



Short Communication

Frequency of Disagreement between Liver Ultrasound and Elastography in the Diagnosis of Cirrhosis

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Abstract

Background and Aims: There are limited data on the frequency of disagreement on cirrhosis between the two methods, and the frequency of a correct diagnosis in instances of disagreement-particularly in a large sample size of patients. The objectives of this study were to access the frequency of disagreement between ultrasound (US) and shear wave elastography (SWE), and to determine each method's frequency of a correct diagnosis in instances of disagreement.

Methods: Both US and SWE were prospectively performed on patients (n=2,156) referred for evaluation for liver disease. When there was disagreement between US and SWE, clinical evaluations (ascites, hepatic encephalopathy, or variceal bleeding), other imaging (CT or MRI), laboratory findings (albumin < 3.2, platelets <125 or INR >1.2), or liver biopsy data that were available or previously collected were used to reconcile disagreement. **Results:** The frequency of disagreement between US and SWE on cirrhosis was 13%. SWE was correct in 56% of cases and US was correct in 44% when there was disagreement. **Conclusions:** SWE vs. US appears to be more often correct in instances of disagreement. Other large prospective studies are needed to replicate the current study's findings.

Keywords: Ultrasound; Elastography; Cirrhosis; Diagnosis

Introduction

Ultrasound (US) is usually used to diagnose sequelae of chronic liver disease such as liver fibrosis and cirrhosis [1-3]. Sonography is widely utilized for surveillance and screening in individuals susceptible to developing hepatocellular carcinoma (HCC), and for assessing hepatic vasculature when utilized with Doppler ultrasound [4,5]. Decompensated cirrhosis with portal hypertension, which manifests through varices, splenomegaly, and ascites, is also well diagnosed on US. Liver surface nodularity, visualized by a linear probe, is well-established as a direct sign of advanced fibrosis, with described sensitivity and specificity of 54% and 95%, respectively [6]. Other features such as enlarged caudate and caudate-right lobe ratio increases sensitivity but limits the specificity of US.

Introduced in 2003, Fibroscan (Echosens) [7] is a non-imaging ultrasound based technique using an externally applied device to generate a shear wave within the liver to measure liver stiffness, termed Transient Elastography (TE). TE is measured in kilopascal (kPa), has excellent reproducibility, but does not image the location of the measurement site, so that large patients and those with ascites, large vessels and masses at the measurement site may yield inaccurate results, and does not assess for disease uniformity.

In 2008, a technique for generating shear waves within the liver by the ultrasound using the ultrasound scanner/transducer was developed, termed Acoustic Radiation Force Impulse (ARFI), obviating the need for an external device to create shear waves in the liver. ARFI uses real time imaging assessment for the placement of region of interest location, improving previous concerns regarding lack of imaging information with TE. ARFI technology is used in both point SWE (pSWE) and two-dimensional SWE (2D SWE) perform the tissue stiffness assessment of liver fibrosis [8].

Liver biopsy has been historically considered the cornerstone and gold standard in the diagnosis of liver cirrhosis. However, the emergence of multiple sensitive and relatively accurate blood tests and imaging tools has limited the use of liver biopsy in the clinical setting, specifically to cases where all other tests are negative. In addition, the safety of these measures as compared to liver biopsy which always carries albeit small but significant risks of bleeding and infection [9].

Many patients with liver disease will have both US and elastography done for evaluation of the presence and extent of liver fibrosis. In some instances, US and elastography will provide divergent results in the diagnosis of cirrhosis (i.e., one method will

indicate cirrhosis and the other will not). There are limited data on the frequency of disagreement on cirrhosis between the two methods, and the frequency of a correct diagnosis in instances of disagreement-particularly in a large sample size of patients. The objectives of this study were to access the frequency of disagreement between US and SWE, and to determine each method's frequency of a correct diagnosis in instances of disagreement.

Methods

Both US and SWE were prospectively performed on patients referred for evaluation for liver disease (n=2,156) in the radiology department at the University of Alabama at Birmingham by credentialed sonographers in a laboratory accredited by the American College of Radiology. US diagnosis of cirrhosis by board certified radiologists with fellowship training in body imaging was based on the presence of at least one of the following: enlarged left lobe, enlarged caudate, increased caudate to right lobe ratio and/or surface nodularity. Point SWE was performed with Philips EPIQ US scanners (Philips Ultrasound), according to established protocol [8]. Prior US or CT/MRI examinations were reviewed at the time of the US, if available. In accordance with the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement, SWE diagnosis of cirrhosis was based on the presence of a liver stiffness value >13 kPa [8]. When there was disagreement between US and SWE, clinical evaluations (ascites, hepatic encephalopathy, or variceal bleeding), other imaging (CT or MRI), laboratory findings (albumin <3.2, platelets <125 or INR >1.2), or liver biopsy data that were available or previously collected were used to reconcile disagreement. Measures of central tendency and frequency distributions were used to characterize 1) the sample, 2) the frequency of disagreement, 3) and the frequency of a correct diagnosis in instances of disagreement. The institutional review board at the University of Alabama at Birmingham approved this study.

Results

The mean age was 53 (13.2) years, and the majority were White (65%) and male (51%) (Table 1). Hepatitis C virus (HCV) (68%) was the most frequent liver disease etiology, followed by non-alcoholic steatohepatitis (NASH) (10%) and hepatitis B virus (HBV) (6%). The mean body mass index (BMI) was 29 (7.2). The frequency of disagreement between US and SWE on cirrhosis was 13% (286/2,156). In cases of disagreement, other imaging modalities (CT or MRI), laboratory findings, clinical judgement, or liver biopsy (if available) data were used to confirm the diagnosis—which were available on 90% (258/286) of cases with disagreement. SWE was correct in 56% (144/286) of cases and US was correct in 44% (114/286) and when there was disagreement.

Variables	Total	%/M (SD)
n=2,156		
Age		53.4 (13.2)
Race/Ethnicity		
White	1,367	65.4%
African American	662	31.7%
Hispanic	2	0.1%
Asian	44	2.1%
Other	16	0.8%
Sex		
Male	1,101	51.1%
Female	1,055	48.9%
Body Mass Index (BMI)		29.3 (7.2)
Liver Disease Etiology		
Hepatitis C virus (HCV)	1,403	67.7%
Non-alcoholic steatohepatitis (NASH)	208	10.3%
Hepatitis B virus (HBV)	115	5.7%
Autoimmune hepatitis	67	3.3%
Alcoholic hepatitis	45	2.2%
Non-alcoholic fatty liver disease (NAFLD)	36	1.8%
Primary biliary cholangitis (PBC)	34	1.7%
Frequency of Agreement and Disagreement		
Agreement	1,864	86.5%
Disagreement	292	13.5%
Type of Agreement and Disagreement		
Agreement: Ultrasound Elastography		
Agreement: Cirrhosis Cirrhosis	141	6.5%
Agreement: No cirrhosis No cirrhosis	1,723	79.9%
Disagreement: Cirrhosis No cirrhosis	212	9.8%
Disagreement: No cirrhosis Cirrhosis	80	3.7%
Frequency of Correct Diagnosis during Disagreement		
Ultrasound (US)	117	43.5%
Shear-Wave Elastography (SWE)	152	56.5%

Table 1: Sample Characteristics and Frequency of Ultrasound (US) and Shear-Wave Elastography (SWE) Agreement and Disagreement.

Discussion

This study accessed the frequency of disagreement between US and SWE, and determined each method's frequency of a correct diagnosis in instances of disagreement. Though US and SWE largely concurred in the diagnosis of cirrhosis in this relatively large prospective study, the frequency of disagreement was 13% and SWE was more often correct in instances of disagreement. Similarly, elsewhere SWE has been found to be superior to US in the evaluation and diagnosis of liver fibrosis and early cirrhosis. [10] SWE has been found to have high levels of intra-observer and inter-observer agreement [11], and a meta-analysis demonstrated that SWE has good to excellent performance in assessment of liver fibrosis and cirrhosis, especially in patients with HBV [12].

SWE does have several notable limitations. Patient fasting is ideal as eating increases hepatic blood flow, which may increase measured liver stiffness. Elevated aspartate aminotransferase (AST) levels (e.g., >5 times normal levels) can yield overestimations in liver fibrosis. Also, ascites and volume overload may increase liver stiffness values [13,14].

The present study had several limitations and strengths. US is operator dependent, and variations in the accuracy of readings may vary by US operator. In some cases, laboratory results were used to reconcile US and SWE disagreement, but indications of cirrhosis on laboratory results can be influenced by other pathological processes. More than three-fourths of the sample was composed of patients with HCV or NASH, limiting generalizability to other liver disease etiologies. In addition, having a liver biopsy as gold standard for diagnosis of liver cirrhosis was not feasible as currently liver cirrhosis mainly diagnosed with noninvasive methods in the United States. Despite these limitations, the study was prospective, included a relatively large sample of patients (n=2,156), more than one-third of the sample was racially/ethnically diverse, and four methods were used to resolve all cases of disagreement.

Non-invasive methods in the diagnosis of cirrhosis have evolved over the years. Though US and SWE may sometimes yield divergent diagnostic findings in the diagnosis of cirrhosis, non-invasive methods have considerable benefits over invasive methods. Other large prospective studies are needed to replicate the current study's findings-frequency of US and SWE disagreement and each method's frequency of a correct diagnosis in instances of disagreement.

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