Ultrasound in Med. & Biol., Vol. 39, No. 9, pp. 1527–1535, 2013

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2013.02.012

● *Original Contribution*

TISSUE DOPPLER IMAGING AND TISSUE STRAIN IMAGING FOR THE EVALUATION OF HEPATIC FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B

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(*Received* 18 *September* 2012; *revised* 16 *February* 2013; *in final form* 20 *February* 2013)

Abstract—We studied the feasibility of evaluating the stages of liver fibrosis with tissue Doppler imaging (TDI) and tissue strain imaging (TSI) for patients with chronic hepatitis B virus infection. One hundred ten patients were divided into two groups: normal adult group ($n = 38$) and chronic liver disease group ($n = 72$, patients infected with HBVs). The chronic liver disease group was divided into three subgroups on the basis of the Scheuer scoring system and clinical evidence: mild fibrosis (S0 and S1, $n = 11$), moderate fibrosis (S2 and S3, $n = 27$) and cirrhosis (S4 and clinically typical cirrhosis, $n = 34$) groups. TDI was performed for a chosen oblique section. Four regions of interest (ROIs), A–D, were chosen in the hepatic parenchyma based on the direction of propagation from the heart to the liver. Strain rate curves were obtained on the basis of TDI and TSI findings. Strain peak rates (SPRs) of all ROIs and the differences in times to SPRs for the four ROIs ($T_{A\text{-}B}$, $T_{B\text{-}C}$ and $T_{C\text{-}D}$) in the hepatic parenchyma were measured with TDI and TSI. Strain rate curves were analyzed for each ROI. The strain rate curves for the normal adult group were synchronous, whereas those for the chronic liver disease group were asynchronous. SPRs of the ROIs gradually decreased with the progression of liver fibrosis. The SPRs of ROI B significantly correlated with chronic liver disease severity ($r = 0.991, p < 0.05$). Areas under the curve (AUCs) of the ROI A and ROI B SPRs at the moderate fibrosis and cirrhosis stages were 0.86 ± 0.06, 0.81 ± 0.56 and 0.90 ± 0.65, 0.92 ± 0.04, respectively. The AUC of the SPRs of ROIs A and B correlated better than the platelet/age/phosphatase/α-fetoprotein/aspartate aminotransferase (PAPAS) index for advanced fibrosis. The differences in time to SPRs among the peaks of the four ROIs ($T_{A\text{-}B}$, $T_{B\text{-}C}$ and $T_{C\text{-}D}$) gradually increased with the progression of liver fibrosis. TDI and TSI with quantitative measurements using tissue Doppler analysis software (TDIQ, GE Medical Systems, Horten, Norway) provided reliable information for evaluating non-invasive liver fibrosis in patients with chronic hepatitis B. (E-mail: wuzhifeng2@yahoo.com.cn) **© 2013 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Tissue Doppler imaging, Tissue strain imaging, Quantitative assessment, Strain peak rates, Liver fibrosis, Cirrhosis.**

INTRODUCTION

Hepatic fibrosis with chronic hepatitis B viruses (HBVs) is associated with a higher risk of hepatocellular carcinoma (Di Bisceglie 2004; Thompson et al. 2008). Patient prognosis strongly depends on histologic severity. At present, liver biopsy is the gold standard for the diagnosis and staging of liver fibrosis (Theise 2007). However, liver biopsy is an invasive procedure accompanied by the risk of various complications, such as pain, hemorrhage and bile peritonitis; thus, it is not suitable for routine clinical follow-up (Al and Shiffman 2007). Furthermore, a liver biopsy sample represents only a small part of the whole liver, and sampling bias is possible (Ratziu et al. 2005; Vuppalanchi et al. 2009). Therefore, to assess the severity of liver fibrosis, non-invasive, tolerable and reliable methods are urgently needed. With recent developments in imaging technology, the role of ultrasound in liver disease has significantly increased.

Nodular hepatic surface, coarse echotexture and signal attenuation, intrahepatic vessel contours and

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spleen length are useful parameters in the diagnosis of cirrhosis (Oberti et al. 1997; Zheng et al. 2003). However, the diagnostic accuracy of routine ultrasound is lower because digestive gas can interfere with ultrasound investigation (Aube et al. 1999). Through the use of Doppler ultrasound signs, including the new hepatic vein spectrum, approximately 90% of patients with compensated chronic liver disease can be correctly diagnosed (Aube et al. 2004). Doppler parameters might not be suitable for assessment of the stage of liver fibrosis by clinicians (Bernatik et al. 2002). Transient elastography shows promise in diagnosing cirrhosis and assessing disease stage (Stebbing et al. 2010); however, transient elastography images are invisible during the measurement stage. With the development of ultrasound contrast agents and specific imaging contrast techniques, contrast-enhanced ultrasound has been reported to perform well and has great potential in the evaluation of liver fibrosis (Liu and Lu 2010; Li et al. 2010); however, the drawbacks of contrast-enhanced ultrasound are that it requires contrast agent injections and depends on operator skill and access to the relevant technology (Bonekamp et al. 2009). Acoustic radiation force impulse imaging has been reported to perform better diagnostically in the evaluation of chronic liver disease severity (Kim et al. 2010; Boursier et al. 2010). Nevertheless, it is not adequate for estimating the early stages of fibrosis (Haque et al. 2010). Tissue strain imaging (TSI) is based on tissue Doppler imaging (TDI), a myocardial examination technique. A recent study using TSI found significant differences in strain values between normal adults and adults with chronic hepatitis and cirrhosis (Hotta et al. 2007). However, the authors did not compare their imaging work with liver biopsy results to study differences between the stages of liver fibrosis. Moreover, the positions of the regions of interest (ROIs) for each group were unclear. Supersonic shear imaging, used as a complementary tool for B-mode ultrasound, could complement morphologic information for fibrosis staging and hepatic lesion imaging (Muller et al. 2009; Bavu et al. 2011). Studies on the evaluation of fibrosis in chronic hepatitis C or non-alcoholic fatty liver diseases are available.

The purpose of this study was to assess the value of using TDI and TSI to evaluate hepatic fibrosis stages in patients with HBVs.

METHODS

Patients

This study included 41 healthy volunteers without hepatic disease history and with normal ultrasound findings (normal adult group) and 74 patients patients infected with HBVs (chronic liver disease group) who had been admitted to the Clinical Medical College of Yangzhou University between February 2010 and April 2012. On the basis of the Scheuer scoring system for liver fibrosis staging (S0, S1, S2, S3 and S4) (Scheuer 1991, 1995) and clinical evidence, the chronic liver disease group was categorized into three subgroups: mild fibrosis (S0 and S1), moderate fibrosis (S2 and S3) and cirrhosis (S4, liver biopsy and clinically typical cirrhosis) groups. Forty-nine patients in the chronic liver disease group underwent liver biopsy or surgery, and twenty-five patients with liver cirrhosis were diagnosed on the basis of clinical criteria. The clinical criteria for liver cirrhosis were as follows: (i) previous episodes of cirrhotic decompensation (encephalopathy, icterus, variceal bleeding or ascites formation); (ii) morphologic signs of liver cirrhosis on ultrasound examination (Aube et al. 1999, 2004); and (iii) endoscopic signs of portal hypertension (Wiechowska-Kozlowska et al. 2008). Each subject who participated in the study provided informed consent. The study protocol conformed to the Declaration of Helsinki and was approved by our institutional ethics committee. The clinical and laboratory assessment findings are summarized in Table 1.

Tissue Doppler imaging and tissue strain imaging examination

All TDI and TSI examinations were performed by a sonographer blind to the patients' clinical data and related information, using a GE Vivid E9 ultrasound machine (GE Medical System, Horten, Norway) with a 2.5-MHz transducer. An oblique anterior approach along the costal margin was employed with a 2.5-MHz transducer on the abdomen at the subxiphoid deviation to the right, and the second hepatic portal (confluence of the hepatic veins) was visualized. Sector scans were used when the confluence of the hepatic veins started to disappear; the right cardiac atrioventricular junction was visualized in the plane of the oblique quadracavity. The angle between the transducer and the body was approximately 45° (Fig. 1). TDI and TSI were performed within 3 d before liver operations or liver biopsies, which were guided by sonography and employed an 18-gauge needle. To reduce measurement error and determine examiner variability, every recording was repeated three times. During TDI and TSI examination, the patients were asked to hold their breath as long as possible, and dynamic images lasting longer than 30 seconds were stored digitally by the ultrasound system in AVI format and written into computer discs.

Analysis of tissue Doppler and tissue strain images

The strain rate from the ROI placed on the right atrioventricular junction included the three peak