

## MINI REVIEW

# Two-Dimensional Shear Wave Ultrasound Elastography for Monitoring Pediatric Liver Transplantation: A Review of Recent Advances

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## ABSTRACT

Pediatric liver transplantation (PLT) is a life-saving procedure for children with end-stage liver disease. However, post-transplant monitoring, particularly the diagnosis and prognosis of complications such as allograft fibrosis, remains challenging. Traditionally, liver biopsy has been the gold standard for assessing allograft fibrosis, despite its invasive nature and inherent procedural risks. Recently, shear wave ultrasound elastography (SWE) has seen increasing use as a noninvasive method to provide real-time, quantitative measurements of liver stiffness as a proxy for fibrosis. In this review, the latest developments in the use of SWE as a method to assess allograft fibrosis post-PLT are presented, including the current technical challenges associated with its clinical implementation.

## 1 | Introduction

Pediatric liver transplantation (PLT) provides life-saving therapy for children with end-stage liver diseases such as biliary atresia, metabolic disorders, and acute liver failure [1]. Advances in surgical techniques have resulted in long-term survival rates exceeding 85% in many high-volume pediatric transplant centers [2]. Despite these improvements, managing PLT patients remains challenging, particularly in diagnosing and monitoring allograft health. Complications such as acute rejection, fibrosis, and biliary strictures can compromise graft function and require early, accurate diagnosis [3]. Compared to adults, pediatric

transplant recipients experience higher rates of infections, rejection, and early poor allograft function, although their long-term survival outcomes are generally more favorable [4, 5]. However, their younger age at transplantation necessitates prolonged follow-up [5].

Liver biopsy remains the gold standard for the clinical assessment and management of liver disease [6]. In cases of persistently abnormal liver tests of unclear etiology, liver biopsy has demonstrated diagnostic utility, with histological analysis providing a specific diagnosis in 84% of cases [7]. Moreover, it is instrumental in staging disease severity, particularly fibrosis,

**Abbreviations:** 2D-SWE, Two-Dimensional Shear Wave Elastography; APRI, Aspartate aminotransferase to Platelet Ratio Index; ARFI, Acoustic Radiation Force Impulse; EFSUMB, European Federation of Societies for Ultrasound in Medicine and Biology; FIB4, Fibrosis-4; HARI, Hepatic Artery Resistance Index; LAF, Liver Allograft Fibrosis; LSM, Liver Stiffness Measurement; METAVIR, Metabolic Evaluation Training Assessment Virus Inflammation Rating; MRI, Magnetic Resonance Imaging; PLT, Pediatric Liver Transplantation; PV, Portal Vein; SRU, Society of Radiologists in Ultrasound; SWE, Shear Wave Elastography; US, Ultrasound; WFUMB, World Federation for Ultrasound in Medicine and Biology.

and in evaluating liver mass lesions. Despite its diagnostic value, liver biopsy has several limitations, including technical factors (e.g., needle diameter, specimen size, and operator expertise) and risks, such as severe pain and hemorrhage. These factors can reduce its diagnostic potential.

Given these limitations, there has been a significant development in noninvasive imaging modalities such as ultrasound (US) and magnetic resonance imaging (MRI) to quantify liver fibrosis. In August 2024, the World Federation for Ultrasound in Medicine and Biology (WFUMB) updated its 2018 guidelines on the use of US elastography, though validated liver stiffness measurement (LSM) cutoffs for identifying pediatric patients at risk for fibrosis post-liver transplant were not provided [8]. This review aims to provide an overview of the developments in shear wave ultrasound elastography (SWE) over the past 5 years as a method for assessing allograft fibrosis in PLT patients, including the technical challenges associated with its clinical implementation.

### 1.1 | Methodology

A Medline, PubMed, OVID, and EMBASE search was conducted to gather relevant studies on 2D-SWE used in monitoring PLT. The primary search was limited to publications from the past 5 years (2019–2024) to ensure the inclusion of the latest advancements in the field. Studies were selected based on their relevance to the application of 2D-SWE in PLT patients, focusing on original research and comprehensive reviews published in English. In addition to the primary search, seminal articles published before 2019 were included to provide supplementary knowledge and foundational context essential for understanding recent developments. Articles that did not specifically address pediatric populations or liver transplantation, or utilized different elastography methods were excluded.

### 1.2 | Shear Wave Ultrasound Elastography

Elastography is an imaging technique that generates quantitative stiffness maps of soft tissue. In the context of liver elastography, research has shown that liver fibrosis is the primary determinant of liver stiffness, making LSM a reliable proxy for assessing liver fibrosis [9, 10]. SWE works on the principle of inducing slow-moving transverse or “shear” waves in the tissue through mechanical stress. This can be achieved using external mechanical methods, as in transient elastography (FibroScan), or through focused ultrasound pulses, known as acoustic radiation force impulse (ARFI). For a comprehensive description of the various US elastography techniques, refer to the review by Sigrist et al. [11]. By tracking the speed of the induced shear wave,  $c_s$  (m/s), and if the density of the material can be estimated,  $\rho$  ( $\text{kg/m}^3$ ), the Young’s modulus,  $E$  (kPa), can be estimated as

$$E = 3\rho c_s^2. \quad (1)$$

This equation is commonly used to describe most types of SWE modes. As a result, tissue elasticity can be directly calculated

from the reconstructed shear wave velocity, which serves as a proxy for liver fibrosis estimation [12].

In two-dimensional shear wave elastography (2D-SWE), multiple ARFI pulses are applied to expand the field of view. This allows for the creation of real-time, color-coded maps of tissue stiffness that can be superimposed on a conventional B-mode image [13]; see Figure 1.

A “cine loop” of multiple frames can be recorded, and the frames displaying the most stable pattern are selected for stiffness measurement. This feature is particularly advantageous for pediatric patients, as it mitigates the challenge of breath-holding during the procedure [13].

### 1.3 | Assessing Liver Disease Pretransplant

Accurate staging of liver disease in PLT candidates is essential to determine the timing and urgency of transplantation. Several studies have explored the efficacy of SWE in this context. For instance, a review by Dike et al. [14] examined the use of SWE in children with biliary atresia, one of the leading causes of PLT. The authors suggested that liver or spleen elastography could be particularly valuable in predicting outcomes such as the progression of portal hypertension and the potential need for liver transplantation.

Gu et al. [15] observed that liver stiffness measurements (LSM) were closely associated with portal vein (PV) maximum velocity, PV flow direction, hepatic artery resistance index (HARI), spleen diameter, and the presence of ascites. These findings are particularly important because, in pediatric patients with severe liver damage, PV blood flow was reduced or even reversed (hepatofugal). The authors concluded that SWE is a feasible and valuable tool for assessing liver damage in children with biliary atresia awaiting transplantation and may serve as a selection criterion for prioritizing children with advanced liver disease for liver transplantation.

## 2 | Diagnosing Post-Transplant Complications

Complications such as acute rejection, fibrosis, and vascular abnormalities are common among liver transplant recipients. Early detection of these complications is crucial for the improvement of long-term outcomes. In this regard, SWE has shown some promise. A study conducted by Monti et al. [16] focused on the use of 2D-SWE in diagnosing acute rejection among 54 PLT recipients in early childhood. In this study, it was determined that increased liver stiffness, measured by 2D-SWE, was strongly associated with histologically confirmed rejection. This could mean that SWE may be employed as a noninvasive marker for graft rejection and facilitate earlier intervention and treatment.

Another study by Gu et al. [15] expanded on these findings by exploring the use of 2D-SWE to assess liver fibrosis in 143 PLT recipients. The study found that 2D-SWE could detect early signs of fibrosis, which is a common complication following

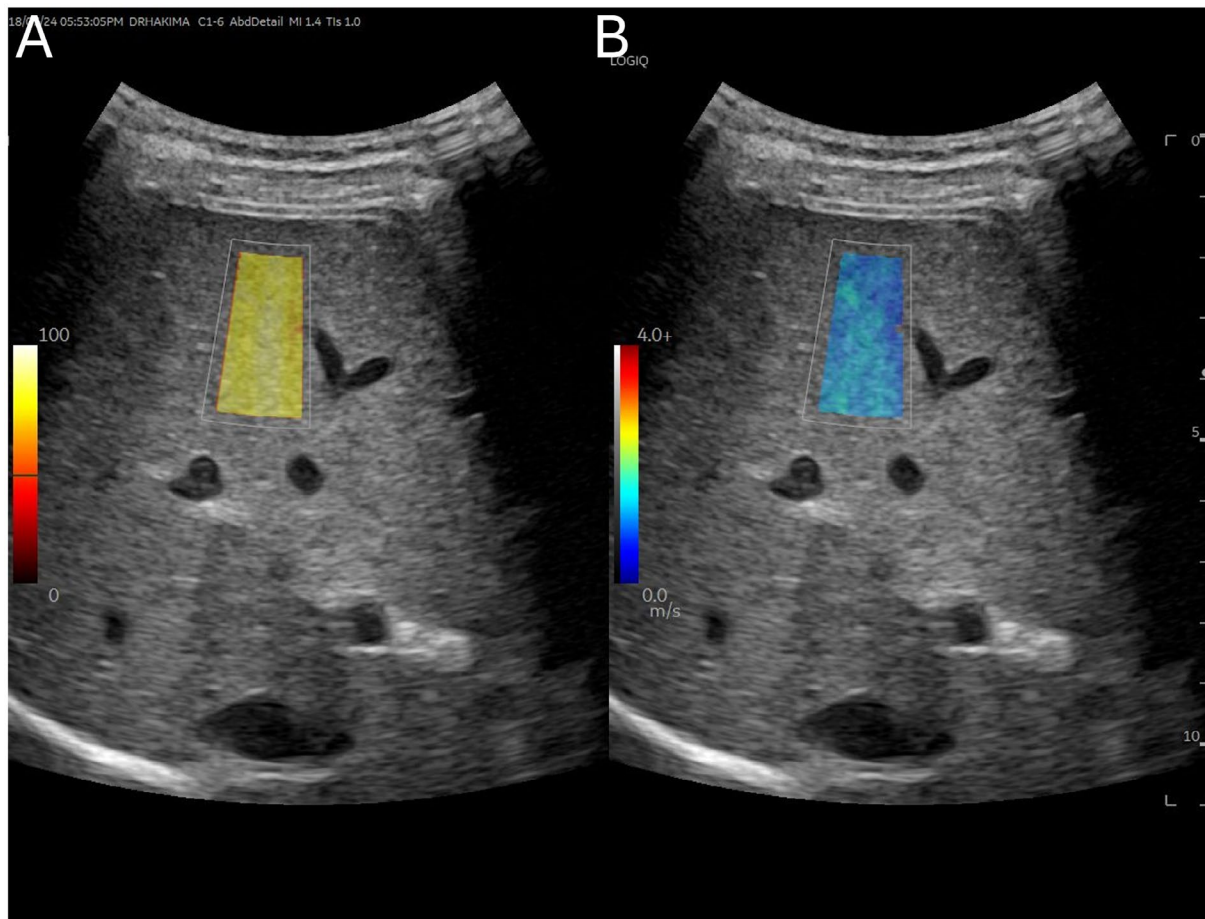


**FIGURE 1** | Two-dimensional shear wave elastography (2D-SWE) image of a pediatric liver using a GE LOGIQ E10 scanner. (A) Quality indicator showing homogeneity of region of interest. (B) Elastogram showing local shear wave speed in the region of interest.

**TABLE 1** | Suggested cut-off values for pediatric liver transplant fibrosis [17, 19, 23–25].

| Year of Study        | Scanner Model Used            | Sample Size | Fibrosis Classification Method | Suggested cut-off value (m/s)                      |
|----------------------|-------------------------------|-------------|--------------------------------|----------------------------------------------------|
| Gu et al. (2022)     | Aixplorer, SuperSonic Imagine | 98          | Scheuer                        | 1.57 $\geq$ S1<br>1.61 $\geq$ S2<br>1.88 $\geq$ S3 |
| Vo et al. (2022)     | Not provided in article       | 22          | Batts-Ludwig                   | 1.2                                                |
| Cetin et al. (2022)  | Canon Medical, Aplio i800     | 32          | Batts-Ludwig                   | 1.25 $\geq$ F2-F4                                  |
| Cetin et al. (2023)  | Canon Medical, Aplio i800     | 48          | Batts-Ludwig                   | 1.25 $\geq$ F2-F4                                  |
| Kehler et al. (2024) | GE Healthcare, LOGIQ E9 & E10 | 62          | METAVIR                        | 1.32 $\geq$ F0<br>1.42 $\geq$ F1<br>1.63 $\geq$ F2 |

liver transplantation. The ability to monitor fibrosis noninvasively could be particularly beneficial in pediatric patients, who may require long-term monitoring to ensure graft health. A further study by Gu et al. [17] in 2022 examined 98 PLT recipients and recorded values of 3.5–4 kPa (1.08–1.15 m/s) for healthy children and 7.5–8.5 kPa (1.58–1.68 m/s) for post-transplant pediatric patients with normal liver function. With cut-off values of 7.35 kPa (1.57 m/s), 7.80 kPa (1.61 m/s), and 10.60 kPa (1.88 m/s) for PLT recipients with fibrosis stages of

$\geq$  S1,  $\geq$  S2 &  $\geq$  S3 according to the Scheuer score system [18], respectively.

Vo et al. [19] investigated the use of blood serum biomarkers and 2D-SWE results in comparison to fibrosis scores using the Batts-Ludwig classification in 22 PLT recipients. It was found that 2D-SWE could be used to distinguish children with significant hepatic graft fibrosis ( $\geq$  F2) from those with no-mild fibrosis (F0-F1). Diagnostic performance was improved further when

combined with serum markers Aspartate aminotransferase to Platelet Ratio Index (APRI) and/or Fibrosis-4 (FIB4). For this study, a cut-off value of 1.2 m/s (4.2 kPa) was reported. Other studies using transient elastography have reported different cut-off values [20–22], but this review will focus on the use of 2D-SWE.

In 2022, Cetinic et al. [23] conducted a prospective feasibility study of 32 PLT recipients comparing 2D-SWE values and fibrosis scores according to the Batts-Ludwig classification. A significant positive correlation between the grade of fibrosis and SWE was found, with a cut-off SWE value of  $\leq 4.7$  kPa (1.25 m/s) yielding 100% sensitivity and 86% specificity to rule out fibrosis scores of F2–F4. However, a further follow-up study by Cetinic et al. [24] in 2023 of 48 PLT recipients revealed a weak positive correlation between the grade of fibrosis and SWE values, with a cut-off SWE value of  $\leq 4.7$  kPa (1.25 m/s) yielding 96% sensitivity and 73% specificity to rule out high-grade fibrosis (F2–F4).

Kehler et al. [25], with a study of 62 PLT recipients, found a significant correlation between LSM using 2D-SWE and the stage of fibrosis according to the Ishak Score, though the Metabolic Evaluation Training Assessment Virus Inflammation Rating (METAVIR) score and liver allograft fibrosis (LAF) scores were also reported. A cut-off value of 1.41 m/s was reported for any fibrosis, with a cut-off value of 1.63 m/s for significant fibrosis which was said to be comparable with the manufacturer cut-off values of 1.35 m/s and 1.55 m/s for any fibrosis and significant fibrosis, respectively.

Table 1 gives a summary of these findings and suggested cut-off values. A large amount of heterogeneity can be observed between these cut-off values.

### 2.1 | Use of 2D-SWE in Post-Transplant Longitudinal Monitoring

As PLT patients require lifelong monitoring, longitudinal monitoring of liver stiffness is essential for assessing graft health over time. Aside from routine biochemical blood tests, there is currently no established method for monitoring allograft function in liver transplant recipients [26]. In many pediatric centers, serial liver biopsies are routinely performed post-transplant to assess histological changes [27]. The value of 1-year protocol biopsies for PLT recipients with normal biochemical liver function varies between centers, with some arguing that the clinical benefit is 0%, with an upper confidence limit of 12% [28]. However, others have found that significant histological abnormalities may be observed in protocol biopsies taken from children who are clinically healthy, have good graft function, and display normal liver biochemistry [29].

As mentioned previously, the inherent invasive nature of liver biopsy has necessitated other modalities to be examined. SWE offers the advantage of measuring liver stiffness in a more diffuse manner, capturing heterogeneity in liver pathology that can be missed through biopsy, as each biopsy can sample only a very small portion of the liver [30]. This is especially important in children undergoing liver transplant, as comprehensive

follow-up has to be performed for the early detection and management of complications.

While this review acknowledges the current need for liver biopsy as a gold standard reference measurement of fibrosis, Kehler et al. argue that 2D-SWE may reduce the number of biopsies required [25]. For example, a high or increasing LSM may indicate the need for a liver biopsy to be taken, rather than have a routine liver biopsy as protocol. Monti et al. also propose the use of SWE as a first-line evaluation before biopsy and to use it as a screening tool that can detect significant alterations in stiffness and therefore specifically target patients requiring biopsies [16]. Both studies acknowledge the need for further studies in this area to determine the optimal frequency and timing of measurements post-transplant.

## 3 | Current Limitations

Despite the growing body of literature on the utility of 2D-SWE, the variability in measurements observed from different ultrasound scanners and centers is a concern. There are several limiting factors to be considered, including difficulties in comparing inter-device results due to differences in technologies and algorithms employed by various manufacturers. A direct comparison between different 2D-SWE scanners was not found in the literature for adult or pediatric liver transplant patients. A study by Vuorenmaa et al. [31] investigated inter-operator and inter-device reproducibility of 2D-SWE results in healthy muscle tissues. The study found no significant differences in the SWE measurements performed by two different operators, indicating that the technique itself is reliable when performed by different users. However, significant differences were observed in the SWE measurements between the two scanners, highlighting the influence of device-specific factors on measurement variability.

While not a direct comparison for 2D-SWE, a study by Atzori et al. [32] compared adult liver elastography results between one scanner utilizing transient elastography and two scanners utilizing point shear wave elastography. It was concluded that there was a “small, but not insignificant variation” with METAVIR F0–1 cut-off values ranging from 7.38 kPa to 8.90 kPa depending on the scanner used. This variability highlights the need for device-specific reference values or calibration methods in clinical practice.

There is also a lack of a standardized approach in imaging, particularly regarding the number of LSM acquisitions. Currently, no consensus exists. Some studies recommend at least six liver stiffness measurements [33], while others found no significant difference between protocols using five or ten measurements [34]. The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) recommends a minimum of three measurements [35], whereas the Society of Radiologists in Ultrasound (SRU) advises five measurements if a quality assessment is provided by the manufacturer or ten measurements if no quality assessment is available [36]. The updated WFUMB guidelines suggest that beginners perform five measurements, with the option to decrease the number

of acquisitions as the operator's expertise increases. No difference in diagnostic accuracy was found between using the mean of three or five acquisitions when a liver biopsy is available as a reference [8].

EFSUMB guidelines advise an intercostal approach along with breath-hold [35]. The updated WFUMB guidelines also advocate an intercostal approach, noting that in the pediatric population, shallow free-breathing while acquiring a long cine loop to identify the best possible frames is acceptable, although measurements may be lower compared to those taken with breath-hold [8, 37]. In some cases, positioning challenges arise. Kehler et al. noted that for patients with an absent right liver lobe, the transducer was repositioned to avoid scar tissue by aligning with the graft location [25]. A comparison of epigastric and intercostal approaches in children did not find a significant difference in LSMs [38].

While both the EFSUMB and WFUMB advise a minimum fasting period of 2 h, studies have acknowledged this can be difficult due to the age and/or clinical routine, and many studies may not strictly adhere to this guideline in all cases [15, 25]. The WFUMB acknowledges this difficulty and advises that measurements can be performed just before the next meal or at the start of eating, though this may increase LSM. These limitations underscore the need for further standardization and research to optimize the clinical utility of 2D-SWE in PLT patients.

## 4 | Conclusion

Over the past several years, 2D-SWE has emerged as a promising noninvasive tool for assessing liver fibrosis and monitoring allograft health in PLT recipients. The ability to provide real-time measurements over a large region of interest offers a significant advantage over traditional liver biopsies, particularly for repeated, long-term follow-up. However, despite its clinical potential, several limitations must be resolved to facilitate its widespread adoption, including inter-device variability and the absence of standardized cut-off values. Pediatric-specific guidelines and more robust clinical studies are also required to optimize its use.

As the field of elastography evolves, and as these challenges are met, 2D-SWE could play a pivotal role in reducing the number of liver biopsies performed post-transplant, improving patient care by enabling early detection of complications and facilitating more personalized management strategies for pediatric transplant recipients.

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## Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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