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● *Original Contribution*

QUANTIFICATION OF ENHANCEMENT OF RENAL PARENCHYMAL MASSES WITH CONTRAST-ENHANCED ULTRASOUND

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Abstract—The purpose of this study was to investigate the value of quantitative assessment of enhancement in diagnosing renal cell carcinoma (RCC) with contrast-enhanced ultrasound (CEUS). A total of 73 solid renal parenchymal masses underwent both conventional ultrasound and CEUS. We compared the difference in maximum diameters on conventional ultrasound and CEUS between the benign and malignant groups. Enhancement features derived from a time-intensity curve were also analyzed. The diameters of renal cancer were found to be larger on CEUS than on conventional ultrasound ($p < 0.05$). When cutoff values of 4.74 s for washout time and 8.52% for enhancement intensity at 60 s for diagnosing RCCs were applied, the sensitivity, specificity and area under the receiver operating characteristic curve were 67.3%, 95.2%, 86.5% and 65.4%, 81.0%, 68.4%, respectively. The sensitivity and specificity for these two enhancement characteristics combined as a criterion for differentiating RCCs from benign lesions were 44.0% and 99.1%, respectively. Early washout in the area of maximal intensity in the interior of the lesion and prolonged washout in the whole area of the lesion are specific CEUS manifestations suggestive of RCC. (E-mail: Du_lf@163.com) © **2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Contrast-enhanced ultrasound, Quantitative analysis, Time-intensity curve, Renal cell carcinoma, Diagnosis.**

INTRODUCTION

Contrast-enhanced ultrasound (CEUS), which employs microbubble contrast agents and complementary harmonic pulse sequences to observe perfusion, has proven to be helpful in the diagnosis and characterization of renal cell carcinomas (RCCs) in many clinical studies in recent years. The advantages of CEUS include a good safety profile, simplicity, patient tolerance, lack of ionizing radiation and real-time multiplanar imaging capability (Piscaglia et al. 2012; Torzilli 2005). Although applications of CEUS in renal tumors have been well developed, there still remain controversies. For example, with respect to the CEUS features of the lesion, some studies indicate that early washout is suggestive of RCC, whereas others found that the CEUS manifestation of prolonged washout is a clue to RCC (Fan et al. 2008; Ignee et al. 2010a; Xu 2011). This study therefore retrospectively analyzed the CEUS imaging findings on RCCs to evaluate their diagnostic value and to characterize the vascular perfusion pattern of lesions.

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METHODS

Patients

Between February 2010 and March 2013, 73 patients (45 men and 28 women; age: 23–86 y [range], 56.3 ± 12.2 y [mean ± standard deviation]) with 73 solid renal parenchymal masses underwent both conventional ultrasound (US) and CEUS. The study was approved by the institutional review board and ethics committee of Shanghai First People's Hospital, and CEUS examinations were conducted after written consent was received from each patient. Patients with solid renal parenchymal masses revealed on US were enrolled in the study. All patients with contraindications according to the guidelines of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) (Piscaglia et al. 2012) were excluded from the study.

Conventional ultrasound and CEUS

Both conventional US and CEUS were performed with a commercially available ultrasound system (Acuson Sequoia 512, Siemens, Munich, Germany) using a 4C1-S convex array transducer (frequency range: 1–4 MHz). One of two experienced radiologists scanned the lesion using gray-scale and color Doppler sonography first. Planes of best visualization were selected to measure the maximum diameters of lesions. Location, echogenicity and color flow signals were also stored for each mass.

Then a 20G cannula was inserted into an antecubital vein for injection of contrast agent and saline solution. The same radiologist activated the contrast pulse sequencing mode (mechanical index = 0.21–0.23) and trained the patient to take a shallow breath or hold his or her breath when asked. The best plane was selected to observe both the renal mass and adjacent parenchyma. After optimization of image quality, a dose of 1.0–1.8 mL contrast agent (SonoVue, Bracco, Milan, Italy), which was chosen individually depending on the weight, height and age of the patient, was administered intravenously as a bolus, immediately followed by a flush of 5 mL 0.9% saline solution. The real-time video record was started from the beginning of the injection for 2 min at least and was stored in the DICOM format.

Imaging analysis

The maximum diameter of lesions was measured on conventional ultrasound and CEUS images. The result of subtracting the diameter measured on conventional ultrasound from that measured on CEUS was recorded as the difference in size. On conventional ultrasonic images, lesions were divided into hyper-echoic, iso-echoic, and hypo-echoic types in comparison to adjacent renal parenchyma. Homogeneity and presence of a hypo-echoic rim were also noted. The color flow signals were classified into two types: rich (defined as diffuse, penetrating or peripheral color flow signals) and poor (defined as focal or dot-like color flow signals).

To quantify contrast enhancement, SonoLiver software (TomTec GmbH, Munich, Germany, and Bracco Research, Geneva, Switzerland) was used, which could depict a time-intensity curve derived from a region of interest (ROI). Further, with the SonoLiver software, the selected ROIs can be coded by red and blue colors according to the intensity of each pixel. Red colors indicate hyper-enhancement in comparison to the reference area, and conversely, blue colors represent hypo-enhancement. With this ability, the ROIs were manually selected by another investigator with 5 y of experience in CEUS who was blinded to the pathologic results. The ROIs selected in this study included: ROI_{mass}, which was placed over the whole area of the mass; ROI_{refer}, which was set to a depth similar to that of the adjacent cortex; and ROI_{IMAX}, which was defined as the area of maximal intensity (IMAX) in the interior of the lesion (Figs. 1 and 2). All ROIs were drawn using more than 200 pixels. In this study, the enhancement intensity of each ROI was expressed in percent of the IMAX of ROI_{refer}, and the IMAX of the ROI_{refer} was set at 100%. In this way, errors resulting from the baseline intensity among different lesion types and different CEUS images were eliminated. ROI_{refer} was chosen to avoid the medulla because of its enhancement features of slow perfusion and hypo-enhancement, which are hemodynamically distinct from those of the cortex. Motion compensation was used to avoid the disturbance of tissue motion.

The enhancement features analyzed in this study included: arrival time (AT), time to peak (TTP), washout time (WT), IMAX and intensity at 60 s (I_{60}) (Table 1). To our knowledge, there is no published quantitative definition for "washout phase." According to EFSUMB guidelines, the transition from hyper- or iso-enhancement to hypo-enhancement is commonly referred to as the start of "washout." To quantify the timing of enhancement, we observed that when the enhancement intensity fell to 50%–65% of maximal intensity in quantification software, the investigator could recognize the transition of enhancement degree by eye; therefore, the time at which 60% of maximal intensity was registered in quantification software was chosen as time point for the washout phase.

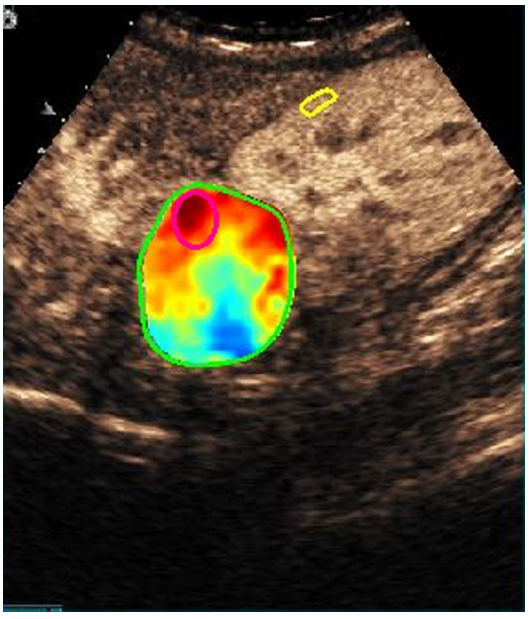

Fig. 1. Region of interest (ROI) definitions. Three regions of ROIs are drawn: ROI_{mass} (green) is placed over the whole area of the mass, ROI_{refer} (yellow) is set to a similar depth of the adjacent cortex, and ROI_{IMAX} (magenta) is defined as the area of maximal intensity (IMAX) in the interior of the lesion. The ROI_{mass} is color-coded with warm and cold colors to represent hyper- and hypo-echoic areas of IMAX.