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● *Original Contribution*

PROSPECTIVE COMPARISON OF THE DIAGNOSTIC PERFORMANCE OF MAGNETIC RESONANCE ELASTOGRAPHY WITH ACOUSTIC RADIATION FORCE IMPULSE ELASTOGRAPHY FOR PRE-OPERATIVE STAGING OF HEPATIC FIBROSIS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Abstract—The purpose of this study was to compare the diagnostic accuracy of magnetic resonance (MR) elastography with that of acoustic radiation force impulse (ARFI) elastography for pre-operative staging of hepatic fibrosis in patients with hepatocellular carcinoma. We prospectively enrolled 77 patients who were scheduled to undergo hepatectomy for hepatocellular carcinoma. Pre-operative MRE and ARFI elastography examinations were performed on the same day, and liver stiffness/velocity values were determined. Fibrosis stage and necro-inflammatory activity of resected specimens were determined histopathologically using the METAVIR scoring system. Correlations between MRE and ARFI elastography findings and histologic findings were determined by receiver operating characteristic (ROC) analysis. Correlation of MRE was excellent and correlation of ARFI elastography was good with fibrosis stage. MRE had better diagnostic performance than ARFI elastography in estimating substantial fibrosis (F2), severe fibrosis (F3) and cirrhosis (F4). The optimal cutoff value and the area under the ROC curve (AUROC) were determined using ROC curve analysis. The highest Youden index was used as a criterion for selecting the optimal cutoff value. ROC analysis revealed that MRE discriminated advanced stages of fibrosis (F ≥ 2) well in patients with hepatocellular carcinoma at a cutoff value of 3.0 kPa with an AUROC value of 0.93, and ARFI elastography did so at a cutoff value of 1.77 m/s with an AUROC value of 0.81 for predicting advanced stages of fibrosis (F ≥ 2). In conclusion, MRE is a more accurate imaging modality than ARFI elastography in estimating advanced stages of fibrosis and cirrhosis. (E-mail: 31560@cch.org.tw)

Key Words: **Acoustic radiation force impulse elastography, Hepatic fibrosis, Necro-inflammatory activity, Magnetic resonance elastography, Ultrasound-based elastography.**

INTRODUCTION

The prognosis and management of chronic liver disease greatly depend on the degree and progression of fibrosis. The onset of liver fibrosis is usually insidious, and most of the related morbidity and mortality occur as the direct consequence of the development of cirrhosis. Prevention of the progression of liver fibrosis to cirrhosis is essential because later stages of the disease are irreversible, resulting in liver failure and death (Bataller and Brenner 2005; Schuppan and Afdhal 2008; Tsochatzis et al. 2012).

Liver biopsy is the gold standard for determining fibrosis stage. However, it is an invasive procedure and has several limitations, including wide inter-observer variability and significant sampling errors (Bedossa et al. 2003; Regev et al. 2002). Non-invasive alternatives to liver biopsy include imaging examinations such as magnetic resonance (MR) imaging, MR elastography (MRE), ultrasound-based elastography and measurement of biomarkers of fibrosis in serum such as aspartate transaminase-to-platelet ratio and levels of hyaluronic acid and type 4 collagen. MRE and ultrasound-based acoustic radiation force impulse (ARFI) elastography are widely used shear wave imaging techniques for staging liver fibrosis (Cui et al. 2016; Meng et al. 2015; Regev et al. 2002; Tang et al. 2015; Yoon et al. 2014). To the best of our knowledge, no

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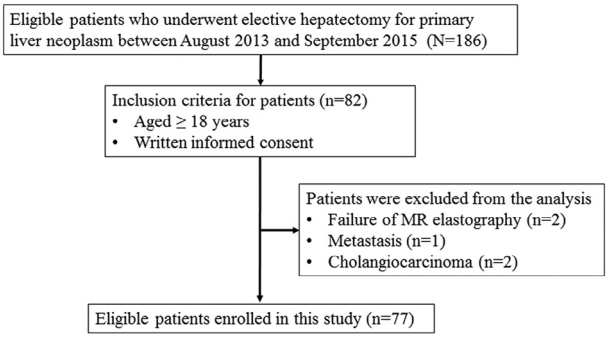

Fig. 1. Flow diagram of patients who underwent elective hepatectomy for hepatocellular carcinoma and were recruited for this study.

prospective studies have compared the accuracy of MRE with that of ARFI elastography in staging fibrosis using surgical specimens as a reference. Therefore, the purpose of this study was to compare the diagnostic accuracy of MRE with that of ARFI elastography for staging hepatic fibrosis in patients with hepatocellular carcinoma.

METHODS

Patients

Patients in this prospective study were derived from a pool of 186 patients who were scheduled to undergo elective hepatectomy for hepatocellular carcinoma during the period August 2013 to September 2015. The preoperative diagnosis of hepatocellular carcinoma (HCC) based on typical enhancing profile (positive enhancement on arterial phase follow by contrast washout on late phase, AASLD practice guideline) (Bruix et al. 2011) or biopsy for tumors with atypical enhancing patterns. The study was approved by the institutional review board of the Changhua Christian Hospital. To be included, patients had to be ≥18 y old and scheduled for liver resection. A total of 82 patients were enrolled consecutively, and written informed consent was obtained from all patients. Patients whose images were of poor imaging (technique failure of elastography) or who had a histologic diagnosis other than HCC (metastatic tumor and cholangiocarcinoma) were excluded from the analysis. Figure 1 is a flowchart of patients who met inclusion criteria. Finally, we prospectively enrolled 77 patients (63 men, 14 women) in the analysis. Blood samples were drawn and MRE/ARFI elastography examinations were performed on the same day after an overnight fast. Imaging examinations and hepatic surgery occurred within 3 d. All patients underwent either partial hepatectomy or wedge resection. The clinical characteristics of the study patients are summarized in Table 1.

Magnetic resonance elastography

All examinations were performed on a 1.5-T MR system (Aera, Siemens, Erlangen, Germany) with a 16-channel phased-array body coil for acquisition of routine clinical MR and MRE images. The MRE system consisted of an acoustic driver system (Resoundant, Rochester, MN, USA) capable of generating acoustic shear waves in human livers. A 19-cm-diameter, 1.5-cm-thick cylindrical passive driver was connected by a flexible plastic tube to an acoustic active driver. The passive driver was placed against the right chest wall centered at the level of the xiphoid process. Continuous acoustic vibrations at 60 Hz transmitted from the active driver were used to produce propagating shear waves in the liver. The propagating shear waves were imaged with axial 2-D gradient-echo sequencing. The parameters of the MRE sequence were as follows: TR/TE, 50/22.7; flip angle, 25°; bandwidth, 260 Hz/pixel; hydrogen resonance frequency, 63.5 MHz; acquisition matrix, 256×64; section thickness, 5 mm; and field of view, 400×400 mm^2. The scanning time of each axial slice was 21 s per breathhold. Patients were asked to hold their breath at the end-expiratory period to obtain a consistent position of the liver for each phase offset. A total of five axial slices were acquired for each patient. All post-processing steps were applied automatically, and liver stiffness measurements were expressed in kilopascals. In cases where a reflective wave, disturbing wave, or artifact was found on wave imaging, the passive driver was re-positioned on the chest wall to obtain well-propagating wave images. The elastograms were reviewed automatically by the intrinsic software for artifacts, such as significant wave interference and oblique wave propagation. Confidence maps providing regions with adequate wave amplitudes were generated automatically by the MRE software.

MRE analysis

All analyses were performed on a dual-screen diagnostic workstation (GE Healthcare, Milwaukee, WI, USA). An abdominal radiologist with more than 20 y of clinical experience in abdominal imaging evaluated the MRE images, including the anatomic image sets, the wave image sets and the elastogram sets. The radiologist was blinded to the patients' clinical data and histopathological results. Figure 2a is a representative anatomic image depicting liver anatomic information on the MRE slice. Figure 2b is a wave image revealing the pattern of a propagating wave. For measurement of liver stiffness, wave images were first checked for adequate wave quality. Presence of a reflective wave, disturbing wave or artifact indicates poor propagating imaging. The liver area with poorly propagating waves should not be measured. With the software of the MR unit, elastograms of the MR elastography slices