A Comparative Analysis of DWI and Ultrasound in Thyroid Nodules

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Abstract

Background

Diffusion weighted imaging and ultrasound are commonly used methods to examine thyroid nodules, but their comparative value is rarely studied. To evaluate the value of diffusion weighted imaging and ultrasound in differentiating benign and malignant thyroid nodules

Methods

A total of 100 patients with 137 nodules were enrolled, who underwent both diffusion weighted imaging and ultrasound before operation. T1 and T2 signal intensity ratio (SIR) of each thyroid nodule was calculated by measuring the mean signal intensity divided by that of paraspinal muscle. The value of ADC, signal intensity ratio (SIR) of benign and malignant thyroid nodules were analyzed by two independent sample t test. The sensitivity, specificity and accuracy of DWI and ultrasound were compared and analyzed by chi-square test.

Results

There was no significant difference in signal intensity ratio between benign and malignant thyroid nodules. The ADC value had significant difference. When the threshold value was 1.12 x10^-3 mm²/s, the maximum area under the curve was 0.944. The sensitivity, specificity and accuracy were 84.9%, 92.2% and 87.6% respectively. The sensitivity and specificity of ultrasound diagnosis were 90.1%, 80.4% and 86.9% respectively.

Conclusion

Ultrasound has high sensitivity in differentiating benign and malignant thyroid nodules, and ADC value has high specificity in differentiating thyroid nodules, but there is no statistical difference in sensitivity and specificity between the two. DWI and Ultrasound have their own advantages in differentiating benign and malignant thyroid nodules.
Introduction

It is reported that the incidence of thyroid malignant tumors has increased significantly in the past decades. The detection rate of thyroid nodules in healthy people is about 16-67% [1]. Statistics from the National Cancer Center [2] showed that the number of new cases of thyroid cancer in 2013 accounted for 16.5% of the world's total. Differentiated thyroid cancer (mainly papillary and follicular carcinomas) accounts for the majority. If early detection and follow-up active treatment can be carried out, the 10-year survival rate of patients can be as high as 90%[3].

Ultrasound is the preferred method for the diagnosis of thyroid tumors. It has good diagnostic ability for the morphological manifestations, calcification and cystic necrosis of thyroid lesions. However, previous studies have shown that the diagnostic results are susceptible to the operator's influence[4]. Recently, Diffusion Weighted Imaging (DWI) has become a hotspot in identifying thyroid nodules. Some researchers have suggested that the T2 SIR signal intensity ratio (SIR) of thyroid nodules can be used as a quantitative parameter to differentiate benign from malignant nodules, which is of great significance in the preoperative diagnosis of thyroid nodules[5]. The purpose of this study was to explore the best diagnostic threshold of DWI in differentiating benign and malignant thyroid nodules, and to compare the diagnostic value of DWI with ultrasound.

Methods

Patients

The Institutional Review Board of Shanghai Ninth People’s Hospital approved this retrospective study and the requirement for informed consent was waived. The following criteria were adopted for patient selection: 1) The mass was primary thyroid tumor; 2) The patients underwent both conventional DWI and Ultrasound scan before treatment; 3)
Masses with short axis ≥ 10 mm; 4) The MR images could be acquired and interpreted.

Through a comprehensive search of our institutional medical report database from July 2017 to January 2019, we identified 100 patients (mean age, 49 years; range, 23–79 years) with 137 nodules (mean short axis, 18 mm; range, 5–76 mm). The final diagnoses were made upon histopathological results in 137 nodules, then the diagnostic results of DWI and ultrasound were compared.

**Image acquisition**

**DWI examination**

All MRI examinations were performed on a 3.0 T scanner (Philips Ingenia 3.0T). The head and neck coils were covered on the thyroid surface. Patients take supine position, neck back, shoulders as far as possible droop, told the patient to breathe calmly, avoid swallowing and coughing movements.

The parameters of MRI acquisition were: T1WI TSE, TR 450 ms, TE 20 ms, thickness 3 mm, gap 1 mm, FOV 240 mm x 240 mm, matrix 300 x 240; T2WI DIXON-TSE, TR 2500 ms, TE 100 ms, thickness 3 mm, gap 1 mm, FOV 240 mm x 240 mm, matrix 300 x 240; DWI, TR 400 ms, TE 70 ms, thickness 3 mm, gap 1 mm, FOV 240 mm x 240 mm, matrix 220 x 180. The b value is 0 and 1000 s/mm².

**Ultrasound examination**

All Ultrasound examinations were performed on a ultrasound scanner (Toshiba-Aplio 400). The probe frequency was 5-12 MHz. The patient was in supine position, head slightly backward, and neck was fully exposed. The probe was placed in the thyroid region. The nodule boundary, echo, blood flow, calcification and peripheral lymph node enlargement were observed.

**Image analysis**

ADC measurements was performed by two radiologists with 3 and 7 years of experience in
head and neck imaging, who were blinded to the clinical information and diagnosis. DWI image analysis was performed on Philips post-processing workstation to measure the average ADC value of each nodule (b value 0,1000 s/mm²) and the signal intensity ratio on T1WI and T2WI. For ADC value, the ROI of the same size on different sections is selected for multi-point measurement, and the average value is obtained at last. The ROI of the same size on different sections is selected to get the region of interest, avoiding cystic degeneration, hemorrhage and necrosis as far as possible. The signal intensity ratio (SIR) was calculated for each sequence as a ratio of signal intensity of the thyroid nodule to that of the paraspinal muscle.

Ultrasound examinations was performed by a radiologist with 7 years of experience in head and neck imaging, who was blinded to the clinical information and diagnosis. TI-RADS classification method was used in the ultrasound diagnosis report, which stipulated that grade 1-3a was benign and grade 3b-5 was malignant. Finally, each nodule was given a definite grading and qualitative diagnosis.

**Statistical analysis**

SPSS 20.0 software was used for statistical analysis. The difference of ADC, T1SIR and T2SIR in patients with benign and malignant thyroid nodules was evaluated by independent sample t test. The difference was statistically significant when P < 0.05. On receiver operating characteristic curve (ROC), the ADC thresholds for differentiating benign and malignant thyroid nodules were obtained. Finally, the diagnostic value of ultrasound and DWI was compared by paired chi-square method.

**Results**

**Pathology**

A total of 137 thyroid nodules were found in 100 patients (21 males and 79 females),
including 79 in the left lobe, 51 in the right lobe and 7 in the isthmus. There were 86 malignant nodules (82 papillary, 2 follicular and 2 lymphoma) and 51 benign nodules (31 nodular goiters, 11 thyroid adenomas and 9 Hashimoto's thyroiditis).

**ADC and SIR**

The average ADC value of benign thyroid nodules (1.36±0.17×10^{-3} mm²/s) was higher than that of malignant thyroid nodules (0.89±0.21×10^{-3} mm²/s), and the difference was statistically significant (P < 0.05), as shown in Figure 1. There was no significant difference in T1SIR and T2SIR between benign and malignant thyroid nodules (P > 0.05). According to ROC curve analysis, the best ADC threshold for differentiating benign and malignant thyroid nodules is 1.12×10^{-3} mm²/s. At this time, the maximum area under the corresponding curve is 0.944, and the sensitivity and specificity are 84.9% and 92.2%, respectively. See Figure 2 for details. The ADC value, T1 and T2 signal intensity ratio of benign and malignant thyroid nodules are detailed in Table 1.

**Diagnostic results of DWI and ultrasonography**

There were 82 papillary thyroid carcinomas and 3 follicular thyroid carcinomas (fig. 3). Most of them showed high or slightly high signal on DWI, and the signal was relatively uniform. Two lymphomas showed nodular high signal on DWI, and the internal signal was relatively uniform. Thirty-one nodular goiters and nine Hashimoto's thyroiditis (Fig. 4) showed nodular slightly higher signal intensity on DWI, and 11 thyroid adenomas showed slightly higher signal intensity on DWI.

of 137 nodules, 77 were malignant, 73 were consistent with pathological findings, and 60 were benign, 47 were consistent with pathological findings. The sensitivity, specificity and accuracy of differential diagnosis of MRI were 84.9%, 92.2% and 87.6% respectively.

TI-RADS classification method was used in the ultrasound diagnosis report, which
stipulated that grade 1-3a was benign and grade 3b-5 was malignant. Among 137 nodules, 88 were malignant, 78 were consistent with pathological findings, 49 were benign and 41 were consistent with pathological findings. The sensitivity and specificity of ultrasound diagnosis were 90.1%, 80.4% and 86.9% respectively. Finally, the qualitative diagnostic results of MR and Ultrasound were matched by chi-square test. The value of MR and Ultrasound in the diagnosis of thyroid nodules was compared in detail in Table 2.

Discussion

In this study, 15 cases of malignant nodules were associated with Hashimoto's thyroiditis and 2 cases with nodular goiter. Previous studies [5] have shown that there is a statistical difference between benign and malignant thyroid nodules in T2SIR (P < 0.001), and Yoshifumi et al. suggested that the presence of dense fibrous tissue in papillary carcinomas led to a decrease in T2SIR. In this study, we found that there was no significant difference between T1 and T2SIR (P > 0.05), and the signal ratio of benign and malignant nodules was smaller than that of previous measurements, which may be related to the type of machine and the type of samples. At present, there are few studies on signal intensity ratio, so the author believes that T2SIR can't be used as a stable index for the identification of thyroid nodules.

According to TI-RADS grading method, nodules were characterized by differential lobes or irregular margins, microcalcification or mixed calcification. Studies [7] showed that the blood flow characteristics of nodules could be used as an important reference index for differentiating benign and malignant nodules. However, there were some overlaps between benign and malignant nodules on sonograms, and some studies suggested [5,8] that Thyroid Imaging Reporting and Data System (TI-RADS) is still controversial. Malignant nodules have blurred boundaries, solid hypoechoic interior, gravel-like calcification and mixed internal blood flow, while lymphoma nodules have abundant internal blood flow.
signals. Studies have shown that enhanced posterior echo of nodules is an important sign of lymphoma differentiating from other malignant thyroid tumors; benign nodules have clear boundaries, low and isoechoic interior, and some of them are accompanied by coarse calcium. Most of the lesions had complete capsule, and the blood flow signals in the nodules were scarce. Circular blood flow signals could be seen around the nodules, while the blood flow signals in the nodules of Hashimoto's thyroiditis were abundant. In this study, the sensitivity of ultrasound diagnosis of nodules was high (90.1%), but the specificity was not high (80.4%). Compared with magnetic resonance imaging, ultrasound is more sensitive to the detection rate of micro-lesions and the display of microcalcification. Almost all calcifications are detected. However, due to the limitations of its own technology, the exploration of deep cervical tissue and the evaluation of peripheral lymph node metastasis are inferior to magnetic resonance imaging.

DWI has always been a research hotspot in differential diagnosis of benign and malignant thyroid nodules. The diffusion coefficient (ADC value) is not only related to the free movement of water molecules, but also affected by microcirculation perfusion. Some scholars have concluded that ADC value is an independent measurement factor in differential diagnosis of benign and malignant thyroid nodules in the multi-parameter study of DWI. In this study, ADC values of benign thyroid nodules were significantly higher than those of malignant thyroid nodules, which was consistent with previous studies. Some scholars have proposed that DWI can provide a lot of information about the microstructure and physiological process of tissues. The existence of organelles and biomacromolecules in tissues limits the free movement of extracellular water molecules. But Schueller-Weidekamm suggests that ADC values in malignant nodules are higher than those in benign nodules. He believes that increased follicular production in malignant nodules increases ADC values. In this study, the ADC value of
malignant nodules (0.89±0.21×10^{-3} mm^2/s) was lower than that of benign nodules (1.36±0.17×10^{-3} mm^2/s). The main reason was that the number and density of malignant nodules were more than that of benign nodules, which resulted in the decrease of intercellular space. At the same time, the malignant nodules were mainly papillary carcinomas, which resulted in the increase of mitotic figures and the increase of nuclear-cytoplasmic ratio, which resulted in the limited intracellular water molecule activity. Qualitative fibrosis also limits the diffusion of water molecules to varying degrees, which is consistent with Yoshifumi [7]. A recently published study [13] It is suggested that irregular margins of nodules are a strong predictor of malignant tendency. Malignant nodules on DWI usually have high signal intensity. Quantitative ADC value obtained by post-processing can objectively evaluate nodules qualitatively. In this study, using 1.12 ×10^{-3} mm^2/s as the threshold, the specificity of DWI diagnosis is higher (92.2%) and the sensitivity is lower (84.9%). Compared with ultrasound, the detection rate of lymph node metastasis is higher. According to Adel Razek[14], diffusion-weighted imaging combined with ADC maps can help to identify metastatic non-necrotic lymph nodes and depict the microscopic information of the solid survival of lymph nodes. Recently, some scholars have concluded that high b value (2000 s/mm^2) [15] has high accuracy in differential diagnosis of benign and malignant thyroid micronodules.

Our study had several limitations. Firstly, it was a retrospective study with relatively small amount of patients, the majority of malignant nodules in the sample selection will inevitably affect some quantitative parameters of DWI. Secondly, only papillary, follicular and lymphoma are found in malignant nodules, and no other malignant nodules are found. we adopted b value of 0 and 1000 s/mm² for DWI. In fact, b values of 800 s/ mm² was more commonly used in previous thyroid studies. Finally, the results of ultrasound
examination are based on the opinion of only one diagnostic physician, which is subjective. Therefore, we will continue to expand the sample size and sample types, and make comparative analysis with ultrasound, and conduct in-depth comparative study of the differences between groups.

Conclusion

The threshold of ADC value for differentiating benign and malignant thyroid nodules is 1.12 ×10^{-3} \text{mm}^2/s. There is no statistical difference in sensitivity and specificity between ultrasound and DWI. Ultrasound is better than DWI in detecting calcification, while MRI is more advantageous in the diagnosis of lymph node metastasis. Both of them play an irreplaceable role in the diagnosis of thyroid nodules.

Abbreviations

ADC: Apparent diffusion coefficient;
AUC: Area under the ROC curve;
DWI: Diffusion weighted imaging;

Declarations

Ethics approval and consent to participate

The study was approved by Institutional Review Board of Shanghai Ninth People’s Hospital. Due to the retrospective study design individual consent was waived.

Consent to publish

Not Applicable.

Availability of data and materials

The dataset supporting the conclusions of this article is available upon request to the corresponding author.

Competing interests
The authors declare that they have no competing interests

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**Authors’ contributions**

XT and WK conceived and designed the study. WK, XY and JR collected the data. WK and XY analyzed the data and wrote the paper. All authors read and approved the final manuscript for publication.

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Figures

![Box plot](Figure 1)

Box plot shows apparent diffusion coefficient (ADC) values for thyroid malignant and benign nodules. Boundaries of boxes closest to zero are 25th percentile, lines in boxes are medians, boundaries of boxes farthest from zero are 75th percentile, error bars are smallest and largest values in 1.5 box lengths of 25th and 75th percentiles.
Figure 2

Graph shows ROC curve of apparent diffusion coefficient (ADC) value used for differentiation between thyroid malignant and benign nodules (b = 1000s/mm²).

The maximum area under the curve is 0.994.
Male, 50 years old, follicular carcinoma of the right thyroid lobe (white arrow). A: Axis TIWI showed iso-signal in right lobe; B: hyperlipidemia on the same level on the same level on the same axis with clear boundary; C: high signal on the same level on DWI; D: pathological section (HE, 10 40) showed that the abnormal follicular cells with dark nuclei surrounded by different sizes of follicular cavity, pink glia, incomplete fibrous envelope on the outside, and nest-like cells infiltrated into the envelope.
Male, 63 years old, bilateral nodular goiter of thyroid with bleeding at different stages (white arrow). A: Axial T1WI showed bilateral lobe enlargement with multiple high-signal and low-signal shadows; B: On the same level, axial T2WI lipid pressure showed multiple high-signal and low-signal hemorrhage foci; C: On the same level, DWI showed diffuse slightly high-signal in bilateral lobes; D: Pathological section (HE, 10 40) showed that the tightly packed follicles were filled with glia, and some of the endocytosins of different sizes absorbed vacuoles, and the microvessel between follicles decreased.

**Supplementary Files**

This is a list of supplementary files associated with the primary manuscript. Click to download.

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