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ORIGINAL ARTICLE

The performance of acoustic radiation force impulse imaging in predicting liver fibrosis in chronic liver diseases

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Abstract Sonography-based noninvasive liver fibrosis assessment is promising in the prediction of treatment efficacy and prognosis in chronic liver disease (CLD) patients. Acoustic radiation force impulse imaging (ARFI) is a newly-developed transient elastography (TE) method integrated into a conventional ultrasound machine. The study aimed to assess the performance of ARFI imaging in the diagnosis of liver fibrosis in Taiwanese CLD patients. We also aimed to search for the optimal cut-off values in different fibrosis stages. A total of 60 CLD patients (40 males; mean age, 51.8 ± 11 years) were consecutively included. They received standard ARFI measurement within 2 weeks at the time of liver biopsy. There were eight patients with Metavir fibrosis stage 0 (F0), 16 patients with F1, 20 patients with F2, eight patients with F3, and eight patients with F4, respectively. The mean values among patient with F0, F1, F2, F3, and F4 were 1.17 ± 0.13, 1.30 ± 0.17, 1.31 ± 0.24, 2.01 ± 0.45, and 2.69 ± 0.91, respectively ($p < 0.001$). The optimal cut-off ARFI value for significant fibrosis ($F \geq 2$) was 1.53 with the accuracy of 0.733, while it was 1.66 for advanced fibrosis ($F \geq 3$) with the accuracy of 0.957. Our

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study demonstrated that ARFI imaging is competent for fibrosis diagnosis, particularly in CLD patients with advanced fibrosis.

Introduction

Chronic liver disease (CLD) of various etiologies, such as chronic hepatitis B (CHB) or chronic hepatitis C (CHC), alcoholic liver disease, and nonalcoholic steatohepatitis (NASH), is the leading cause of hepatocellular carcinoma (HCC) globally. The main pathogenic mechanism underlying hepatocarcinogenesis is necroinflammation and its subsequent fibrogenesis [1,2]. Therefore, severity estimation of liver fibrosis is important for treatment efficacy, prognosis, HCC surveillance and determining the best treatment strategies in CLD patients [3,4].

Liver biopsy, as the gold standard method for the assessment of liver fibrosis, is an invasive method associated with patient discomfort and sometimes with serious complications [5,6]. Biopsy is associated with a bleeding risk of 1% and a mortality rate of ~0.01% [3,5]. Additionally, liver biopsies are often considered "imperfect" surrogate markers for liver fibrosis assessment because of inherent limitations. These include invasiveness, risk of life-threatening complications, intra- and inter-observer variability, and sampling error.

In addition to serum biomarkers, several ultrasound-based methods have been vigorously developed and validated for assessing the degree of fibrosis and cirrhosis by measuring liver stiffness in the past decade. These ultrasound-based methods shed a new light in the aspect of noninvasive evaluation of liver fibrosis. They have provided good diagnostic accuracy in a clinical setting [7,8]. Acoustic radiation force impulse (ARFI) imaging is a newly-developed transient elastography (TE) method integrated into a conventional ultrasound machine and can be performed with ultrasound probes during an abdominal ultrasound examination [8]. Previous studies have indicated that it is a good predictor of liver fibrosis stages in CLD patients, particularly in CHC patients [8,9]. However, the performance of ARFI in Asians across different etiologies remains to be clarified and validated.

The aim of the study was to assess the performance of ARFI in the diagnosis of liver fibrosis in Taiwanese CLD patients. The optimal cut-off values were also evaluated according to different fibrosis stages in a clinical basis.

Methods

Patients

Between October, 2013 and November, 2014, a total of 60 CLD patients were consecutively included in this study. All patients received a liver biopsy aiming to elucidate their histopathological manifestations in a clinical setting. The Ethics Committee of Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, approved the study before it began. The study was conducted according to the Declaration of Helsinki. Written informed consent for anthropomorphic measurements, ARFI measurement, blood sampling, and medical record review were obtained from patients prior to enrollment.

ARFI measurement

ARFI measurement was performed with curved-array transducer (6CI probe) of the Siemens ACUSON S2000 ultrasound system (Siemens Medical Solutions, Erlangen, Germany). The 10 mm $\times$ 5 mm region of interest was focused on the right liver lobe via an intercostal approach. All patients were measured on the right lobe at a depth of ~2—3 cm below the capsule during relaxed breath-holding. Food intake increased shear wave values significantly, especially when consumed $<$ 3 hours prior to measurements. Therefore all patients had enough fasting time ($>$ 10 hours). The mean shear wave velocity (m/s), standard deviation, and number of effective measurements were recorded. At least 10 successful acquisitions were measured for each patient.

ARFI-failure was defined as no successful ARFI measurement after 10 attempts and an interquartile range greater than 30%. The interquartile range is defined as the difference between the 75th percentile, essentially the range of the middle 50% of the data.

Histology grading and staging

Liver biopsy was performed within 2 weeks of ARFI measurement using an echo-assisted method. For each patient, a liver biopsy specimen of at least 1.5 cm in length was taken and fixed in 10% formalin buffer. Biopsy samples were stained with hematoxylin-eosin and the results were then reported by a dedicated liver pathologist blinded to each patient.

Histological grading was performed based on the histological activity index (HAI) by Knodell et al. [10]. Fibrosis score (F0—F4) was determined according to the Metavir scoring systems [11]. Significant fibrosis and advanced fibrosis are defined as F2, and F3—4, respectively.

Statistical analyses

The demographic data were expressed as mean values $\pm$ standard deviation (SD). ARFI results were expressed as mean values $\pm$ SD and were compared between groups using analysis of variance. The diagnostic performances of ARFI in the diagnosis of fibrosis stages were evaluated by receiver—operator characteristic (ROC) curves. The area