Ultrasound in Med. & Biol., Vol. ■■, No. ■■, pp. ■■–■■, 2018

0301-5629/$ - see front matter

https://doi.org/10.1016/j.ultrasmedbio.2018.02.010

● *Original Contribution*

ACOUSTIC STRUCTURE QUANTIFICATION VERSUS POINT SHEAR WAVE SPEED MEASUREMENT FOR THE ASSESSMENT OF LIVER FIBROSIS IN VIRAL HEPATITIS B

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(*Received* 10 *July* 2017; *revised* 5 *December* 2017; *in final form* 22 *February* 2018)

Abstract—This study was conducted to evaluate the value of acoustic structure quantification (ASQ) technology versus that of point shear wave speed measurement (PSWSM) imaging technology for the assessment of liver fibrosis stage. A total of 104 patients with chronic hepatitis B (CHB) and 30 healthy control patients underwent ASQ and PSWSM examinations. Seven quantitative parameters were obtained from ASQ, and a principal component analysis was used to establish the integrative indicators. A quantitative parameter, known as the shear wave speed (SWS, m/s), was obtained from the PSWSM. The METAVIR scores for the assessment of pathologic liver fibrosis were used as a benchmark. Liver fibrosis stages exhibited a good correlation with the integrative indicators and SWS ($r = 0.682$, $p < 0.001$; $r = 0.651$, $p < 0.001$). The areas under the receiver operating characteristic curves for ASQ and PSWSM were 0.705 and 0.854 for mild liver fibrosis ($F \geq 1$, $p = 0.045$), 0.813 and 0.743 for significant liver fibrosis ($F \geq 2$, $p = 0.115$), 0.839 and 0.857 for severe liver fibrosis ($F \geq 3$, $p = 0.417$) and 0.874 and 0.971 for liver cirrhosis ($F = 4$, $p = 0.016$), respectively. In conclusion, both ASQ and PSWSM were promising ultrasonic methods for assessing liver fibrosis in patients with CHB; however, PSWSM was more valuable for identifying mild liver fibrosis ($F \geq 1$) and cirrhosis ($F = 4$) than ASQ, and the combination of PSWSM and ASQ improved the accuracy of diagnosing severe liver fibrosis ($F \geq 3$). (E-mail: arfi2014@126.com, linshumei123@126.com)

Key Words: **Liver fibrosis, Non-invasive diagnosis, Acoustic structure quantification, Point shear wave speed measurement, Chronic hepatitis B, Liver biopsy.**

INTRODUCTION

Liver fibrosis is the main characteristic of chronic liver disease. Overall, 20%–40% of chronic liver disease cases progress to liver fibrosis or cirrhosis. Severe liver cirrhosis can cause bleeding from esophageal and gastric varices, hepatic encephalopathy and hepatic failure (Ramachandran and Iredale 2012). Moreover, progressive liver fibrosis is closely related to hepatocellular carcinoma (El-Serag 2002). Chronic viral infection is the main factor involved in liver fibrosis and liver cirrhosis. In China, chronic viral infections account for 60%–80% of liver fibrosis and liver cirrhosis (Wang et al. 2014). An accurate assessment of the extent of liver fibrosis is important for the treatment, prognosis and monitoring of viral hepatitis B.

Liver biopsy (LB) remains the gold standard for the diagnosis of liver fibrosis (Gebo et al. 2002). However, LB is an invasive examination that terrifies some patients. Pain may occur during liver biopsy; 25% of patients experience pain after this procedure (Sebastiani 2009). Other uncommon complications include intra-abdominal hemorrhage, infection, bile leakage, hemothorax and pneumothorax (Filingeri et al. 2015), and the mortality rate is 0.05% (Bravo et al. 2001). Because of the unevenness of liver fibrosis, liver biopsy strips (which account for only 1 of 50,000 livers) are not adequate to reflect the extent

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Conflict of Interest: The authors do not have conflicts of interest to disclose.

of fibrosis of the whole liver (Duarte-Rojo et al. 2012). Additionally, inter-observer and intra-observer differences in pathologic observations can influence the accuracy of the assessment of liver fibrosis (Regev et al. 2002).

Ultrasound-based elastography is a non-invasive and quantitative tool for the assessment of tissue stiffness. Liver fibrosis, which is caused by the excessive deposition of extracellular matrix, results in increased tissue stiffness, prompting the use of ultrasound elastography to assess these changes. Currently, the most commonly used technologies in clinical research and applications are transient elastography (TE, FibroScan, Echosens, Paris, France) and ultrasound shear wave elastography (USWE). The main difference between TE and USWE is the nature of the excitation. The external excitation in TE punches the body surface to generate shear waves propagating through the tissue along the "A line" (Shiina et al. 2015). USWE does not require external pressure to assess elastic information from deep tissue. Instead, it emits focused acoustic radiation pulses (0.05–1 ms) to induce the tissue to produce a shear wave propagating along the transverse direction (Nightingale et al. 2003). Both measure the propagation of the shear wave in one direction. Compared with USWE, TE has been used in clinical practice for a longer time and has been included in the Guidelines for the Diagnosis and Management of Chronic Liver Diseases (European Association for the Study of the Liver [EASL] 2012). Some studies have indicated that performance of point shear wave measurement (PSWSM) is comparable to that of TE in the diagnosis of liver fibrosis (Bota et al. 2013). However, FibroScan has limitations when it is used in patients with obesity or ascites (Castéra et al. 2010). In addition, TE does not provide a guiding B-mode image. Obesity is a limitation for the application of PSWSM, and the rate of failed PSWSM in obese patients (body mass index [BMI] ≥ 30 kg/m^2) was reported as 17.6% (Bota et al. 2014).

Ultrasonic elastography can be used to assess the stiffness of tissues. Acoustic structure quantification (ASQ) is a new tool for assessment of the structure of tissues that are not categorized as elastography. ASQ is software that analyzes the statistical information of the acquired echo signals and is based on the raw gray-scale data. The raw data are collected before the scan converter and lateral filter are applied. ASQ is thought to be less subjective and less dependent on the operator than conventional ultrasound imaging because it can offer both qualitative visual results (parametric imaging) and quantitative results. ASQ software has been commercialized and is available in Toshiba ultrasound scanners. Preliminary studies have obtained encouraging results in terms of the assessment of liver fibrosis using ASQ (Krämer et al. 2014; Ricci et al. 2013).

The present study was aimed at determining the diagnostic value of ASQ versus that of PSWSM for the assessment of liver fibrosis in chronic hepatitis B (CHB).

METHODS

Patients

This study was approved by the Baoji Central Hospital Ethics Committee. Informed consent for all examinations was provided in writing by the patients or their family members. A total of 104 patients (aged 13–64 y, mean age: 30.5 ± 11.1 y) with chronic viral hepatitis B, including 70 males (aged 13–64 y, mean age: 29.0 ± 10.5 y) and 34 females (aged 16–62 y, mean age: 32.8 ± 11.7 y), were recruited from the Department of Infectious Diseases of Baoji Central Hospital between February 2015 and May 2016. All patients underwent LB under ultrasonic guidance after ASQ and PSWSM, but did not receive antiviral therapy. The inclusion criteria were the presence of hepatitis B virus (HBV) deoxyribonucleic acid (DNA) in the sera and positivity for HBV surface antigen for at least 6 consecutive mo. The exclusion criteria were hepatitis B associated with a fatty liver, liver congestion, primary biliary hepatitis, autoimmune hepatitis and other types of viral hepatitis such as viral hepatitis C. The criterion for hepatitis C was positive for hepatitis C virus antibody. The criterion for the diagnosis of fatty liver was biopsy pathology revealing liver steatosis >5% (Kleiner et al. 2005).

Thirty healthy volunteers, including 15 males and 15 females (aged 18–45 y, mean age of 32.4 ± 11.7 y), were enrolled as controls. All volunteers had normal levels of serum liver enzymes (alanine aminotransferase [ALT], aspartate aminotransferase [AST], γ-glutamine transferase [γ-GGT] and alkaline phosphatase [ALP]) and serum bilirubin (total bilirubin, direct bilirubin and indirect bilirubin). The volunteers were negative for hepatitis B virus surface antigen and hepatitis C virus antibody and had no history of diabetes, hyperlipidemia or alcoholism. Conventional ultrasonic scans did not reveal abnormalities of the liver.

Acoustic structure quantification

After fasting for more than 8 h, each subject underwent ASQ examination by a radiologist with 3 mo of experience in ASQ examinations using a Toshiba Aplio 500 ultrasound machine (Toshiba Medical Systems, Osaka, Japan) at a frequency of 5.0 MHz. The subject was placed in the left lateral decubitus position with the right hand placed behind the head. The probe was placed in the right intercostal area for scanning. Subjects were advised to hold their breath at maximum inspiration while the ASQ imaging was initiated. The frame rate for the collection was 8 frames per second (fps) for 3 s. Images were stored and copied to a computer. Segment V of the right anterior lobe of the liver was selected as the region of interest (ROI). The de-