliary atresia, progresses rapidly before and even after successful bile drainage surgery, leading to biliary cirrhosis and portal hypertension [2]. One of the important cirrhotic complications is esophageal varices. Since more than 50% of the patients with biliary atresia suffer

from esophageal varices before the age of 2 years [3], endoscopic surveillance and prophylactic endoscopic therapy are needed to prevent variceal bleeding [4]. Liver transplantation is the only curative treatment for biliary atresia patients showing complications associated with cirrhosis [1, 5] It can achieve satisfactory short- and long-term outcomes [6]. Thus, monitoring liver fibrosis and esophageal varices is essential for patients with biliary atresia to prevent fatal bleeding from esophageal varices [4], and to determine the optimal timing for liver transplantation [7].

To date, the gold standard methods for assessing liver fibrosis and esophageal varices are invasive, involving liver biopsies and upper gastrointestinal endoscopy [8]. Liver and spleen stiffness measurements, which are surrogate noninvasive markers for liver fibrosis and portal hypertension, have been investigated recently [8-10] using acoustic radiation force impulse (ARFI) imaging with Virtual Touch[™] quantification (Siemens Medical Solutions, Mountain View, CA, USA), which is a commercially available US-based elastography method used to evaluate tissue stiffness. Tissue stiffness measurements using ARFI imaging are accomplished by simply pushing a button during real-time B-mode imaging after determining the region of interest, which is displayed graphically at a size of $1.0 \text{ cm} \times 0.6 \text{ cm}$ using the convex probe. Tissues in the region of interest are excited mechanically by impulsive acoustic radiation forces, generating shear waves within the tissue, and the velocity of these shear waves, which is proportional to the square root of the tissue elasticity, is quantitatively expressed as the stiffness of the tissue in meters per second [9, 11].

Hospitalization and general anesthesia are necessary to obtain liver biopsies from and perform upper gastrointestinal endoscopy in patients, all of which are associated with notable complication rates and a considerable amount of labor [12, 13]; hence, a noninvasive method for diagnosing liver fibrosis and esophageal varices would be very beneficial. This study evaluated the diagnostic value of liver and spleen stiffness measurements for diagnosing liver fibrosis and esophageal varices in patients with biliary atresia using ARFI imaging.

Materials and methods

Patients and ethical considerations

Between July 2011 and January 2014, we performed liver and spleen stiffness measurements using ARFI imaging at around the time of liver histology examinations and/or endoscopic screening in patients with biliary atresia who were surviving with their native livers. Twenty-eight patients underwent liver and/or spleen stiffness measurements and liver histology and/or upper gastrointestinal endoscopy evaluation. Eight of the 28 patients were enrolled in the study before their initial surgeries. The ARFI imaging examinations were performed within 4 days prior to surgery, and in conjunction with liver histology examinations during surgery. Six of the 8 patients underwent postsurgical follow-up ARFI imaging examinations and endoscopic screening 7-11 months after surgery. Enrollment for this study is illustrated in Fig. 1. The study population comprised 13 males and 15 females, and the median age of the patients at the time of the first examination was 9.9 years (range = 0.1-33.6). Type 1 biliary atresia (atresia of the common bile duct) was diagnosed in 5 patients, type 3 biliary atresia (atresia at the porta hepatis) was diagnosed in 21 patients, and the disease type was unknown in 2 patients. The initial bile drainage surgeries undertaken were a hepaticoenterostomy in 1 patient and hepatoportoenterostomies in 26 patients, and the median age at the time of the surgery was 57 days (interquartile range: 46-74).

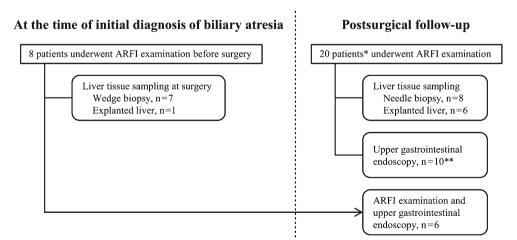


Fig. 1 Enrollment of the study population. Eight of the 28 patients were enrolled in the study before their initial surgeries. Acoustic radiation force impulse (ARFI) examinations were performed before surgery, in conjunction with liver histology examinations during surgery. Six of the eight patients underwent postsurgical follow-up ARFI examinations and endoscopic screening. The remaining 20 patients were enrolled at the time of postsurgical follow-up. *Four of the 20 patients had a history of splenectomy. **After excluding patients with a history of treatment for esophageal varices and/or splenectomy

One patient underwent primary liver transplantation at the age of 194 days.

This study was exploratory, and conformed to the ethical guidelines within the 1975 Declaration of Helsinki, and it was approved by the institution's ethical committee. Written informed consent was obtained from either the patients or from their parents.

Liver and spleen stiffness measurements using acoustic radiation force impulse imaging

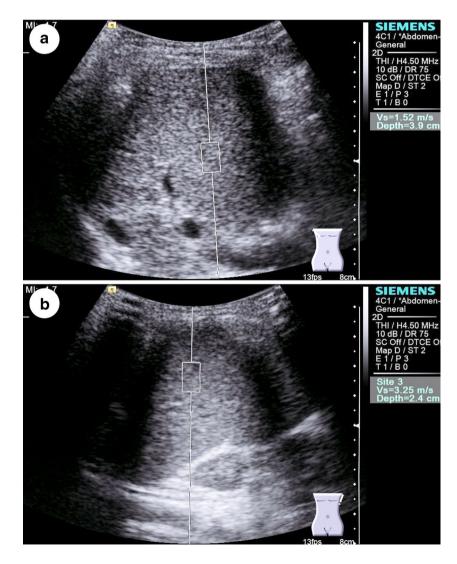
Liver and spleen stiffness measurements were performed by 1 of 7 radiologists or radiology technicians with 1 year to 30 years (median: 13 years) of experience in US examinations who were blinded to the histological and endoscopic findings. A Siemens Acuson S2000 (Mochida Siemens Medical Systems Co., Ltd., Tokyo, Japan) was used with Virtual TouchTM quantification and a convex probe (4C1). Liver and spleen stiffness measurements were determined through the right and left intercostal spaces, respectively. The examiner

Fig. 2 Liver and spleen stiffness measurements using acoustic radiation force impulse (ARFI) imaging in a 2-year-old female. The examiner places the convex probe on the right and left intercostal spaces, and defines the region of interest at a 3-cm depth from the liver surface (a) and at the center of the splenic parenchyma (b), respectively. By pushing the measuring button, the tissue stiffness in the region of interest is quantitatively expressed as the velocity of the shear wave in meters per second

defined the region of interest at a 3-cm depth from the liver's surface and at the center of the spleen's parenchyma, while avoiding the large vessels (Fig. 2). The measurements were repeated 5 times at each site when the patient was in the supine position, resting and not holding their breath, and at the end of exhalation. The median values were used for the analyses. In addition, we devised a combined liver and spleen stiffness measurement, which was simply calculated by adding together the liver and spleen stiffness values.

Histological evaluation

Liver tissue samples were acquired for clinical use after obtaining written informed consent in 22 patients. Those tissue samples obtained within 3 months of the ARFI imaging examinations were examined histologically. Surgical wedge biopsies were obtained through surgical resection from the edge of the liver during laparotomy, including hepatoportoenterostomy. Percutaneous needle biopsies were performed under US guidance using an 18-gauge suction needle. Explanted livers were



obtained during liver transplant surgery. The histological findings were retrospectively re-evaluated by a liver pathologist (Y.M.) with 8 years of experience who was blinded to the other information relating to the patients. The liver fibrosis grade was evaluated in accordance with the Metavir scoring system [14] as follows: F0 indicates no portal fibrosis, F1 indicates portal fibrosis without septa, F2 indicates portal fibrosis with rare septa, F3 indicates numerous septa without cirrhosis and F4 indicates cirrhosis.

Endoscopic evaluation

Upper gastrointestinal endoscopies were performed at our clinic after obtaining written informed consent in 24 patients. Endoscopic findings obtained within 3 months of the ARFI imaging examinations were referred. One experienced endoscopist (N.H.) with 16 years of experience who was blinded to the other information relating to the patients retrospectively re-evaluated the endoscopic findings in accordance with the criteria described by the Japan Society for Portal Hypertension [15], as described next. The forms of the esophageal and gastric varices were described as F0, no varicose appearance; F1, straight small-caliber varices; F2, moderately enlarged, beady varices; and F3, markedly enlarged, nodular or tumor-shaped varices. High-risk esophageal varices were defined as varices showing the F2-F3 forms with or without red color signs, or varices showing the F1 form with red color signs.

Other data collected

The patients' clinical courses and the results from laboratory and imaging tests, undertaken within 3 months of the ARFI imaging examinations, were collected from the patients' medical records. Spleen stiffness and spleen size measurements could not be obtained from four patients with histories of splenectomies, and the blood platelet count data were discarded. From the assessment of esophageal varices, eight patients with a history of treatment for esophageal varices and/ or splenectomy were excluded; one patient had a history of splenectomy, five patients had a history of treatment for esophageal varices and two patients had both histories. The noninvasive liver fibrosis/portal hypertension markers, namely, the aspartate aminotransferase to platelet ratio index [16], the clinical prediction rule [17] and the varices prediction rule [18], were calculated using the following formulas:

Aspartate aminotransferase to platelet ratio index = (aspartate aminotransferase [/upper normal limit] \times 100)/platelet count (10⁹/l), where a serum aspartate aminotransferase level of 35 IU/l was used as the upper normal limit.

Clinical prediction rule = $(0.75 \times \text{platelet count } [10^9/\text{l}])/$ (spleen size z score+5)+2.5 × albumin (g/dl), where the spleen size *z* scores were calculated based on the pediatric age-specific reference values from Greece [19] for patients aged <10 years, or values from China [20] for patients aged ≥ 10 years.

Varices prediction = albumin (g/l) × platelet count $(10^{9}/l)$ /1,000

Statistical analysis

The intraobserver reliability of the liver and spleen stiffness measurements was assessed using the intraclass correlation coefficient, which ranges from 0 (no reliability) to 1 (perfect reliability), and a value >0.75 is generally considered to signify excellent reliability [21]. The noninvasive quantitative test results were treated as continuous data. The liver fibrosis grades (F0-F4) were treated as ordinal data. The differences among continuous data sets were assessed using the Kruskal-Wallis test or the Mann-Whitney U test. The accuracy of the noninvasive tests for diagnosing the liver fibrosis grades and high-risk esophageal varices was assessed using receiver operating characteristic curves, where an area under the curve of 1.0 indicates a test with perfect diagnostic power, and an area under the curve of 0.5 indicates a test without any diagnostic power. The cutoff values were determined by maximizing the sums of the sensitivity and specificity. The confidence intervals for the sensitivity and specificity were calculated using binomial tests. P-values <0.05 were considered statistically significant. The statistical analyses were performed using IBM[®] SPSS[®] software version 22.0 (IBM, Armonk, N.Y., USA) and R software version 3.1.0 (The R Foundation for Statistical Computing Vienna, Austria; http://www.R-project.org/).

Results

Findings from the invasive tests

The liver histology findings were evaluated in 22 patients. The median age at the time of examinations was 6.3 years (range: 0.1–33.6 years). The liver tissue samples comprised seven surgical wedge biopsy specimens, eight percutaneous needle biopsy specimens and seven explanted livers. The median length of the needle biopsy samples was 17 mm (interquartile range: 16–19 mm), and the median number of portal tracts they contained was 10 (interquartile range: 7–12). All of the wedge biopsy specimens contained >20 portal tracts. The liver fibrosis grades were as follows: F0, n=2; F1, n=3; F2, n=5; F3, n=8; and F4, n=4.

The upper gastrointestinal endoscopy findings were evaluated in 16 patients. The median age of the patients undergoing examinations was 6.3 years (range: 0.7–

33.5 years). The esophageal varices grades were as follows: no varices, n=11; low-risk varices, n=2; and high-risk varices, n=3.

Liver and spleen stiffness measurements

The study included 4 patients with histories of splenectomies; therefore, 34 liver stiffness measurements and 30 spleen stiffness measurements were obtained. The intraclass correlation coefficients for the liver and spleen stiffness measurements, which were repeated 5 times at each site, were 0.97 (95% confidence interval=0.96– 0.99, P<0.001) and 0.88 (95% confidence interval=0.79–0.94, P<0.001), respectively.

The liver and spleen stiffness measurements stratified according to the liver fibrosis and esophageal varices grades are shown in Fig. 3. The liver stiffness measurements showed significant differences among the different grades of liver fibrosis (P=0.009), and showed higher values in the patients with high-risk esophageal varices than in the other patients (P=0.04). The spleen stiffness measurements showed no significant differences

regarding liver fibrosis grades (P=0.26) or the presence of high-risk esophageal varices (P=0.15).

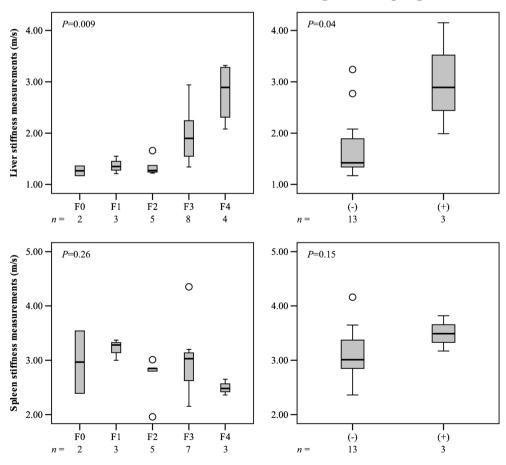
Diagnosis of liver fibrosis

The diagnostic value and receiver operating characteristic curves of the liver stiffness measurements for diagnosing liver fibrosis are shown in Table 1 and Fig. 4, compared with the aspartate aminotransferase to platelet ratio index. The areas under the receiver operating characteristic curves of liver stiffness measurements for liver fibrosis grades \geq F2, \geq F3 and =F4 were 0.83 (95% confidence interval=0.65-1.00, P=0.03), 0.93 (0.82-1.00, P<0.001) and 0.94 (0.85-1.00, P=0.006), respectively. The cutoff values for the liver stiffness measurements were identified as 1.61 m/s for \geq F2, 1.70 m/s for \geq F3 and 2.00 m/s for =F4. The diagnostic accuracies were 72.7% (95% confidence interval = 49.8 - 89.3% for \geq F2, 90.9% (70.8 - 98.9%) for > F3, and 86.4% (65.1 – 97.1%) for = F4. The aspartate aminotransferase to platelet ratio index showed a significant diagnostic value for the \geq F3 fibrosis grade only, with an area under the curve of 0.86 (95% confidence interval = 0.69-1.00, P=0.007).

Fig. 3 Liver stiffness measurements and spleen stiffness measurements stratified according to the grades of liver fibrosis and esophageal varices. The box plots show the median values of the tests with the interquartile ranges. The error bars indicate the lowest and highest values that are within 1.5 box-lengths of the upper and the lower quartiles. Outliers are represented by individual circles. The differences in the liver and spleen stiffness measurements among the groups were assessed using the Kruskal-Wallis test or the Mann-Whitney U test

Grade of liver fibrosis

High-risk esophageal varices



Fibrosis grade	Area under the curve (95% confidence interval)	P-value	Cutoff values	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Accuracy (95% confidence interval)			
Liver stiffness measurements (shear wave velocity, m/s)									
\geq F2	0.83 (0.65 - 1.00)	0.03	1.61	64.7% (38.3 - 85.8%)	100% (47.8-100%)	72.7% (49.8-89.3%)			
\geq F3	0.93 (0.82 - 1.00)	< 0.001	1.70	83.3% (51.6-97.9%)	100% (69.2-100%)	90.9% (70.8 - 98.9%)			
=F4	0.94 (0.85 - 1.00)	0.006	2.00	100% (39.8-100%)	83.3% (58.6-96.4%)	86.4% (65.1-97.1%)			
Aspartate aminotransferase to platelet ratio index									
\geq F2	0.67(0.40-0.93)	0.28	0.65	80.0% (51.9-95.7%)	60.0% (14.7-94.7%)	75.0% (50.9-91.3%)			
\geq F3	0.86 (0.69 - 1.00)	0.007	1.32	80.0% (44.4-97.5%)	90.0% (55.5-99.7%)	85.0% (62.1 - 96.8%)			
=F4	0.71 (0.49 - 0.92)	0.27	1.39	100% (29.2 - 100%)	70.6% (44.0-89.7%)	75.0% (50.9-91.3%)			

 Table 1
 Diagnostic value of the liver stiffness measurements and aspartate aminotransferase to platelet ratio index for the diagnosis of liver fibrosis grades analyzed by receiver operating characteristic curves

Diagnosis of high-risk esophageal varices

Table 2 and Fig. 5 show the diagnostic values of the noninvasive markers and the receiver operating characteristic curves for the diagnosis of high-risk esophageal varices using the noninvasive markers. The cutoff value for the liver stiffness measurements was 1.94 m/s, with a diagnostic accuracy of 81.3% (95% confidence interval = 54.4–96.0%). The diagnostic values improved when the liver and spleen stiffness measurements were combined. The combined liver and spleen stiffness measurements showed an area under the curve of 0.92 (95% confidence interval = 0.79 - 1.00, P = 0.03), sensitivity of 100% (95% confidence interval=29.2-100%), specificity of 84.6% (54.6-98.1%), and accuracy of 87.5% (61.7 -98.4%). The spleen stiffness measurements, the aspartate aminotransferase to platelet ratio index, the clinical prediction rule and the varices prediction rule did not show statistically significant diagnostic power, which may be due to the small number of patients.

Discussion

Although liver fibrosis and cirrhosis are common among biliary atresia patients, few reports have described the noninvasive diagnosis of liver fibrosis in biliary atresia patients surviving with their native livers. The aspartate aminotransferase to platelet ratio index, which was developed to detect cirrhosis in hepatitis C patients [16], was reported to be a good marker of liver fibrosis in 35 patients who had undergone Kasai portoenterostomies and whose liver tissue samples were removed at the time of surgery [22], and in 23 patients following successful Kasai portoenterostomies whose liver tissue samples were removed approximately 4 years after surgery [23]. We recently developed the biliary atresia liver fibrosis score to diagnose the liver fibrosis grade in biliary atresia patients older than 1 year, based on histological findings from 180 liver samples and the corresponding standard liver test results obtained from 62 patients [7]; however, the score has not yet been validated. One reason for the limited amount of data

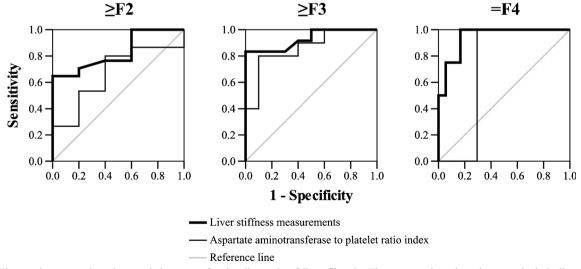


Fig. 4 The receiver operating characteristic curves for the diagnosis of liver fibrosis. The presented noninvasive tests include liver stiffness measurements (*thick line*) and the aspartate aminotransferase to platelet ratio index (*thin line*)

Test	Area under the curve (95% confidence interval)	P- value	Cutoff value	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Accuracy (95% confidence interval)
Liver stiffness measurements	0.90 (0.73 - 1.00)	0.04	1.94	100% (29.2-100%)	76.9% (46.2 - 95.0%)	81.3% (54.4-96.0%)
Spleen stiffness measurements	0.79(0.57 - 1.00)	0.12	3.14	100% (29.2 - 100%)	69.2% (38.6 - 90.9%)	75.0% (47.6-92.7%)
Combined liver and spleen stiffness measurements	0.92 (0.79 - 1.00)	0.03	5.13	100% (29.2 - 100%)	84.6% (54.6 - 98.1%)	87.5% (61.7-98.4%)
Aspartate aminotransferase to platelet ratio index	0.79 (0.45 - 1.00)	0.12	4.87	66.7% (9.4-99.2%)	100% (75.3 - 100%)	93.8% (69.8-99.8%)
Clinical prediction rule	0.76 (0.48 - 1.00)	0.18	106	66.7% (9.4-99.2%)	84.6% (54.6-98.1%)	81.3% (54.4-96.0%)
Varices prediction rule	0.85 (0.66 - 1.00)	0.07	7.16	100% (29.2 - 100%)	76.9% (46.2-95.0%)	81.3% (54.4-96.0%)

 Table 2
 Diagnostic values of several noninvasive tests for the diagnosis of high-risk esophageal varices analyzed using receiver operating characteristic curves

Tissue stiffness as measured by shear wave velocities (m/s)

relating to liver fibrosis markers in biliary atresia patients is that liver biopsies are not commonly performed except at the time of surgery [2], and liver transplantation is the only curative treatment for biliary atresia patients. However, surrogate markers of fibrosis, including liver stiffness measurements, would be useful for monitoring fibrosis progression in a future interventional trial [2, 7]. Two studies describing 32 and 39 patients with pediatric liver disease that involved 16 and 3 biliary atresia patients, respectively, reported that liver stiffness measurements using ARFI imaging correlated with liver fibrosis [24, 25].

The noninvasive detection of esophageal varices in biliary atresia patients appears to be of great importance in clinical practice. Three reports have described liver stiffness

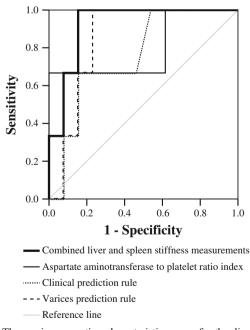


Fig. 5 The receiver operating characteristic curves for the diagnosis of high-risk esophageal varices using several noninvasive tests. The presented noninvasive tests include combined liver and spleen stiffness measurements (*thick line*), the aspartate aminotransferase to platelet ratio indices (*thin line*), the clinical prediction rule (*dotted line*) and the varices prediction rule (*dashed line*)

measurements using transient elastography as good markers of the presence of esophageal varices (area under the curve = 0.88–0.92) in postsurgical biliary atresia patients [13, 26, 27]. The aspartate aminotransferase to platelet ratio index might also be able to diagnose the presence of esophageal varices in postsurgical biliary atresia patients, with reported areas under the curves of 0.87-0.88 [13, 27]. Gana et al. [17] developed the clinical prediction rule to predict esophageal varices, and reported an area under the curve of 0.93 from a study of 51 pediatric patients with liver disease or portal vein thrombosis, and the validation studies showed areas under the curves of 0.80 and 0.77 [28, 29]. The varices prediction rule was developed more recently from a study of 195 biliary atresia infants as a novel predictor of significant varices at 6 months post-Kasai portoenterostomy (area under the curve=0.75; sensitivity=86%; specificity=71%). The current study demonstrated that liver and spleen stiffness measurements using ARFI imaging may be potential noninvasive markers for high-risk esophageal varices, which really require endoscopy procedures for their prophylactic treatment.

We recently reported that liver fibrosis in postsurgical biliary atresia patients is strongly correlated with the liver biochemistry results [7]. Another recent report by Lampela et al. [23] also described close correlations between liver fibrosis and the liver biochemistry results. However, we wonder why some biliary atresia patients show many of the symptoms associated with portal hypertension despite having relatively good liver biochemistry results. The previously reported cutoff values for liver stiffness measurements using transient elastography for diagnosing esophageal varices (9.7-12.7 kPa) are lower than those found in adults [13, 26, 27, 30]. Unfortunately, the current study could not assess patients who showed a discrepancy between liver fibrosis and portal hypertension because such patients were mostly excluded from the assessment of esophageal varices due to prior treatment for esophageal varices and hypersplenism. However, we suggest that factors other than liver fibrosis - for example, an increase in the hepatic vascular tone and/or an increase in the splanchnic blood flow - may be important causes of portal

hypertension in biliary atresia patients, which would be similar to other patients with liver disease and cirrhosis [7]. Hence, we emphasize that assessing liver and spleen parameters separately might be useful in the follow-up of biliary atresia patients. ARFI imaging has the advantage of producing two noninvasive quantitative parameters relating to the liver and spleen easily and simultaneously. A previous report from a study of adults with cirrhosis similarly explained that combining liver and spleen stiffness measurements that were determined using transient elastography had a good diagnostic accuracy for diagnosing esophageal varices [31].

Although we have demonstrated the clinical utility of liver and spleen stiffness measurements using ARFI imaging in biliary atresia patients, there are several limitations to the study. First, our study involved a small sample size and the patients had heterogeneous backgrounds. Thus, we could not determine which noninvasive markers were preferable for diagnosing the grade of liver fibrosis and high-risk esophageal varices. The second limitation is associated with the reference standards, especially the liver histology findings. To grade the fibrosis of the livers, about one-third of the liver tissue samples were obtained using percutaneous needle biopsies and another one-third using surgical wedge biopsies. Because a liver biopsy specimen involves only a small part of the whole liver, and liver fibrosis often shows heterogeneous distribution, liver biopsy examination may be limited by sampling error [32]. In addition, subjective histological assessment has the potential for intraobserver and interobserver variability [33]. These issues may have affected the diagnostic accuracy of the tests, including the liver and spleen stiffness measurements. The third limitation is attributable to the ARFI imaging examination; only one of the seven examiners assessed liver and spleen stiffness for each patient, and thus we were unable to determine the interobserver variability of the examinations. Despite these limitations, liver and spleen stiffness measurements using ARFI imaging have the desirable characteristics of a diagnostic test, that is, they are noninvasive, safe, easy to perform, inexpensive and accurate [8]. Long-term serial measurements of liver and spleen stiffness must be conducted in large numbers of biliary atresia patients to determine the clinical utility of ARFI imaging more precisely.

Conclusion

In patients with biliary atresia who are surviving with their native livers, liver and spleen stiffness measurements using ARFI imaging may offer a potential methodology for the diagnosis of the grade of liver fibrosis and the presence of highrisk esophageal varices. Acknowledgments This study was supported by the Japan Society for the Promotion of Science (JSPS KAKENHI, Grant-in-Aid for Young Scientists (B), Grant Number 26870570).

Compliance with ethical standards

Conflicts of interest None

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