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● *Original Contribution*

CONTRAST-ENHANCED ULTRASOUND IN THE CHARACTERIZATION OF HEPATOCELLULAR CARCINOMAS TREATED BY ABLATION: COMPARISON WITH CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING

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Abstract—The purpose of this study was to evaluate the clinical utility of low-mechanical-index contrast-enhanced ultrasound (CEUS) in assessing the response to percutaneous microwave ablation in patients with hepatocellular carcinoma by comparing the results with those of contrast-enhanced magnetic resonance imaging (CEMRI). Between August 2005 and July 2011, 182 patients with 231 lesions treated by microwave ablation were included in the study. One month after microwave ablation, CEUS and CEMRI were performed to evaluate therapeutic responses. The difference in diagnostic accuracy between the two methods was analyzed to evaluate the value of contrast-enhanced ultrasound after microwave ablation. The final diagnosis was based on computed tomography and MRI typical findings of therapeutic response of hepatocellular carcinoma, proven serum tumor marker levels and additional follow-up. The sensitivity of CEUS and CEMRI in evaluating the therapeutic effect of hepatocellular carcinoma was 86.5% and 84.6%; the specificity, 98.3% and 98.9%; and the accuracy, 95.7% and 95.7%.There was no significant statistical disparity between CEUS and CEMRI ($p > 0.05$).The sensitivity, specificity and accuracy were 98.1, 97.2 and 97.8% when CEUS was used in combination with CEMRI to evaluate the therapeutic response of hepatocellular carcinoma to microwave ablation. CEUS examination was proven to be a tolerable and easy modality for assessment of the therapeutic effect of microwave ablation and can provide results comparable to those obtained with CEMRI. Combining the results of these two examinations may reduce false-positive and false-negative diagnoses. (E-mail: Dyuxl301@yahoo.com.cn) © **2013 Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Hepatocellular carcinoma, Microwave ablation, Contrast-enhanced ultrasound, Magnetic resonance imaging.**

INTRODUCTION

Hepatocellular carcinoma (HCC) is the second leading cause of death related to malignancies in China, with more than 200,000 victims each year, which accounts for 53% of all liver cancer deaths worldwide (Tang 2006). Although HCC can be treated successfully by surgical resection, the majority of patients are not suitable for resection because of diagnosis at an advanced tumor stage and underlying liver cirrhosis (Bismuth et al. 1993; Lai et al.1995).

With the development of modern imaging systems, several image-guided minimally invasive techniques have been developed as alternatives to surgery. Image-guided percutaneous ablation therapy for hepatocellular carcinoma has been used worldwide (Lau et al. 2003). The survival benefit for patients with HCC undergoing resection or percutaneous ablation is mostly dependent on tumor size (Liang et al. 2005). The most widely used modalities are radiofrequency ablation and microwave ablation. The success of ablative treatment is strongly dependent on complete tumor destruction, which requires both accurate placement of ablative probes in the center of lesions and a thorough understanding of the ablative range (Antoch et al. 2002; Solbiati et al. 2001). However, the local recurrence rates after treatment remain high. To evaluate the therapeutic effect and detect residual tumor, much effort has been expended to identify an imaging technique that permits early post-therapeutic localization of surviving tumor tissue. Residual tumor blood flow on contrast-enhanced ultrasound performed ≥2 d after trans-arterial chemoembolization may be predictive of tumor outcome; currently, reliable detection of residual tumor blood flow by computed tomography

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(CT) and/or magnetic resonance imaging (MRI) requires 3 mo (Kono et al. 2007). Therefore, the aim of our study was to compare the imaging features and roles of contrast-enhanced ultrasound (CEUS) and contrast-enhanced MRI (CEMRI) in assessing the therapeutic response of HCC to, and detection of residual carcinoma after, microwave ablation.

METHODS

Patient population

Between August 2005 and July 2011, 182 consecutive patients (150 men and 32 women, aged 30–86 y, mean ± standard deviation = 58.1 ± 10.3 y) with 231 HCC nodules detected on either conventional sonography or contrast-enhanced CT/MRI were enrolled in this study (Table 1). All of them underwent microwave ablation with curative intention in our institution, and the protocol was proposed in accordance with the patients' medical history, laboratory data, and CT/MRI results. The maximum diameter of lesions in our study ranged from 1.0−7.8 cm (2.6 ± 1.4 cm). One hundred thirty-three patients had only a single lesion, and the other 49 patients had two lesions. This study was approved by our institutional human research review committee. Written informed consent was obtained from all patients. Inclusion criteria for our study were nonresectable cancer or patient refusal to undergo surgery; single HCC lesion ≤8 cm; no more than two HCC lesions with a maximum diameter ≤6 cm; absence of portal vein thrombosis or extrahepatic metastases; prothrombin time <25 s; prothrombin activity >40%; and platelet count >40 cells × 10^9/L. The exclusion criteria were severe cardiopulmonary disease, severe infection and so on. On the basis of these criteria, two patients were excluded because of portal vein thrombosis (these two patients were not included in our study group).

Pre-ablation imaging workup

All patients had undergone conventional ultrasound, CEUS, contrast-enhanced CT (CECT) and/or gadolinium-enhanced MRI to delineate the target tumor before microwave ablation. Baseline liver assessment was performed in each patient using conventional gray-scale ultrasound and color/power Doppler to evaluate and record the number, location, size, shape, border and internal echogenicity of the lesion and the intralesional blood supply. Maximum diameters of the index tumors were measured on CEUS images during the portal-venous phase before microwave ablation because the necrotic zone in this phase is avascular. To determine if tumor was persistent, ablated lesions were assessed in all vascular phases. CEUS examinations were carried out using the low-mechanical-index (MI ≤ 0.2) contrast-dedicated method contrast pulse sequencing (Cadence CPS, Siemens, Mountain View, CA, USA). The contrast agent used in this study was SonoVue (Bracco, Milan, Italy), an aqueous suspension of phospholipid-stabilized sulfur hexafluoride (SF_6) gas microbubbles supplied as a lyophilized powder (Schneider et al. 1995). Contrast-enhanced images (all vascular phases) were acquired digitally on the hard disk of the US system, as well as continuously on digital video tape, and were evaluated in consensus by two expert doctors who had at least 5 y experience using CEUS and were blinded to clinical and imaging information on the patients. All MRI studies were carried out using the same 1.5-T unit (Signa Echo-Speed, GE Medical Systems, Milwaukee, WI, USA); same contrast medium (Magneviest, Schering, Berlin, Germany, 0.1 mmol/kg body weight); and same sequences. According to at least two modalities of contrast imaging, all lesions were hypervascular (Fig. 1). Histologic diagnoses of all lesions were obtained by ultrasound-guided tumor biopsy using an 18-gauge needle in all patients. In patients with multiple nodules that appeared similar on contrast-enhanced images, at least one biopsy was performed and they were definitely diagnosed by follow-up.

Table 1. Baseline clinical characteristics of patients

Age (years)	58.1 ± 10.3*
Sex	
Males/females	150/32
Etiology of chronic liver disease	
None/HBV/HCV/HBV + HCV	25/123/28/6
Hepatic cirrhosis/none	154/28
Maximum diameter of lesions (cm)	
Mean ± SD (range)	2.6 ± 1.4*

HBV = hepatitis B virus; HCV = hepatitis C virus.
* Mean ± standard deviation.

Microwave ablation protocol

All treatments were performed in our institution. Before microwave ablation, all patients were examined by conventional ultrasound or CEUS to choose an appropriate puncture route. For lesions <1.7 cm in diameter, a single antenna was used; for those ≥1.7 cm in diameter, we used two or more antennas (Liang et al. 2003). Afterward, the antenna was inserted into the tumor and placed at located sites percutaneously. General anesthesia (propofol, 6–12 mg/kg per hour; ketamine, 1–2 mg/kg) was instituted after correct placement of antennas (Dong et al. 2003). If the lesion was adjacent to the bile duct, gallbladder or bowel (≤5 mm), a 21-gauge thermocouple was placed percutaneously at a designated location to monitor temperature in real time (Zhou et al. 2009). The temperature was kept at 50–54°C for no longer than 3 min, with intermittent emission of microwaves (Liang et al. 2009). If the lesion is near the diaphragmatic dome, artificial ascites should be used. An 18-gauge