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● *Original Contribution*

USEFULNESS OF CONTRAST PERFUSION ECHOCARDIOGRAPHY FOR DIFFERENTIAL DIAGNOSIS OF CARDIAC MASSES

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Abstract—The aim of this study was to assess the usefulness of contrast perfusion echocardiography in the differential diagnosis of different types of cardiac masses. Conventional echocardiography and contrast perfusion echocardiography were performed in 72 patients with cardiac masses. The degree of contrast enhancement of the mass and an adjacent section of myocardium after injection of contrast agent was determined by visual inspection and quantitative time–signal intensity curve analysis. The difference in maximal steady-state pixel intensity between the mass and the adjacent myocardium ($\Delta A_{mass–myocardium}$) was calculated. All masses had a pathologic diagnosis or resolved after anticoagulation. All 16 cardiac masses without enhancement on visual inspection were confirmed to be cardiac thrombi. Twenty-four masses with incomplete enhancement on visual inspection were recognized as benign tumors with validation methods. Of the 32 cardiac masses with complete enhancement, 30 were confirmed as malignant tumors and two as benign tumors with validation methods. The sensitivity and specificity of $\Delta A_{mass–myocardium}$ in differentiating thrombi from tumors were 93% and 100%, respectively, and 100% and 97% in differentiating malignant tumors from benign tumors and thrombi. Both visual and quantitative assessment of degree of enhancement of cardiac masses in relation to the adjacent myocardium during contrast perfusion echocardiography had high diagnostic accuracy for differentiation of a thrombus from a tumor or a benign tumor from a malignant tumor. (E-mail: ybdeng2007@hotmail.com) **© 2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Contrast perfusion echocardiography, Cardiac mass, Thrombus, Tumor.**

INTRODUCTION

Two-dimensional echocardiography is considered the first-line diagnostic imaging modality for the evaluation of cardiac masses, with a reported sensitivity of 93% for transthoracic echocardiography and 97% for transesophageal echocardiography (Meng et al. 2002). However, conventional echocardiography is not a reliable method for differentiation between different types of cardiac masses, including thrombi and benign and malignant tumors.

Advances in contrast perfusion echocardiography have enabled characterization of the vascularity of cardiac masses, which may provide additional information to differentiate a thrombus from a tumor or benign tumor from a malignant tumor (Porter et al. 2014). There have been some studies on differentiation of cardiac masses using contrast perfusion echocardiography, but most were case reports or involved limited numbers of patients (Kirkpatrick et al. 2004; Mansencal et al. 2009). Furthermore, few studies have evaluated the accuracy of contrast perfusion echocardiography in the differential diagnosis of cardiac masses. The primary objective of this study was therefore to evaluate the usefulness of contrast perfusion echocardiography in the differential diagnosis of cardiac masses in a relatively large sample of patients.

METHODS

Study population

Our institution is a tertiary referral teaching hospital. Between January 2008 and August 2014, we prospectively

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studied 72 consecutive patients (42 men and 30 women, mean age: 50 ± 15 y, age range: 12–85 y) with cardiac masses. All patients underwent a conventional examination and a contrast perfusion echocardiographic examination. This study was approved by the hospital ethics committee, and informed consent was obtained from all patients before contrast perfusion echocardiography.

Conventional and contrast perfusion echocardiographic imaging

Conventional echocardiographic imaging and contrast perfusion echocardiographic imaging were performed with a commercially available ultrasound machine and M3S transducer (Vivid 7 Dimension, GE Medical Systems, Horten, Norway) with a transmission frequency of 1.7–3.4 MHz. Two-dimensional images of cardiac masses were acquired in parasternal, apical four-chamber, apical two-chamber and apical long-axis or other non-standard planes if necessary. All images were digitally stored on the hard disk in the machine for off-line analysis (EchoPAC 6.1, GE Medical Systems).

The patients then underwent contrast perfusion echocardiography. During the continuous intravenous infusion of 2.4 mL SonoVue (Bracco, Geneva, Switzerland) through the antecubital vein, cardiac masses were imaged using the preset real-time myocardial contrast perfusion imaging modality with coded pulse inversion technique. To reduce microbubble destruction, we preset the mechanical index to 0.08 and the frame rate to 22/s. Image depth was adjusted to 12–15 cm according to the size of the heart, and the focus position was set at the level of the mass. Time gain compensation was adjusted to achieve a homogeneous signal intensity of the heart. All these settings were kept constant throughout each examination. When the cardiac masses were opacified with contrast agents, a high-mechanical-index (1.0) ultrasound impulse was transmitted for at least 20 frames to destroy microbubbles within cardiac masses and myocardium. This method allowed visualization of the gradual contrast replenishment of the mass after this impulse.

A real-time contrast perfusion cine loop revealing the entire process of contrast replenishment was acquired after injection of contrast material. The cine loop was digitally stored for later analysis. Patients were observed for complications for 30 min before leaving.

Imaging analysis

Contrast enhancement of the cardiac masses after the high-mechanical-index impulse was assessed visually only in relation to the enhancement in the adjacent myocardium and categorized as follows by two independent observers who were blinded to the clinical information and the final diagnosis of the patients: grade 1 = no enhancement within cardiac mass; grade 2 = partial or incomplete enhancement within cardiac mass lower than that within the adjacent myocardium; grade 3 = complete enhancement within cardiac mass higher than that within the adjacent myocardium.

Contrast enhancement of masses was also quantitatively analyzed off-line with time–signal intensity curve analysis software (EchoPAC 6.1, GE Medical Systems). Regions of interest were drawn both within the cardiac mass and within the section of adjacent ventricular myocardium. Time–signal intensity curves for the mass and adjacent myocardium during the process of replenishment after the high-mechanical-index impulse were automatically produced and fitted to the exponential function $y = A \cdot (1-e^{-k \cdot t})$, where A reflects the post-impulse maximal steady-state pixel intensity level, and k represents the initial rate of contrast replenishment after the high-mechanical-index impulse. The difference in the value of A between mass and adjacent myocardium ($\Delta A_{\text{mass–myocardium}}$) was calculated.

Methods for validation of diagnosis of a cardiac mass

Diagnoses of cardiac masses were confirmed with validation methods, including pathologic examination of surgical specimens, mass resolution after anticoagulation and detection in serial echocardiographic studies during follow-up. Moreover, in patients with an extra-cardiac primary malignant tumor, a cardiac mass that decreased or resolved after chemotherapy targeting the specific histologic type of the extra-cardiac malignant tumor was diagnosed as a metastasis. Results of visual inspection and quantitative analysis of perfusion imaging were compared with the final diagnoses determined with the validation methods described.

Inter-observer and intra-observer reproducibility

To assess the reproducibility of the quantitative measurements, $\Delta A_{\text{mass–myocardium}}$ was measured in 10 patients by two independent observers on the same day and twice by one observer, with measurements taken 1 wk apart. Inter-observer and intra-observer variability was calculated as the percentage of the absolute difference between the two measurements divided by the mean value of the measurements.

Statistical analysis

We used SPSS Version 13.0 software (SPSS, Chicago, IL, USA) for statistical analysis. Continuous variables were expressed as the mean ± one standard deviation. Continuous variables were compared using Student's *t*-test. The sensitivity and specificity of $\Delta A_{\text{mass–myocardium}}$ in the differential diagnosis of different types of cardiac masses were derived using receiver operating