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Pediatric Liver Ultrasound Elastography

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A B S T R A C T

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Ultrasound elastography is an easy, relatively affordable, noninvasive method that can be used to assess for hepatic fibrosis. The aim of this article is to present an introduction to ultrasound elastography and provide case examples to show when its use can be beneficial.

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Introduction

Ultrasound (US) is often used for advanced imaging in the pediatric population. It is noninvasive, easily accessible, lacks ionizing radiation, and often does not require sedation. Common US examinations include evaluation of the head/neck, soft tissues, vessels, joints, and various abdominal structures. The use of advanced US techniques has continued to expand in evaluation and diagnoses of various disease processes in pediatric patients. One such emerging technique, US elastography, has been shown to accurately assess the elasticity or stiffness of tissues (Sigrist et al., 2017). Developed in the 1990s and becoming more widely available in the last 5 years, elastography is pertinent especially as it relates to the promising applications of assessments for signs of liver disease such as fibrosis and hepatic vascular congestion (Andersen et al., 2016). Applications in musculoskeletal and small organ imaging are also being evaluated for clinical significance (Thumar et al., 2018). Stiffness measurements can also be obtained using magnetic resonance elastography. The advantages of US elastography over magnetic resonance elastography are that US is cost-effective, can be performed portably, takes less time, does not require postimage processing, and it is easier to interpret.

How US Elastography Works

US elastography uses sound waves to assess the stiffness or elasticity of the tissues by applying a force and measuring the

resultant pressure or displacement. The two main US elastography techniques are strain elastography (STE) and shear wave elastography (SWE) (Sigrist et al., 2017). STE uses an external force applied to the tissue of interest. The amount of displacement compared to surrounding tissues is displayed in color in a strain image. In most instances, this technique does not directly quantify the tissue stiffness but rather compares the displacement relative to other tissues. In SWE, a force is applied to the tissue by using an acoustic radiation force impulse that is generated by the US transducer (Sigrist et al., 2017; Taljanovic et al., 2017). This force is applied to a focal area of tissue, and the shear waves are measured (Taljanovic et al., 2017). The speed of the shear waves directly correlate to the stiffness of the tissue. The stiffer the tissue interrogated, the faster the shear waves.

US Elastography Uses

The most common application for US elastography is the evaluation of a number of different liver pathologies. The most widely studied is the efficacy of US elastography to predict liver fibrosis. Several literature reviews have shown US elastography to be an excellent, noninvasive way to diagnose and grade hepatic fibrosis with high correlation to histologic grading on biopsies (Andersen et al., 2016). A meta-analysis by Kim et al. determined that US elastography has a sensitivity of 81% and a specificity of 91% to detect stage 2 liver fibrosis and even greater accuracy for higher stages of fibrosis (Kim et al., 2018). This has led to the use of US elastography in several conditions that may result in liver fibrosis. Such instances include grading of hepatic fibrosis in cirrhosis (Barr et al., 2015), evaluation of liver stiffness in patients after the Fontan procedure for congenital heart disease (Chen et al., 2016), nonalcoholic fatty liver disease (Ferraioli et al., 2018), and biliary atresia (Hanquinet et al., 2015). In a study performed at Children's Mercy Hospital, increasing shear wave elastography velocities were detected in patients with hepatic veno-occlusive disease (also

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Table 1

The mean elastography velocity can be used to estimate the histopathologic grade of fibrosis

Ultrasound elastography velocity correlation to pathology (Ishak grade)	
Ishak 0-1	1.46 m/s (mean velocity)
Ishak 2-3	1.82 m/s
Ishak 4-6	2.15 m/s

known as sinusoidal obstruction syndrome) after hematopoietic cell transplantation before other clinical or US changes (Reddivalla et al., 2018). In the clinical setting, this advanced detection is beneficial for monitoring such patients and detecting hepatic diseases earlier than the standard clinical signs. In the future, US elastography may serve as a noninvasive alternative to liver biopsy in the assessment and diagnosis of hepatic fibrosis in various patient populations.

There have been several studies which have examined the application of US elastography in various small organs for the evaluation of the elasticity of different tissues and to find noninvasive ways of monitoring and diagnosis. Studies in the kidney, for example, have looked at use of shear wave elastography in determining changes in the renal parenchyma in chronic renal disease, although results have been inconsistent (Bruno et al., 2016). Future studies may focus on complications of renal transplant or evaluation of benign versus malignant lesions (Aydin et al., 2018). Studies involving pancreatic tissues and musculoskeletal lesions have examined the application of US elastography to distinguish between benign and malignant lesions in such tissues (Park et al., 2014; Taljanovic et al., 2017). Other applications include the evaluation of muscle stiffness in cerebral palsy and congenital torticollis and differentiating between benign and malignant thyroid nodules (Brandenburg et al., 2015; Kwon & Park, 2012; Lin et al., 2014; Opfer & Chan, 2019).

Discussion

In our clinical practice, we are only using US elastography to assess liver stiffness. Liver US elastography is typically performed in addition to a right upper quadrant or complete abdominal US. At our institution, we acquire 12 shear wave measurements in a similar region in the right hepatic lobe per the Society of

Radiologists in Ultrasounds guidelines (Barr et al., 2015). US elastography typically adds approximately 2 minutes of additional technologist time. We report the median shear velocity and the interquartile range over median ratio. When that ratio is under 0.3, it gives us confidence that the examination is valid because the central range of the repeated measurements is small. In addition, the images should also be assessed by a radiologist for quality control to determine that the measurements were obtained in appropriate regions of the liver away from blood vessels and bile ducts. A table is included with the radiology report, which correlates shear wave velocity to the Ishak histopathology grade (Table 1) (Dillman et al., 2015).

Case Presentations

Case 1

The first case example (Figure 1) is that of a girl who had jaundice with elevated serum bilirubin values as a newborn. A liver biopsy and lab work were performed at 2 months of age, and she was diagnosed as having alpha-1 antitrypsin (AAT) deficiency. The liver biopsy also demonstrated portal fibrosis and focal bridging fibrosis. Patients with AAT deficiency are at risk for developing hepatic fibrosis. Because of the increased risk for cirrhosis in these patients, it's common for patients with AAT to get serum lab values and US examinations every 6-12 months for surveillance of any developing cirrhosis and possible hepatocellular carcinoma. The traditional grayscale appearance of her liver was normal during her second year follow-up examination. Only with the addition of US elastography during that examination was an abnormality noted with mildly elevated shear wave velocities. Given that her serum lab values were within normal range, it was decided to do follow-up imaging to assess the trend over time. Because of the increased sensitivity of US elastography for detecting small changes in liver stiffness, the intervals between invasive procedures may be able to be lengthened. More studies are needed to determine best clinical practices.

Case 2

The second case (Figure 2) is that of a 14-year-old boy with history of liver transplant when he was one-year old for biliary

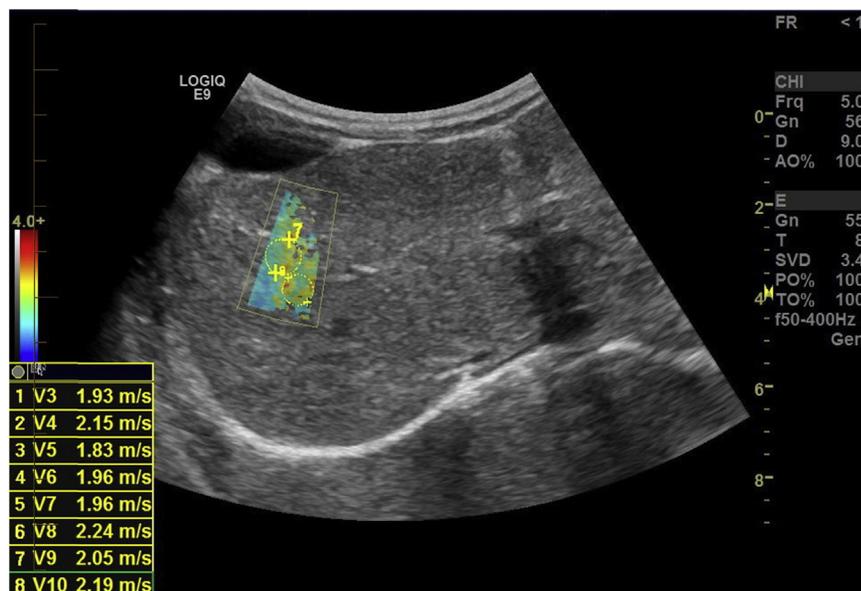


Figure 1. Two-year-old girl with history of alpha-1 antitrypsin (AAT) deficiency. Grayscale appearance of the liver was normal. US elastography demonstrates elevated mean velocity (1.9 m/s) indicating fibrosis. Biopsy showed portal fibrosis with focal bridging fibrosis. US = ultrasound.

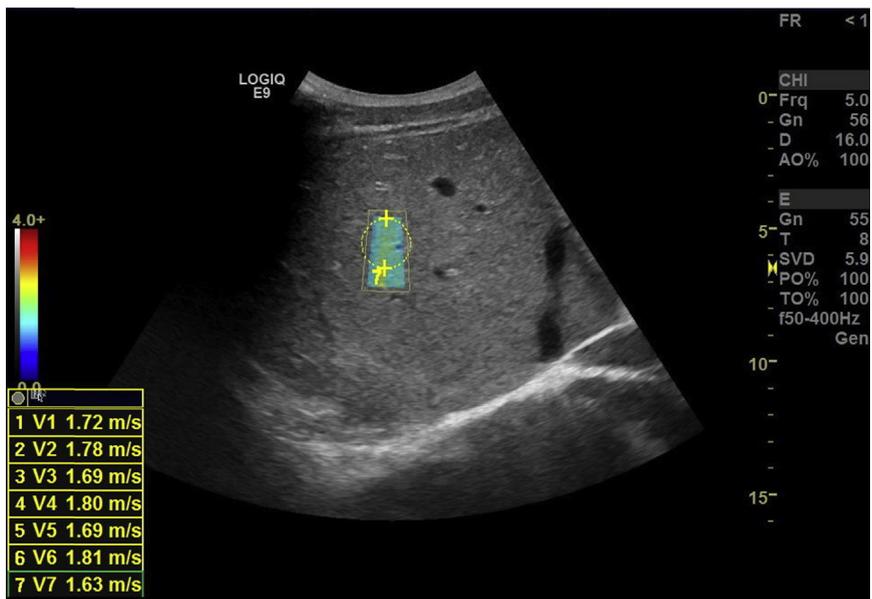


Figure 2. Fourteen-year-old boy with history of liver transplant. US elastography demonstrates mild elevation of mean velocity. Liver biopsy showed mild to moderate portal fibrosis, focal bridging, and sinusoidal fibrosis. US = ultrasound.

atresia who was being monitored for long-term complications from his liver transplant. US elastography demonstrated elevated velocities that correlated with mild to moderate fibrosis, and liver biopsy performed the following day was concordant showing mild to moderate liver fibrosis. His biopsy from 2 years before that showed only mild liver fibrosis. Because the US elastography and liver biopsy were concordant and both showed increasing liver fibrosis, medical management was optimized as the patient had been noncompliant with antifibrosis drug therapy. Follow-up biopsy in 18 months demonstrated decreased mild portal fibrosis. The standard of care procedure for surveillance of liver fibrosis after transplant is liver biopsy. Similar to the first case, if US elastography can be shown to be a good surrogate marker for surveillance of

fibrosis, this could potentially lengthen the time intervals between biopsies or completely eliminate them altogether, thus reducing risks.

Case 3

The third case (Figure 3) is from a 17-year-old boy with a history of chronic myelogenous leukemia who was treated with a hematopoietic cell transplant. He was enrolled as part of a research study where we were studying US elastography's ability to diagnose a transplant-related complication called veno-occlusive disease. Five days after his transplant, his elastography velocities had increased 24% from the baseline values. This was well before he met clinical criteria for this diagnosis and before the clinicians suspected



Figure 3. Seventeen-year-old girl with history of stem cell transplant for chronic myelogenous leukemia (CML) was being monitored for potential complication of stem cell transplant called veno-occlusive disease (VOD). US elastography showed abnormal elevation of the liver stiffness with increased velocities. Liver biopsy showed VOD with centrilobular hepatocyte damage with hemorrhage and early focal microvesicular steatosis. US = ultrasound.

that this mild abdominal pain and liver function test abnormalities could be due to veno-occlusive disease. At 12 days after transplant, the clinical team was starting to be concerned for veno-occlusive disease and obtained another elastography examination. At day 13 after transplant, he finally met the clinical (modified Seattle) diagnostic criteria for veno-occlusive disease when he had hepatomegaly and his weight was 4% over his baseline weight (Corbacioglu et al., 2018). At day 29 after transplant, liver biopsy was performed because of clinical concern for graft versus host disease. Histopathology confirmed the diagnosis of veno-occlusive disease with acute hepatocyte injury with no signs of graft versus host disease. This patient initially did well under supportive care with aggressive diuretics and pain management. However, the elastography values kept increasing as did his weight and right upper quadrant pain. He was then treated with defibrotide on day 30 after his transplant. Luckily, he did not progress to multiorgan failure and was discharged on day 53 after transplant.

The importance of identifying veno-occlusive disease in the setting of stem cell transplant is that disease mortality is profoundly impacted if treatment is initiated early in the disease course. In fact, mortality from veno-occlusive disease with multiorgan failure has been shown to be as high as 84% (Coppell et al., 2010); however, treatment with defibrotide has been shown to decrease 100-day mortality rates to anywhere from 29 to 59% (Richardson et al., 2019). US elastography can be used for close surveillance of these patients after transplant and can be used to help guide potential therapies to improve patient outcomes.

Radiology Nursing Role

The role of the radiology nurse includes playing a supportive role in the care for the patient and also providing education to the patient in regard to some of the basics of the radiologic examinations. Due to US imaging not requiring sedation, education could have different facets including reasons why imaging is being performed, patient preparation before imaging, and explaining benefits, risks, and alternatives of getting imaging. The radiology nurse should also be prepared to encourage distraction techniques and coach the patient through breath holds or quiet shallow breathing for patients unable to hold their breath. The supportive role that nurses perform varies greatly from patient to patient based on what their clinical history is and their current performance status. As in our case examples, many patients benefitting from US elastography have underlying liver disease, are transplant recipients (liver or stem cell), and are medically complex with input from many health care providers. Being able to communicate effectively with the different providers and with the patient is another very important role.

Conclusion

US elastography is an emerging technique that offers promising applications in relation to several disease processes within the pediatric population. As can be seen from our case examples, the addition of elastography to regular US can enhance sensitivity for detecting underlying liver disease. The advantages of US elastography over liver biopsy are that it is noninvasive. US elastography carries no risk compared with the risks inherent when performing a liver biopsy.

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