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ORIGINAL ARTICLE

Diagnostic value of contrast-enhanced ultrasound in thyroid nodules with calcification

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Abstract The aim of this study was to investigate the diagnostic values of conventional ultrasound and contrast-enhanced ultrasound (CEUS) in benign and malignant thyroid nodules with calcification. Conventional ultrasound and CEUS were performed in 122 patients with thyroid nodules with calcification. The thyroid nodules were characterized as benign or malignant by pathological diagnosis. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accordance rate of the two imaging methods were determined. The area under the receiver operating characteristics curve (AUC) was used to assess the diagnostic values of the two imaging methods. In 122 cases of thyroid nodules with calcification, 73 benign nodules and 49 malignant nodules were verified by pathological diagnosis. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accordance rate of conventional ultrasound were 50%, 77%, 59%, 69%, and 66%, respectively, and those of CEUS were 90%, 92%, 88%, 93%, and 91%, respectively. There were significant differences between the two imaging methods. AUCs of conventional ultrasound and CEUS were 0.628 ± 0.052 and 0.908 ± 0.031, suggesting low and high diagnostic values, respectively. CEUS has high diagnostic values, being significantly greater than those of conventional ultrasound, in differential diagnosis of benign and malignant thyroid nodules with calcification.

Conflicts of interest: All authors declare no conflicts of interest.

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Introduction

In clinical practice, the incidence of thyroid nodules is high. Thyroid nodules are found in 50% of autopsy cases [1], and approximately 5% of these nodules are malignant [2]. Kuhn et al [3] reported that thyroid papillary carcinoma is the most common type of thyroid carcinoma, accounting for more than 85% of thyroid carcinomas. Ultrasound is the preferred examination method for thyroid diseases [4], and thyroid nodules with calcification are often detected with this modality. Previous studies have shown that calcification occurs in 19.8—32.1% of thyroid nodules [5,6]. As reported by Kim et al [7], the calcification rates in malignant and benign thyroid nodules are approximately 40.2% and 22.2%, respectively. In malignant thyroid nodules, the microcalcification and massive calcification rates are 42.9% and 26.7% [7]. Therefore, to avoid unnecessary surgery, a reliable method for identification of the malignant lesions in a large number of thyroid nodules with calcification is the focus of clinical attention [8].

Many researchers have attempted to distinguish benign and malignant thyroid nodules according to the calcification type [9,10]. However, because calcification may occur both in benign and malignant nodules, the application of conventional ultrasound in diagnosis of thyroid nodules has been restricted. Contrast-enhanced ultrasound (CEUS) is a new technology developed in recent years and has yielded favorable results in the examination of parenchymal organs such as abdominal organs [11—13], but its application in thyroid diseases is still in the exploratory stage. In this study, the diagnostic value of CEUS in identifying benign and malignant thyroid nodules with calcification was investigated. The objective was to assist clinicians in selecting the correct therapeutic approach for thyroid nodules.

Methods

Patients

One hundred and twenty-two patients who underwent surgery for thyroid nodules with calcification at our hospital between February 2010 and March 2012 were enrolled in this study. There were 37 male and 85 female patients, aged 18—72 years, with an average age of 46 $\pm$ 12 years. There were 122 thyroid nodules, one nodule in each patient. The nodule size was 0.35—4.2 cm, with an average of 1.5 $\pm$ 0.40 cm, and the maximum major diameter of the calcification lesions was 10 mm. According to the pathological diagnosis results, the 122 thyroid nodules were divided into a malignant group (49 nodules) and a benign group (73 nodules).

Methods

An ACUSON Sequoia 512 (Siemens Healthcare, Erlangen, Germany) ultrasound scanner was used in the present study. The scanner was equipped with a model 15L8w high-frequency linear transducer array. The scanner has a spatial resolution of 0.1 mm. Contrast pulse sequencing (CPS) with a transmitting frequency of 7.0 MHz and a mechanical index (MI) of 0.32 was used, as recommended, for CEUS procedures [14].

The SonoVue (Bracco SpA, Milan, Italy) contrast agent was used for all patients. The agent was prepared by mixing with 5 mL saline and shaking vigorously until a milky-white microbubble suspension was obtained. A bolus injection of 2.4 mL of the SonoVue preparation was administered via the cubital vein, followed by injection of 5 mL saline to flush the syringe. Immediately thereafter, real-time harmonic gray-scale ultrasound examination of the thyroid nodule was conducted, and the dynamic images were recorded. Finally, the ultrasound images were independently evaluated by two experienced sonographers.

CEUS results were categorized as follows. (1) According to the comparison of echo intensity at peak enhancement between the thyroid nodule and the surrounding thyroid parenchyma, the enhancement degree was categorized as hypo-enhancement, iso-enhancement, or hyper-enhancement. (2) According to the uniformity of echo intensity of the lesion at peak enhancement, the enhancement uniformity was categorized as homogeneous enhancement or inhomogeneous enhancement (including local nonenhancement). Quantitative parameters of CEUS, including time to enhancement, time to peak, and peak intensity, were obtained using 2D Cardiac Performance Analysis (CPA) magnetic resonance (MR) quantification software (TomTec Imaging Systems, Unterschleissheim, Germany) [15]. According to Zhou et al [16], inhomogeneous hypo-enhancement was defined as the diagnostic standard for malignant thyroid nodules.

Statistical analysis

Data were expressed as mean $\pm$ SD. Statistical analysis was performed using SPSS 18.0 statistical software (SPSS Inc., Chicago, IL, USA). The t test and Chi-square test were performed for analyzing the measurement data and enumeration data, respectively. A p value <0.05 was considered statistically significant. The pathologically diagnosed malignant thyroid nodules were used as standards, and the receiver operating characteristics (ROC) curves of multivariate observations were drawn, with the sensitivity of the malignant nodule imaging diagnosis as ordinate and 1-specificity as abscissa.

Results

CEUS findings in benign and malignant thyroid nodules

In the malignant group, all 49 thyroid nodules were papillary carcinomas, including 44 nodules with microcalcification and five nodules with coarse calcification. After the injection of contrast agent, 29 nodules with microcalcification and two nodules with coarse calcification were categorized as inhomogeneous hypo-enhancement (Fig. 1). Thirteen nodules with microcalcification displayed inhomogeneous hypo-enhancement with penetration of contrast agent into the surrounding thyroid parenchyma and point-like appearance of contrast agent in the center of the nodule. Two nodules with microcalcification and two nodules with coarse