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● *Original Contribution*

NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS WITH ElastPQ: COMPARISON WITH TRANSIENT ELASTOGRAPHY AND SEROLOGIC FIBROSIS MARKER TESTS, AND CORRELATION WITH LIVER PATHOLOGY RESULTS

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Abstract—We investigated the feasibility of using ultrasound shear wave elastography point quantification (ElastPQ) for liver fibrosis staging and compared it with other non-invasive tools with respect to efficacy in liver stiffness measurement. A total of 106 patients who underwent liver stiffness measurements, using ElastPQ and biochemical investigations, before parenchymal liver biopsy or surgery were included. Among these, 51 also underwent transient elastography (TE). Correlations of ElastPQ, TE and aspartate aminotransferase-to-platelet ratio index (APRI) with histopathological findings (as the reference standard) were determined using Spearman's correlation coefficient. The diagnostic performance of ElastPQ, TE and APRI was evaluated using receiver operating characteristic (ROC) curve analysis. ElastPQ had good diagnostic accuracy in identifying each liver fibrosis stage, with an area under the ROC curve (AUC) of 0.810 to 0.864. Stiffness values obtained using ElastPQ, TE and APRI were significantly positively correlated ($r = 0.686$, $r = 0.732$ and $r = 0.454$, respectively) with histologic fibrosis staging ($p < 0.001$). According to the AUC for the diagnosis of significant fibrosis (≥F2) and cirrhosis (=F4), ElastPQ had better diagnostic accuracy (AUC = 0.929 and 0.834, respectively) than APRI (AUC = 0.656 and 0.618, respectively) ($p < 0.05$), and was similar to TE (AUC = 0.915 and 0.879, respectively). ElastPQ is a promising ultrasound-based imaging technique for evaluation of liver fibrosis, with a diagnostic accuracy comparable to that of TE. (E-mail: shinks@cnu.ac.kr) © **2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **ElastPQ, Hepatic fibrosis, Liver cirrhosis, Ultrasonography, Shear wave elastography, Transient elastography.**

INTRODUCTION

Chronic liver disease associated with viral hepatitis B or C, or other etiologies, is an increasingly prevalent clinical problem (Sebastiani et al. 2011). It can cause various parenchymal liver injuries, lead to progressive liver fibrosis and result in liver cirrhosis and its various complications, including portal hypertension and hepatocellular carcinoma (Pinzani and Rombouts 2004). Although cirrhosis is relatively irreversible, early fibrosis is reversible. Therefore, early detection and staging of liver fibrosis are vital for optimal treatment planning.

Liver biopsy is the most commonly used reference standard for the assessment of liver fibrosis (Bravo et al. 2001). However, it has several limitations, including possible procedure-related complications, sampling error and intra- or inter-observer variability, leading to the over- or understaging of fibrosis (McGill et al. 1990; Van Thiel et al. 1993). Therefore, the limitations of liver biopsy have prompted the development of alternative non-invasive methods that can be used for diagnosing and staging liver fibrosis (Schmeltzer and Talwalkar 2011). To date, several non-invasive methods, such as serologic fibrosis marker tests, including the aspartate aminotransferase (AST) to platelet ratio index (APRI), and imaging tools, including magnetic

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resonance-based and ultrasonography (US)-based elastography techniques, have been investigated for the assessment of fibrosis (Annet et al. 2007; Huwart et al. 2007; Lee et al. 2014; Yoon et al. 2013).

Most US-based elastography techniques, including transient elastography (TE), acoustic radiation force impulse (ARFI) imaging, ultrasound shear wave elastography point quantification (ElastPQ) and shear wave elastography (SWE), use shear waves for absolute soft tissue stiffness quantification (Barr et al. 2015; Ferraioli et al. 2014a, 2015). Among these, TE was one of the earliest investigated methods for measuring liver stiffness, and had high accuracy and precision for assessing liver fibrosis stage (Barr et al. 2015; Friedrich-Rust et al. 2008). However, the use of TE to measure liver stiffness is limited in obese patients and/or individuals with ascites (Foucher et al. 2006). On the other hand, ARFI imaging, ElastPQ and SWE have high technical success rates, even in patients who may be difficult to assess (Barr et al. 2015; Samir et al. 2015; Yoo et al. 2016). Furthermore, they have been incorporated into conventional real-time US systems. Compared with TE, these techniques have the advantages of both qualitative assessment of morphologic changes and quantitative measurements of liver stiffness during liver US examination (Ferraioli et al. 2014b; Kircheis et al. 2012; Samir et al. 2015).

ElastPQ and ARFI imaging are reliable tools that have exhibited acceptable accuracy in the assessment of liver fibrosis (Friedrich-Rust et al. 2012; Kircheis et al. 2012; Samir et al. 2015). Although the two methods incorporate point shear wave elastography technology with similar physical principles, the cutoff values for liver fibrosis staging are system dependent and not interchangeable, according to previous studies (Ferraioli et al. 2015; Ling et al. 2013; Sporea et al. 2014). Because ElastPQ is a relatively new technique, only a few studies assessing its efficacy have been published (Lu et al. 2016; Ma et al. 2014; Yoo et al. 2016). Consequently, there have been few comparisons of the diagnostic performance of ElastPQ with that of other non-invasive tools for the staging of liver fibrosis using histologic liver fibrosis stage as a reference standard. Although Sporea et al. (2014) performed a comparative study between ARFI and ElastPQ, they did not evaluate diagnostic performance using histologic liver fibrosis stage as a reference standard. To our knowledge, there have been no multi-comparison studies assessing ElastPQ, TE and APRI—with liver histology as the reference standard—in the same patient population.

Accordingly, the purpose of the present study was to evaluate the feasibility of using ElastPQ for liver fibrosis staging and to compare the diagnostic accuracies of ElastPQ, TE and APRI at each stage of fibrosis using liver histology as the reference standard.

METHODS

Study design and population

This retrospective study was approved by the institutional review board; the requirement for informed patient consent was waived. Between March 2013 and August 2015, a computerized search revealed 111 patients who had undergone successful liver stiffness measurements using ElastPQ on the same day or within several days of liver surgery or liver biopsy. After a study coordinator reviewed the US-based elastographic technique and pathologic results, five patients were excluded from the analysis for inadequate liver specimen to establish a histologic diagnosis of liver fibrosis (n = 2) and previous major liver surgery (n = 3). Finally, a total of 106 patients (64 men and 42 women; age range: 19–86 y, mean age: 57 y) were included. Of these 106 patients, 51 underwent successful TE with reliable measurements and were included in comparisons of diagnostic performance in assessing liver stiffness.

Blood markers

All patients in the present study underwent hematological and biomedical investigation. Blood samples were obtained from the patient after overnight fasting on the same day the liver biopsy was performed or before surgery was performed. The following routine blood markers were assessed: AST, alanine aminotransferase, albumin, γ-glutamyltransferase and platelet count. As an indicator of the non-invasive serologic fibrous marker test, the APRI was calculated using the formula

$$\mathrm{APRI} = (\mathrm{AST}/\mathrm{AST}_{\mathrm{ULN}} * 100)/\text{platelet count}$$

where $\mathrm{AST}_{\mathrm{ULN}}$ is the upper limit of the normal AST value (40 IU/L) (Lin et al. 2011). Viral hepatitis B infection was diagnosed using positive serology tests for serum hepatitis B surface antigen; viral hepatitis C infection was diagnosed by the presence of antibodies against hepatitis C virus.

Point shear wave elastography

ElastPQ was performed using an ultrasound system (iU-22, Philips Medical Systems, Bothell, WA, USA) by one of the authors (L.J.E.), who had 3 y of ultrasound elastography and 7 y of liver ultrasound experience. The examiner was blinded to all clinical data during the measurements. Examinations were performed *via* the intercostal approach in the right lobe of the liver, 1 to 2 cm under the liver capsule, with the patient lying supine with the right arm in maximum abduction. Using real-time B-mode imaging, the examiner positioned the ElastPQ measurement box (approximate 0.5 cm× 1.5 cm) in a region free of visible ducts or vessels. The patients were instructed to hold their breath while the examiner pressed the "update" button to acquire stiffness measurement in real-time. Stiffness is expressed in kilopascals of Young's