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● *Original Contribution*

ACOUSTIC RADIATION FORCE IMPULSE AND SUPERSONIC SHEAR IMAGING VERSUS TRANSIENT ELASTOGRAPHY FOR LIVER FIBROSIS ASSESSMENT

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Abstract—Our study compared three elastographic methods—transient elastography (TE), acoustic radiation force impulse (ARFI) imaging and supersonic shear imaging (SSI)—with respect to the feasibility of their use in liver fibrosis evaluation. We also compared the performance of ARFI imaging and SSI, with TE as the reference method. The study included 332 patients, with or without hepatopathies, in which liver stiffness was evaluated using TE, ARFI and SSI. Reliable measurements were defined as a median value of 10 (TE, ARFI imaging) or 5 (SSI) liver stiffness measurements with a success rate ≥60% and an interquartile range interval <30%. A significantly higher percentage of reliable measurements were obtained using ARFI than by using TE and SSI: 92.1% versus 72.2% ($p < 0.0001$) and 92.1% versus 71.3% ($p < 0.0001$). Higher body mass index and older age were significantly associated with inability to obtain reliable measurements of liver stiffness using TE and SSI. In 55.4% of patients, reliable liver stiffness measurements were obtained using all three elastographic methods, and ARFI imaging and TE were similarly accurate in diagnosing significant fibrosis and cirrhosis, with TE as the reference method. (E-mail: isporea@umft.ro) © **2013 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Liver stiffness, Liver fibrosis, Transient elastography, Acoustic radiation force impulse elastography, Supersonic shear imaging.**

INTRODUCTION

Chronic liver diseases are quite common in daily practice. In some areas, chronic viral hepatitis B and/or hepatitis C are dominant, and in others, non-viral chronic hepatopathies (alcoholic or non-alcoholic steatohepatitis) are more common. To assess the severity of chronic liver diseases, the hepatologist can use invasive (liver biopsy) or non-invasive techniques.

After its introduction into daily practice, the first liver biopsy being performed in 1923 (Bingel 1923), percutaneous liver biopsy became an indispensable tool for the evaluation of liver diseases. Because liver biopsy offers information regarding fibrosis stage, necro-inflammation and fatty infiltration and reveals specific markers in certain hepatic diseases, this morphologic examination is considered the "gold standard" method for assessment of liver diseases (Grant and Neuberger 1999; Rockey et al. 2009). However, we must consider that after diagnostic liver biopsy, minor or serious complications, including death, may occur in 1–5% of cases (Piccinino et al. 1986), and that liver biopsy has limitations because of the uneven distribution of liver fibrosis (Bedossa et al. 2003), the small size of the specimen (approximately 1/50,000th of the total volume of the liver) (Afdhal 2006) and inter- and intra-observer diagnostic discrepancies in biopsy assessments of liver fibrosis (Bedossa et al. 1994). For these reasons, several non-invasive methods for liver fibrosis assessment have been developed in the last 10–15 y.

Serologic tests were the first ones to be developed; they can be used evaluate liver fibrosis (Guha et al. 2008) and activity and fibrosis (Poynard et al. 2004). Subsequently, transient elastography (TE), commercialized as the FibroScan, a shear wave ultrasound elastographic method, began to be used for liver fibrosis assessment. Several published studies and meta-analyses (Friedrich-Rust et al. 2008; Sandrin et al. 2003; Tsochatzis et al. 2011) have reported that TE is a reliable diagnostic tool for the non-invasive evaluation of liver fibrosis, especially in patients with chronic

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hepatitis C (Castera et al. 2005; Tsochatzis et al. 2011), but also in those with chronic hepatitis B (Chon et al. 2012; Marcellin et al. 2009) and non-alcoholic steatohepatitis (Wong et al. 2010) and in post-transplant patients (Adebajo et al. 2012). TE also has some limitations: it is hampered by the presence of ascites because TE waves cannot penetrate into ascites; obesity significantly decreases the rate of reliable measurements (Castera et al. 2010); aminotransferases flares are associated with falsely elevated TE values (Coco et al. 2007, Viganò et al. 2010); and extra-hepatic cholestasis (Millonig et al. 2008) and high central venous pressure (Millonig et al. 2010) falsely increase the liver stiffness values assessed by TE. Also, the FibroScan device is quite expensive and, thus, in some countries, the number of available systems is limited.

In the last 3 y, several real-time elastographic methods have been used for the non-invasive assessment of liver fibrosis. They can be classified into two categories: *train methods*, such as real-time tissue elastography (Havre et al. 2008), and *shear wave methods*, such as acoustic radiation force impulse (ARFI) elastography (Friedrich-Rust et al. 2007) and supersonic shear imaging (SSI) (Bavu et al. 2011). Unlike TE, real-time elastographic methods are included in standard ultrasound systems that can be used for many other purposes (standard ultrasound examination, Doppler evaluation, contrast-enhanced ultrasound), so that these devices are more cost effective. Another advantage is that patients with ascites can also be evaluated by means of real-time techniques.

Among the real-time elastographic methods, ARFI has been studied the most. A recently published meta-analysis (Friedrich-Rust et al. 2012) indicated that it is a good method for liver fibrosis evaluation, with accuracies of 0.87 in predicting significant fibrosis ($F \geq 2$), 0.91 in predicting severe fibrosis ($F \geq 3$) and 0.93 in predicting liver cirrhosis. SSI is the latest to appear on the market, and there are few, although promising, published studies regarding this technique (Bavu et al. 2011, Ferraioli et al. 2012).

The main aim of this study was to compare the feasibility of using the three elastographic methods involving ultrasound shear waves (TE, ARFI and SSI). The secondary aim was to compare ARFI elastography and SSI with respect to performance in the assessment of liver fibrosis assessment, with TE as the reference method, because TE has already been validated for the evaluation of liver fibrosis (Adebajo et al. 2012; Castera et al. 2005; Chon et al. 2012; European Association for the Study of the Liver 2011, 2012; Marcellin et al. 2009; Tsochatzis et al. 2011; Wong et al. 2010).

METHODS

Patients

Our study included 332 consecutive patients for whom liver stiffness (LS) was evaluated in the same session using three elastographic methods: TE, ARFI and SSI. The subjects were: healthy volunteers (medical students, nurses and medical doctors from our hospital: none had a history of liver disease, but additional tests, such as biological tests and viral markers, were not performed, with the exception of an ultrasound examination, which was normal); patients with chronic hepatitis B and C; patients with chronic non-viral hepatitis (such as alcoholic or non-alcoholic steatohepatitis, autoimmune hepatitis, primary biliary cirrhosis); and patients previously diagnosed with liver cirrhosis on the basis of clinical, biologic, ultrasonographic, morphologic and/or laparoscopic criteria.

All patients included in our study had a homogeneous liver structure (without focal liver lesions) and no ascites on abdominal ultrasound examination.

All patients signed an informed consent before elastographic measurements; the study was approved by the local ethics committee and was performed in accordance with the Helsinki Declaration of 1975.

Transient elastography

Liver stiffness was measured by means of TE using the FibroScan device (EchoSens, Paris, France), which incorporates a 5-MHz ultrasound transducer probe mounted on the axis of a vibrator. The vibrator generates a completely painless vibration (50-Hz frequency and 2-mm amplitude), which induces an elastic shear wave propagating through the skin and the subcutaneous tissue to the liver, which is tracked using the coaxial ultrasound transducer. The wave velocity is directly related to tissue stiffness, which is calculated by the device and expressed in kilopascals (Sandrin et al. 2003).

For each patient, 10 valid TE measurements were performed under fasting conditions. The patient was in the supine position, by the intercostal approach, with the right arm in maximum abduction. A standard M-probe was used. The median value was calculated and expressed in kilopascals. A reliable measurement was defined as the median of 10 valid LS measurements with a success rate (SR = ratio of number of successful acquisitions to total number of acquisitions) $\geq$60% and an interquartile range (IQR = difference between 75th and 25th percentiles, essentially the range of the middle 50% of the data) $<$30% (Fig. 1). The median of 10 valid measurements was considered as indicative of the severity of fibrosis.