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● *Original Contribution*

RADIOFREQUENCY ABLATION FOR HEPATOCELLULAR CARCINOMA: UTILITY OF CONVENTIONAL ULTRASOUND AND CONTRAST-ENHANCED ULTRASOUND IN GUIDING AND ASSESSING EARLY THERAPEUTIC RESPONSE AND SHORT-TERM FOLLOW-UP RESULTS

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Abstract—The purpose of this study was to assess the efficacy of conventional ultrasound (US) and contrast-enhanced ultrasound (CEUS) in guiding and assessing early therapeutic response to radiofrequency (RF) ablation for hepatocellular carcinomas (HCCs; up to 3 lesions, each ≤3 cm in diameter) and to report the short-term follow-up results. Between September 2011 and January 2013, 63 patients with 78 HCCs (≤3 cm) underwent conventional US- and CEUS-guided percutaneous RF ablation. CEUS was repeated after 20–30 min to assess therapeutic response, and local efficacy was further confirmed by contrast-enhanced magnetic resonance imaging (MRI) 1 mo after tumor ablation. Patients were followed periodically to look for local tumor or disease progression. Survival probability was estimated with the Kaplan–Meier method. Complete ablation was achieved for 76 (97.4%) of 78 HCCs in one (n = 73) or two (n = 3) sessions. No major complications were observed in any patient. The overall concordance in assessment of therapeutic efficacy of RF ablation between CEUS and MRI was 97.4% (76/78 tumors). The concordance test gave a value of $\kappa = 0.74$ ($p < 0.001$), indicating that CEUS had a high diagnostic agreement with MRI. During a mean follow-up of 20 mo, the local tumor progression rate was 5.3% (4/76 tumors). The 1-, 1.5- and 2-y cumulative survival rates were 98.4%, 96.1% and 92.6%, respectively. Although CEUS has some intrinsic limitations, the combined use of conventional US and CEUS provides a safe and efficient tool to guide RF ablation for HCCs 3 cm or smaller, with encouraging results in terms of survival rate and minimal complications. Moreover, the immediate post-procedural CEUS can be a reliable alternative to contrast-enhanced MRI for assessing the early therapeutic response to RF ablation. (E-mail: fenghua-li@163.com and renjizhaibo@163.com) **© 2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Hepatocellular carcinoma, Liver, Radiofrequency ablation, Contrast-enhanced ultrasound, Therapeutic response.**

INTRODUCTION

Radiofrequency (RF) ablation is a safe and effective local treatment option for patients with hepatocellular carcinoma (HCC; Lee et al. 2014). Some studies have even advocated that percutaneous RF ablation can be used successfully as a first-line treatment modality for early-stage HCC (Choi et al. 2007; Kim et al. 2013b; Lee et al. 2014). Although RF ablation can provide potentially curative results for HCC, the procedure is intrinsically dependent on imaging for its planning and assessment of the final outcome. For guiding RF ablation of HCC, various imaging modalities, including ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI), can be used (Goldberg et al. 2009). Among them, conventional gray-scale US has been the most widely used guiding modality, thanks to its easy accessibility, low cost, real-time imaging capability and no radiation hazard to the patients. However, not all HCCs are suitable for conventional gray-scale US-guided RF ablation. For

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example, some HCCs less than or equal to 3 cm are often less conspicuous due to either their isoechoic nature and/or their locations in the sonographic blind spots such as the liver dome (Lee et al. 2010). In addition, the identification of target lesions is also difficult when the true HCC nodules must be distinguished from many large regenerative nodules in a cirrhotic liver (Minami et al. 2004). Therefore, accurate detection and localization of the true index tumor is essential for successful local ablation treatment of HCCs 3 cm or smaller.

Implementation of contrast-enhanced US (CEUS) can be helpful to enhance the technical feasibility of US-guided RF ablation of HCCs, and it has various advantages in guiding ablation procedure and assessing the therapeutic efficacy (Minami and Kudo 2011; Meloni et al. 2006; Solbiati et al. 2004). CEUS provides a relatively longer time window to the operator to perform RF ablation, allows real-time visualization, can be used in patients with compromised renal function, and has been shown to be a further option to contrast-enhanced CT and MRI for assessing therapeutic response (Frieser et al. 2011; Rajesh et al. 2013). Moreover, CEUS is especially helpful for localizing the index tumors with poor sonographic conspicuity during percutaneous US-guided RF ablation of HCCs (Minami et al. 2004; Minami and Kudo 2011; Rajesh et al. 2013). However, for HCCs 3 cm or smaller, applying CEUS to a RF ablation procedure is still difficult since some tumors do not show typical enhancement characteristics and deep-seated small lesions are easily missed on CEUS due to attenuation of the US beam (Gaiani et al. 2004; Kim et al. 2013a). The combined use of conventional gray-scale US and CEUS might achieve the advantage complementation of two modalities to guide RF ablation. In terms of the post-procedural assessment, the early and accurate evaluation of tumoral response to ablation therapy using imaging modalities is important for determining whether the tumor is completely treated or needs additional treatment (Kim et al. 2005; Sparchez et al. 2009). Having an excellent accuracy in depicting the micro-vascularization of an HCC nodule, CEUS has been used to detect residual tumor immediately after the RF ablation (Gallotti et al. 2009; Meloni et al. 2012; Sparchez et al. 2009). Even though many previous clinical trials documented local response rate and various clinical results of RF ablation (Choi et al. 2007; Kim et al. 2013a; Mazzaferro et al. 2004; Pompili et al. 2013), there have been few reports that focused on combined conventional US- and CEUS-guided percutaneous RF ablation for HCCs 3 cm or smaller and early assessment of therapeutic response with CEUS.

The purpose of our study, therefore, was to assess the efficacy of the combined use of conventional US and CEUS in guiding percutaneous RF ablation for HCC (up to three lesions, each ≤3 cm), and to determine the utility of CEUS in the early assessment of therapeutic response to RF ablation. The short-term follow-up results were also reported in the evaluation of post-ablation complications, the local tumor progression rate and survival rates of patients.

MATERIAL AND METHODS

Patient population

This prospective study was approved by the institutional review board, and written informed consent was obtained from all patients before imaging examinations and ablation procedures. All the patients underwent dynamic contrast-enhanced MRI within 1 mo prior to RF ablation treatment to assess the location, number and size of the tumors. Inclusion criteria for this study were (i) up to 3 lesions per patient; (ii) maximum tumor diameter smaller than or equal to 3 cm; (iii) lesion located at least 3 mm away from the main, right or left portal vein and the gallbladder; and (iv) Child–Pugh class A or B liver cirrhosis, prothrombin time ratio >50% and platelet count >50,000/μL. Lesions with a large exophytic component, adjacent organ or bowel invasion or associated tumor thrombosis of the portal vein or extra-hepatic metastases were excluded. The lesions that could not be detected by both conventional US and CEUS were excluded and had to switch to an alternate guiding method to complete the ablation procedure. The lesions with lack of at least 10 mo follow-up contrast-enhanced MRI were also excluded from our study. The diagnosis of HCC was based on the typical imaging features (arterial phase hyper-enhancement followed by portal venous or delayed phase washout) of the dynamic contrast-enhanced CT and/or MRI or biopsy (Bruix et al. 2011).

Between September 2011 and January 2013, 76 patients with 93 HCCs 3 cm or smaller were enrolled consecutively in this study. Four of the 76 patients were excluded from the study population because their four HCC nodules could not been detected by both conventional US and CEUS as a result of coarse parenchymal echotexture of a cirrhotic liver and poor sonic window associated with shrunken liver volume. A total of 72 patients with 89 HCCs underwent conventional gray-scale US and CEUS-guided percutaneous RF ablation. Nine patients with 11 tumors were excluded who did not have the required follow-up contrast-enhanced MRI following RF ablation treatment; within 10 mo after tumor ablation, only one or two times follow-up contrast-enhanced MRIs were performed in these nine patients, and then they were lost to

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