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● *Original Contribution*

COMPARISON OF ACOUSTIC RADIATION FORCE IMPULSE IMAGING AND TRANSIENT ELASTOGRAPHY FOR NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B

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Abstract—The aims of this study were to compare the performance of acoustic radiation force impulse (ARFI) elastography and transient elastography (TE) in the assessment of liver fibrosis in patients with chronic hepatitis B and to evaluate the impact of elevated alanine transaminase levels on liver stiffness assessment using ARFI elastography. One hundred eighty consecutive patients with chronic hepatitis B were enrolled in this study and evaluated with respect to histologic and biochemical features. All patients underwent ARFI elastography and TE. ARFI elastography and TE correlated significantly with histologically assessed fibrosis ($r = 0.599$, $p < 0.001$, for ARFI elastography; $r = 0.628$, $p < 0.001$, for TE) and necro-inflammatory activity ($r = 0.591$, $p < 0.001$, for ARFI elastography; $r = 0.616$, $p < 0.001$, for TE). Areas under the receiver operating characteristic curves for ARFI elastography and TE were 0.764 and 0.813 ($p = 0.302$, ≥stage 2), 0.852 and 0.852 ($p = 1.000$, ≥stage 3) and 0.825 and 0.799 ($p = 0.655$, S = 4), respectively. The optimum cutoff values for ARFI elastography were 1.63 m/s for stage ≥2, 1.74 m/s for stage ≥3 and 2.00 m/s for stage 4 in patients for whom alanine transaminase levels were evaluated. The cutoff values decreased to 1.24 m/s for ≥ stage 2, 1.32 m/s for ≥ stage 3 and 1.41 m/s for stage 4 in patients with normal alanine transaminase levels. ARFI elastography may be a reliable method for diagnosing the stage of liver fibrosis with diagnostic performance similar to that of TE in patients with chronic hepatitis B. In addition, liver stiffness values obtained with ARFI elastography, like those obtained with TE, may be influenced by alanine transaminase levels. (E-mail: zdk002@163.com) **© 2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Acoustic radiation force impulse elastography, Transient elastography, Chronic hepatitis B, Liver fibrosis, Liver stiffness.**

INTRODUCTION

Chronic hepatitis B (CHB) infection affects nearly 350–400 million people worldwide (European Association for the Study of the Liver [EASL] 2012). It is a major cause of liver cirrhosis and hepatocellular carcinoma. Staging of liver fibrosis is important for prognostic and therapeutic decisions in patients with CHB. Recent international treatment guidelines clearly state the importance of liver fibrosis as a pre-treatment assessment of CHB (Liaw et al. 2012; Lok and McMahon 2009). Currently, liver biopsy (LB) is the gold standard for the diagnosis and staging of fibrosis in patients with CHB. This procedure, however, is invasive and is associated with a relatively high risk of complications (Thampanitchawong et al. 1999). In addition, the accuracy of LB is limited by intra-observer and inter-observer variability and sampling errors (Regev et al. 2002; Bedossa et al. 2003). Therefore, LB is not a perfect reference standard, leading to an increasing demand for a non-invasive and reliable test.

Elastography techniques have recently been developed as potential non-invasive techniques for assessment of chronic liver diseases with promising results. Many recent studies have evaluated the performance transient elastography (TE), a currently well-established ultrasound-based method for non-invasive liver fibrosis staging worldwide, in the diagnosis of fibrosis stage (Cardoso et al. 2012; Chon et al. 2012; Sporea et al. 2013; Suzuki et al. 2013). However, the performance of

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TE has been reported to be unsatisfactory in patients with ascites, obesity or narrow intercostal spaces (Foucher et al. 2006). One study reported that TE is less accurate in the diagnosis of liver cirrhosis in CHB and non-alcoholic fatty liver disease than in the diagnosis of chronic hepatitis C (Gaia et al. 2011). Recently, acoustic radiation force impulse (ARFI) elastography has been proposed as a novel ultrasound-based and alternative elastography method for assessment of liver elasticity. It enables exact localization of the ARFI measurement site during B-mode ultrasound. However, very few studies have reported its performance in patients with CHB (Friedrich-Rust et al. 2013; Sporea et al. 2012). The purpose of our study was to evaluate the value of ARFI elastography in the assessment of liver fibrosis and to compare the accuracy of ARFI elastography and TE in patients with CHB only, with respect to the severity of fibrosis assessed histologically. We also investigated the impact of necro-inflammatory activity on ARFI elastography.

METHODS

Patients

Between October 2011 and June 2013, we enrolled 197 consecutive patients with CHB who underwent LB, ARFI elastography and TE in our hospital. CHB infection was diagnosed by positive serology tests for serum hepatitis B surface antigen (HBsAg) for at least 6 mo. None of the patients were receiving antiviral therapy at the time of enrollment. The indication for LB was determination of the severity of liver fibrosis and inflammation. For each patient, comprehensive blood liver tests (*i.e.*, aspartate transaminase, alanine transaminase [ALT], serum albumin, γ-glutamyltransferase, total bilirubin, triglycerides, cholesterol and platelet count) and all elastography measurements were performed no more than 3 d before the LB. The study was performed in accordance with the ethical guidelines of the Helsinki Declaration and approved by the ethics committee of our institute. All study patients gave written consent before being enrolled in the study.

Acoustic radiation force impulse elastography

In our study, the Acuson S2000 ultrasound system (Siemens, Beijing, China) was used for ARFI elastography measurements in all patients. Three trained operators (each with >3 y of experience with conventional US examination and more than 100 elastography measurements) who were blinded to the liver biopsy and clinical data performed measurements. The ultrasound transducer probe automatically produces mechanical energy using short-duration acoustic pulse to generate localized displacements in the examined liver tissue. The displacements result in propagation of shear waves away from the region of excitation that are tracked using US correlation-based methods (Nightingale et al. 2002). ARFI elastography measurements were performed in the right liver lobe through the intercostal space. Patients were positioned supine with the right arm in abduction and were asked to hold their breath for a moment to minimize breathing motion when being examined. ARFI elastography measurements were performed so as to avoid large vessels and ducts in the liver; the 1–2 cm below the surface of the liver was chosen as the measuring depth. A total of 10 valid measurements were performed in every patient and the median value was calculated, the result being expressed in meters per second.

Transient elastography

In our study, TE was performed with the FibroScan device (Echosens, Paris, France). The vibrator generates shear waves that propagate through the skin into the liver tissue. TE measurements were performed in the right lobe of the liver, through the intercostal space. Patients were positioned supine with the right arm in abduction. After the place of measurement was located, the operator pressed the button of the probe to start the measurement. A total of 10 valid measurements were performed in every patient, and the median value was calculated, the result being expressed in kilopascals.

Liver histology assessment

LB was performed using 16G disposable Trucut needles (C. R. Bard, Covington, GA, USA) under ultrasonographic guidance in the Department of Ultrasound. Liver specimens were stained with hematoxylin and eosin and assessed by an expert liver pathologist (with 20 y of experience) without knowledge of liver stiffness (LS) measurements and clinical data. A liver sample was excluded from histologic analysis if it was shorter than 15 mm and contained fewer than six portal tracts. Liver fibrosis and necro-inflammatory activity were evaluated histologically according to the Scheuer scoring system (Theise et al. 2007). Fibrosis was staged on a scale from 0 to 4: stage 0 (S0) = absence of fibrosis; stage 1 (S1) = fibrous portal expansion; stage 2 (S2) = periportal or rare portal–portal septa; stage 3 (S3) = fibrous septa with architectural distortion; and stage 4 (S4) = cirrhosis. Necro-inflammatory activity was graded as follows: grade 0 (G0) = no portal/periportal and lobular necro-inflammatory activity; grade 1 (G1) = portal/periportal inflammation and minimal, occasionally spotty, lobular inflammation; grade 2 (G2) = mild piecemeal portal/periportal necrosis and mild or focal lobular necrosis; grade 3 (G3) = moderate piecemeal portal/periportal necrosis and moderate or noticeable hepatocellular change inside the lobule; and