Usefulness of Liver Stiffness on Ultrasound Shear-Wave Elastography for the Evaluation of Central Venous Pressure in Children With Heart Diseases

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Background: Liver stiffness on ultrasound shear-wave elastography (SWE) reflects central venous pressure (CVP) in adult patients with heart failure, but the association of liver stiffness on SWE with CVP in pediatric patients is not clear. The present study evaluated whether liver stiffness on SWE is useful as a non-invasive indicator of CVP in pediatric patients.

Methods and Results: Liver stiffness was measured using ultrasound SWE in 79 patients aged <20 years with congenital heart diseases. None of the patients was found to have liver disease. Correlations between liver stiffness and other clinical variables, including CVP, were analyzed. CVP was the only factor independently and significantly correlated with liver stiffness in multivariate analysis. However, variables related to hepatic fibrosis did not correlate with liver stiffness.

Conclusions: Liver stiffness on ultrasound SWE is useful as a non-invasive indicator of CVP in children with heart diseases.

Key Words: Central venous pressure; Children; Congenital heart disease; Liver stiffness; Ultrasound shear-wave elastography

Ultrasound shear-wave elastography (SWE) is being widely used for the non-invasive measurement of tissue stiffness. Its use is prevalent in the field of hepatology, and the quantitative stiffness of the liver is known to correlate with the degree of fibrosis. In the field of adult cardiology, liver stiffness is known to reflect central venous pressure (CVP). However, the association between SWE findings of the liver and CVP among children with heart diseases has not been clarified. In children, because vascular access is limited, the evaluation of CVP has mainly relied on classic indices such as body weight and skin edema. Therefore, clarification of the relationship between liver stiffness on SWE and CVP in children might change the practice of pediatric heart care and intensive care.

In this study, we measured liver stiffness using ultrasound SWE in children with heart diseases to evaluate whether it is useful as a non-invasive indicator of CVP in this population.

Methods

Study Subjects
This study was approved by the Institutional Review Board of Fukuoka Children’s Hospital and informed consent was obtained appropriately. Ultrasound SWE was performed in 79 patients aged <20 years with congenital heart diseases who underwent cardiac catheterization between August 2017 and August 2018. The medical records of the patients were reviewed to retrieve information about the diagnosis and previous treatments.

Ultrasound SWE
SWE of the liver was performed just before catheterization in the same room using Logic S8 equipment (GE Healthcare, Chicago, IL, USA). The fasting time was at least 4 h in all cases. SWE was performed 10 times on the right lower lobe of the liver to a depth of 2–4 cm from the liver surface while the patient was upright. In some cases of situs inversus or if the size of the right lobe was inadequate, the left lobe was used. The size of the SWE box was 3.0 × 1.5 cm and the region of interest was 1.25 cm in diameter. Thick and obvious vessels were excluded from the region of interest. The patients included infants and toddlers for whom breath holding was difficult, so all examinations were performed during a motionless period of respiration while free breathing. The median of 10 measurements was used for analysis.

Statistical Analysis
Continuous variables are expressed as mean±standard deviation. Categorical variables are expressed as number (percentage). Pearson’s correlation coefficient and multiple regression models were used to evaluate the correlations between liver stiffness on SWE and other variables in the
A total of 79 patients were enrolled in the present study. Their characteristics are shown in Table 1: 45 patients had biventricular diseases, such as transposition of the great arteries and tetralogy of Fallot, and none had liver diseases;
and cardiac index significantly correlated with liver stiffness (Table 2). On the other hand, indicators of hepatic fibrosis, such as type IV collagen, type III procollagen peptide, and Mac-2 binding protein glycosylation isomer, did not show significant correlations with liver stiffness. The subsequent multivariate analysis revealed that CVP was the only factor that independently and significantly correlated with liver stiffness, among all the factors identified in the univariate analysis. This relatively strong correlation between CVP and liver stiffness (Figure 1) was noted even in the subgroups of patients with biventricular disease (Figure 2A) and those who underwent the Fontan procedure (Figure 2B).

**Discussion**

In this study, we showed that ultrasound SWE of the liver was useful for the evaluation of CVP in children, including those with biventricular disease and those with Fontan circulation. Our findings are valuable, as reports on the use of ultrasound SWE in children with heart diseases, especially biventricular circulation, are limited.

The usefulness of ultrasound SWE in the field of adult cardiology is already known. Liver stiffness is known to reflect CVP,\(^8\)\(^\text{–}\)\(^10\) which is reversed by treatment of congestion,\(^8\)\(^\text{–}\)\(^12\) so SWE can be used to evaluate the sufficiency of treatment. Although estimating cardiac output and congestion is crucial in the treatment of heart failure, quantitative measurement of CVP is sometimes difficult, because invasive procedures, such as Swan–Ganz catheter insertion, are usually required. Because SWE is a non-invasive procedure, it is preferable, especially for pediatric patients in whom invasive procedures have high risks, such as occlusion of large vessels and respiratory failure associated with sedation.

In the field of pediatric cardiology, ultrasound SWE has often been reported as an evaluation tool for hepatic fibrosis after the Fontan procedure.\(^13\)\(^\text{–}\)\(^15\)\(^\text{–}\)\(^22\)\(^\text{–}\)\(^24\) However, it is not known whether liver stiffness after the Fontan procedure truly reflects the degree of hepatic fibrosis, because these patients have high venous pressure to some degree, which may result in increased stiffness. Some previous studies have shown a relationship between liver stiffness and fibrosis severity according to the blood sample score among Fontan

![Figure 1](image1.png)  
**Figure 1.** Significant correlation between liver stiffness on SWE and CVP in all patients (<20 years old). CVP, central venous pressure; SWE, shear-wave elastography.

![Figure 2](image2.png)  
**Figure 2.** Significant correlations between liver stiffness on SWE and CVP in patients with biventricular diseases (A) and those who underwent the Fontan procedure (B). Abbreviations as in Figure 1.
patients. However, it is not clear whether the fibrosis score, which is frequently used in adult patients with liver diseases, can be applied in Fontan patients. Kutty et al reported a substantial correlation between the degree of histological fibrosis and liver stiffness on ultrasound SWE among 10 patients after the Fontan procedure. On the other hand, some studies have reported significant increase in liver stiffness immediately after the Fontan procedure, and it should be noted that liver stiffness reflects venous congestion to some extent. The present study revealed a significant correlation between liver stiffness and CVP in patients after the Fontan procedure as well as biventricular repair. We also revealed no significant relationships between liver stiffness and serum indices of hepatic fibrosis such as type IV collagen, type III pro-collagen peptide, and Mac-2 binding protein glycosylation isomer. Although the histological data of the patients were not assessed, we believe that liver stiffness on SWE is useful as an index of CVP rather than as an index of hepatic fibrosis in children with heart diseases.

Study Limitations
First, as this was an observational cross-sectional study, the reversibility of liver stiffness was not investigated. Therefore, it remains unclear whether ultrasound SWE is useful for the evaluation of temporal changes in CVP. Second, histological data on hepatic fibrosis were lacking in this study, and the poor correlation between hepatic fibrosis and liver stiffness was derived only from the serum indices of fibrosis. Further studies are required to address these limitations and confirm the present findings.

Conclusions
Liver stiffness on ultrasound SWE may be a useful non-invasive indicator of CVP in children with heart diseases, including those with biventricular disease and those with Fontan circulation.

Grants
None.

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