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The Value of Virtual Touch Tissue Quantification Technique in Differential Diagnosis of Thyroid Microcarcinomas*

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ABSTRACT Objective: Virtual touch tissues quantification (VTQ) is a new elastography method which can evaluate the tissue stiffness noninvasively and quantitatively. The aim of this study is to investigate the clinical value of VTQ technique in differential diagnosis of thyroid microcarcinomas (TMCs). **Methods:** Virtual touch tissue quantification (VTQ) was used to examine 114 thyroid nodules and the adjacent thyroid tissues in 110 patients. The values of shear wave velocities (SWV) of nodules and the adjacent thyroid tissues were obtained and analyzed. Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic performance of VTQ and to define the optimal cut-off point. **Results:** 114 nodules included 32 benign lesions (30 nodular goiters and 2 adenomas) and 82 malignant lesions (papillary microcarcinomas). The mean SWV in benign nodules and the adjacent thyroid tissues were 2.30± 0.49 m/s (range: 1.39~4.03 m/s), 2.08± 0.40 m/s (range: 1.30~2.79 m/s), respectively, while in malignant nodules and the adjacent thyroid tissues were 3.12± 0.97 m/s (range: 1.96~8.34 m/s), 2.06± 0.46 m/s (range: 1.05 3.13 m/s), respectively. The mean SWV of malignant thyroid nodules was significantly higher compared with benign thyroid nodules (t=5.911, P<0.0001). A significant difference was found between malignant thyroid nodules and the adjacent tissues of thyroid (P<0.0001), while no statistical difference was found between benign thyroid nodules and the adjacent thyroid tissues (P>0.05). The area under ROC curve (AUC) was 0.833, using 2.30 m/s was the cut-off point, the sensitivity and specificity of VTQ were 90.2 % and 62.5 %, respectively. **Conclusion:** Mean value of SWV of malignant thyroid nodules were significantly higher than that of benign ones. VTQ technique could be an effective tool in the differential diagnosis of TMCs by providing quantitative infor- mation about tissue stiffness.

Key words: Virtual touch tissue quantification; Elastography; Thyroid nodule; Microcarcinoma

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Introduction

Thyroid microcarcinoma (TMC) is defined as a tumour ≤ 1 cm in the greatest dimension [1]. As occult primary focus, clinical symptoms are not typical, and thus missed diagnosis and misdiagnosis rate are higher. With the development of high-frequency ultrasound, the detection rate of TMCs increased, however, there are some limitations of conventional ultrasound in differential diagnosis of TMCs[2]. Despite fine needle aspiration biopsy (FNAB) has been proved an effective method for thyroid carcinoma diagnosis, it is an invasive examination and has a strong dependence on operator [3,4]. Elastography was first proposed in the year of 1991by Ophir et al [5], and was used to assess the stiffness of the tissue by measuring the degree of distortion under external force. Virtual touch tissues quantification (VTQ) is an emerging elastography technique which can evaluate the tissue stifiness noninvasively and quantitatively. It estimates the tissue stiffness by measuring shear wave velocity (SWV) in the regions of interest (ROI) and can be performed during routine ultrasound examinations. Compared with conventional ultrasound elastography, VTQ has been considered to be highly reproducible and more objective for assess the stiffness of target tissue. At present, VTQ technique has been mainly applied to assess hepatic fibrosis and has a good diagnostic accuracy for the staging of liver fibrosis[6-8]. In addition, VTQ technique has been used to evaluate other organs, such as pancreas, spleen, kidney and prostate, as well as breast[9-11]. Recently, the feasibility of VTQ for evaluating thyroid disease was shown [24-25]. However, the report about VTQ technique in differentiation of TMCs is few. The aim of the current study is to explore the clinical value of VTQ technique in differentiating TMCs. In this study, we measured SWV of all the enrolled nodules by using VTQ technique. Values of SWV of TMCs were compared with that of the benign thyroid nodules. Clinical value of VTQ in differentiating malignant nodules from benign ones were detected by ROC curves.

1 Materials and Methods

1.1 Patients

A total of 125 thyroid nodules in 121 consecutive patients were selected from September 2012 to July 2013 in a affiliated

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hospital of a university. All patients underwent conventional US followed by VTQ elastography by one sonographer with 15 years of experience of ultrasound and about 1 month of special training in performing VTQ on thyroid nodules.

The inclusion criterion were the presence of a thyroid nodules ≤ 1 cm in diameter, solid or almost solid thyroid nodules, no treatment performed on the nodules and all nodules were confirmed by histopathology after surgery. The nodules that displayed X.XX m/s were excluded. Finally, 114 thyroid nodules in 110 patients (84 females and 26 males; age mean 45.3 ± 12.0 years, range, 14~77 years) were enrolled in this study. The mean diameter of nodules was 0.73± 0.16 cm (range, 0.4~1.0 cm). All patients who participated in this study were given informed consent in advance.

1.2 Conventional US

All examinations were performed using an Siemens-Acuson S2000 US system (Siemens Medical Solutions, Mountain View, CA, USA) equipped with a 9L4-linear array transducer with frequency ranged from 7.0 MHz to 9.0 MHz. Conventional US features of thyroid nodules were evaluated for size, margin, shape, echogenicity, halo-sign, spot microcalcification (hyperechoic spots less than 2 mm, without acoustic shadowing). Then color Doppler flow imaging (CDFI) was performed.

1.3 VTQ elastography

VTQ elastography was performed on the longitudinal axis section with the same equipment and the same probe after the conventional US examination. The probe should come into contact with the surface of skin gently. The patients were positioned in a supine position and were asked to hold breath and then VTQ function was initiated. The shear wave velocity (SWV) within a ROI was estimated by system automatically and displayed on the screen, the results being expressed in meters per second (m/s) (Fig. 1). Firstly, the ROI cursor was moved onto the center of the nodules, avoiding coarse calcifications and liquefaction necrosis. And then, the ROI was moved to the surrounding thyroid tissue and the same procedure was repeated. In each patient, at least 5 valid SWV measurements were performed in nodules and the adjacent thyroid tissues, then the mean value were calculated.

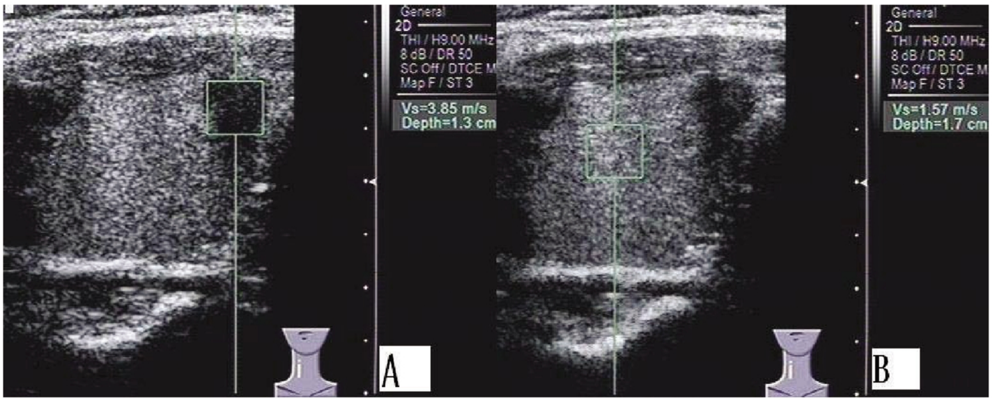

Fig.1 The SWV of a thyroid nodule in ROI was 3.85 m/s. B: The ROI placed in the adjacent tissue measuring the SWV was 1.57 m/s in the same patient. Pathologic findings revealed papillary carcinoma.

1.4 Statistical analysis

We used SPSS17.0 statistical software package (SPSS Inc, Chicago, IL) for statistical analysis. The continuous data were expressed as mean ± SD. The difference between two different groups were compared with independent t test. P<0.05 was found to be statistically significant. Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic performance of VTQ. The area under ROC curve (AUC) and 95 % confidence intervals (CI) were determined. The maximum value of Youden's index (sensitivity specificity 1) was performed to define the optimal cut-off point for VTQ, and the sensitivity and specificity of this cut-off point were calculated.

2 Results

2.1 Pathologic findings

Totally 110 patients with 114 nodules with pathological diagnosis were enrolled in this study. Among the 32 benign nodules in 31 cases, 30 were nodular goiters and 2 were adenomas. The remaining 82 nodules in 80 cases were all papillary thyroid microcarcinomas.

2.2 VTQ elastography

The mean SWV in benign nodules and the adjacent thyroid tissues were 2.30± 0.49 m/s (range: 1.39~4.03 m/s), 2.08± 0.40 m/s (range: 1.30~2.79 m/s), respectively, while in malignant nodules and the adjacent thyroid tissues were 3.12± 0.97 m/s (range: 1.96~8.34 m/s), 2.06± 0.46 m/s (range: 1.05~3.13 m/s), respectively. Mean SWV of malignant thyroid nodules was significantly higher compared with benign nodules (t=5.911, P<0.0001) (Figure 2). A significant difference was found between malignant thyroid nodules and the adjacent tissues of thyroid (P<0.0001), while no statistical difference was found between benign thyroid nodules and the adjacent thyroid tissues (P>0.05).

2.3 ROC analysis

The AUC for the SWV in differentiating benign from malignant thyroid nodules was 0.833(95 % CI 0.751-0.916) (Fig. 3). Using 2.30 m/s as the best cut-off point for VTQ, the corresponding sensitivity and specificity of VTQ for detection of malignancy were 90.2 % and 62.5 %, respectively. The distribution of VTQ elastography in TMCs was shown in Table 1.

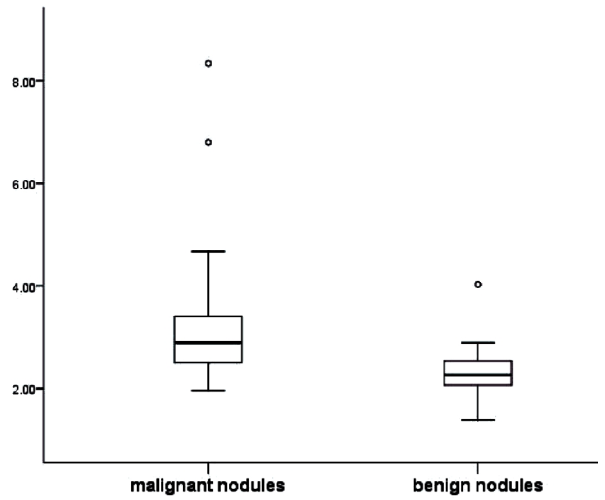

Fig.2 Mean SWV assessed by VTQ elastography in malignant and benign thyroid nodules

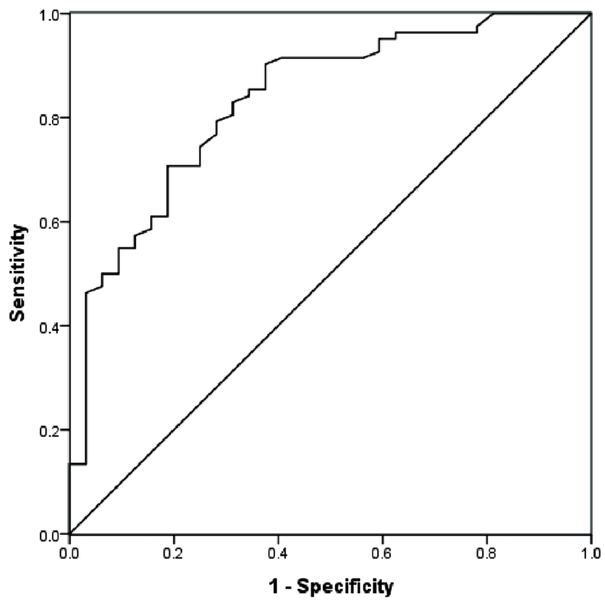

Fig.3 ROC curve for VTQ elastography of TMCs

Table 1 The distribution of VTQ in TMCs

SWV	Nodules (n)	Pathologic finding	
		Malignant	Benign
≥ 2.30 m/s	87	74	13
<2.30 m/s	27	8	19

3 Discussion

The incidence of thyroid cancers has been increasing year by year [12], TMC is a specific subgroup of thyroid carcinoma. It is reported that more than 30 % of patients with TMC [13]. Ultrasound has become the first choice as a convenient and noninvasive tool for the examination of thyroid lesions. Previous studies showed that microcalcification, marked hypoechogenicity, taller-than-wide shape and spiculated margin were the ultrasound specific features of thyroid malignancy[14-16]. However, the accuracy of these features was lower. Real-time tissue elastography (RTE) provides qualitative and semi-quantitative information about the tissue stiffness[17], the applications in clinical medicine are more extensive. Numerous studies have demonstrated that RTE plays a role in differentiating malignant thyroid nodules from benign ones [18-20]. Although there are many advantages of RTE, it has limitations in that elastographic images acquisition and interpretation which are highly dependent on the operator. As the images are produced by applying repetitive compression with the probe to the skin, so it is inevitable there are variabilities within and across observers[21].

VTQ is a newly quantitative method which is used to measure the stiffness of tissue by measuring the velocity of shear waves within a ROI. It exploits a short-duration, high-intensity acoustic pulses to generate localized tissue displacements. At the same time, a shear wave speed is obtained by tracking these displacements of the tissue in the vertical direction. The shear wave velocity represent the local elasticity properties of the tissue in ROI, and is proportional to the square root of the tissue elasticity[22]. The stiffer the tissue is, the higher the SWV[23]. Recent studies have proved that it has high applied value in diagnosis of thyroid carcinoma[24,25], and yet, there have been rare reports on TMCs.

In the present study, the mean SWV of benign and malignant nodules were 2.41 ± 1.36 m/s and 5.02 ± 2.94 m/s, respectively. The SWV in malignant nodules was significantly higher than those of benign ones. It indicated that SWV associated with pathologic components. In papillary carcinoma, the differentiations of tumor cells are variant. Fibrosis and psammoma bodies are often found in mesenchyme, which makes nodular stiffness increased[26], thus the SWV is higher. Compared with papillary carcinoma, the benign lesions such as nodular goiter and adenoma, organizations constituted by follicles, which contain colloids, so the nodular stiffness is relatively reduced, thus, the SWV is lower. In addition, some benign nodules with calcification or fibrosis and some malignant nodules with hemorrhage or cystic change may effected on tissue stiffness. In this study, there were 8 malignant nodules that of SWV<2.30 m/s and 13 benign nodules that of SWV≥ 2.30 m/s. 8 nodules displayed X.XX m/s, this was because the SWV went out of the setting scope 0~9 m/s, so we excluded these cases. AUC was 0.833, which indicated that VTQ was a useful index in the differential diagnosis of TMCs.

Our study had some limitations. First, all selected malignancies were papillary thyroid carcinoma, therefore, our study can't reflect VTQ elastography of other pathologic types of TMC. Second, there are some limitations of VTQ technique. The VTQ-ROI measuring is fixed to the size of 6 mm× 5 mm, which can not be adjusted freely. Hence, the SWV of the nodules diameter 7 mm may be affected because the adjacent normal thyroid tissue is included in ROI. Third, the setting range of SWV is 0~9 m/s, if the stiffness of the tissue beyond the range is displayed as X.XXm/s, which cannot reflect its stiffness. Fourth, the SWV value is higher for the nodules with macrocalcification because during the measurement it is difficult to avoid the macrocalcification. Fifth, the sample size of the present study is relatively small. Further larger studies are needed to confirm the clinical value of VTQ elastography.

In conclusion, we found that ① malignant nodules of thyroid were much stiffer than benign ones, and this could be useful in the differential diagnosis in clinical. ② Value of SWV of TMCs were significantly higher than that of benigns. ③ VTQ could be an effective tool in differenting malignant nodules from benign ones by providing quantitative information of thyroid stiffness. However, papillary carcinomas bigger than 1 cm were not include in this study. Clinical value of VTQ in the diagnosis of other kind of pathological nodules should be studied in future, as well as the intra- and inter-observer reproducibility.

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声触诊组织定量技术鉴别诊断甲状腺微小癌的价值 *

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摘要 目的: 声触诊组织定量技术(VTQ)是一种新的弹性成像方法,能够定量、无创地评价组织硬度信息。本文的研究目的是探讨声触诊组织定量技术在鉴别诊断甲状腺微小癌(TMCs)中的应用价值。**方法:** 应用 VTQ 技术对 110 例共 114 个结节(最大直径≤1 cm)进行检测,获取并分析结节及周边甲状腺组织的横向剪切波速度(SWV)。利用 ROC 曲线对测量结果进行分析,评价 VTQ 技术的诊断价值并确定最佳诊断界值。**结果:** 114 个结节中良性结节 32 个(30 个为结节性甲状腺肿,2 个为腺瘤),恶性结节 82 个(均为乳头状癌)。甲状腺良性结节及周边甲状腺组织的 SWV 平均值分别为(2.30± 0.49) m/s、(2.08± 0.40) m/s,恶性结节及周边甲状腺组织的 SWV 平均值分别为(3.12± 0.97) m/s、(2.06± 0.46) m/s。恶性结节的 SWV 值明显高于良性结节,两者之间差异具有统计学意义(t=5.911,P＜0.0001);恶性结节与其周边甲状腺组织比较有显著差异(P＜0.0001);而良性结节与其周边甲状腺组织无统计学差异(P＞0.05)。ROC 曲线下面积为 0.833,以 2.30 m/s 诊断界值点时,敏感度、特异度分别为 90.2%、62.5%。**结论:** 甲状腺恶性结节的 SWV 值明显高于良性结节。VTQ 技术能够提供组织硬度信息,在鉴别诊断甲状腺微小癌方面具有一定的临床应用价值。

关键词: 声触诊组织定量;弹性成像;甲状腺结节;微小癌

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