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Diagnostic value of elastosonography for thyroid microcarcinoma

Hailing Wang [a], Lihui Zhao [a], Xiaojie Xin [a], Xi Wei [a], Sheng Zhan [a,*], Yigong Li [b], Ming Gao [b]

[a] *Department of Ultrasonographic Diagnosis and Therapy, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China*

[b] *Department of Thyroid and Neck Tumor, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China*

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A B S T R A C T

Objective: To assess the diagnostic value of elastosonography for thyroid microcarcinoma (TMC), particularly with regard to elasticity score (ES) and strain ratio (SR).

Methods: Conventional ultrasound and elastosonography were performed for 487 thyroid micronodules before surgery. We set the histology as the reference standard. The ES and SR values, as well as their diagnostic threshold and efficiency, were compared and analyzed by the receiver-operating characteristic (ROC) curve. Additional comparisons between TMC patients with and without extracapsular extension were also performed.

Results: Statistically significant differences ($P < 0.05$) in both ES and SR values were detected among the TMC and benign groups. The area under the ROC curve of SR was significantly greater than that of ES (0.956 and 0.844, respectively; $P < 0.05$). Using ES $\geqslant$ 3 and SR $\geqslant$ 3.65 as diagnostic threshold values, the diagnostic sensitivity, specificity, and accuracy of ES for differentiating benign and malignant nodules were 79.9%, 72.3%, and 80.5%, respectively, whereas those of SR were 86.6%, 85.3%, and 89.4%, respectively. The maximum diameter, microcalcification status, aspect ratio, bilateral cervical lymph node metastasis, and SR values of nodules with extracapsular extension (A1 subgroup) were greater than those of nodules without extracapsular extension (A2 subgroup).

Conclusions: Elasticity imaging technology not only can help differentiate between benign and malignant thyroid micronodules but also allow SR values to provide accurate and objective information on tissue hardness and to predict TMC extracapsular extension or even bilateral cervical lymph node metastasis.

1. Introduction

Thyroid microcarcinoma (TMC) refers to thyroid tumors with a diameter less than or equal to 10 mm. Most patients do not exhibit clinical manifestations because of the small size of TMC lesions; therefore, the early diagnosis rate among these patients is low. Minuscule nodules of the thyroid generally receive clinical attention only when noted by the patient, typically as an incidental finding during routine physical examination. Therefore, the clinical importance and utility of these nodules in diagnosis is mainly associated with the need to exclude a thyroid cancer diagnosis.

Certain sonographic criteria may increase the suspicion index of malignant nodules; these criteria include hypoechoic texture, ill-defined edges, absence of a halo, presence of punctate microcalcification, increase in central color flow, and anteroposterior-to-transverse diameter greater than 1 [1]. Ultrasound elastosonography is a newly developed dynamic imaging technique that detects tissue elasticity by measuring the degree of distortion under the application of an external force. Malignant lesions are often characterized by their greater stiffness than normal tissue [2]. Many studies have reported the utility of ultrasound to differentiate benign and malignant thyroid nodules [3–6]. Previous research has typically used the elasticity score (ES) and strain ratio (SR) to identify benign and malignant thyroid nodules. However, a few reports have assessed their diagnostic value for TMC [7–9]. Therefore, this study assessed the value of ultrasonic ES and SR for identifying the properties of thyroid micronodules and for evaluating tumor infiltrate surrounding organs and tissues.

Abbreviations: TMC, thyroid microcarcinoma; ES, elasticity score; SR, strain ratio; ROC, receiver-operating characteristic; TNM, tumor-node-metastasis stage; AUC, area under the ROC curve.

* Corresponding author. Tel.: +86 022 23340123.
E-mail address: zs19620112@126.com (S. Zhan).

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2. Materials and methods

2.1. Patients

This study was approved by the ethics committee of Tianjin Medical University Cancer Institute and Hospital. From January 2010 to December 2011, patients with nodules less than or equal to 10 mm determined by both conventional ultrasound and elasticity imaging in our hospital were enrolled in this study. These patients subsequently underwent surgery in conjunction with histopathological confirmation. Inclusion criteria required solid tiny nodules located in both lobes of the thyroid with a diameter of 2–10 mm. Exclusion criteria included patients with abnormal neck anatomy or mass with eggshell calcifications that caused observable posterior acoustic attenuation. In total, 431 consecutive patients with 487 very small thyroid nodules were included.

All patients were divided into a TMC or benign nodule group based on the pathologic results after surgery. In 325 patients (102 male, 223 female; aged 21–76 years old, average age 47.67 ± 10.68 years), 375 nodules were proven to be TMC, including 372 papillary thyroid carcinomas and 3 follicular carcinomas. In 106 patients (34 male, 72 female; aged 25–80-years-old, average age 46.35 ± 10.46 years), 112 nodules were confirmed to be benign lesions, including 101 multinodular goiters and 11 thyroid adenomas.

2.2. Equipment

Both conventional sonography and real-time elastosonography were performed with a Philips iU22 digital ultrasound scanner system (Philips Bothell, Washington, USA) equipped with a linear transducer array with a wide bandwidth of 5–12 MHz. We operated the transducer in the resolution mode (10–12 MHz) for real-time elastosonography. All examinations were performed by a sonologist (H.L.W) with more than 8 years of experience in scanning with B-mode and Doppler, and training in thyroid elastosonography data acquisition. The training was processed as follows. First, the sonographers attended nationwide Q-lab software training courses (Beijing, China) held by Philips Company, passed the final examination, and obtained the training certificate. Second, the sonographers participated in the standardized training on scoring system and operating procedure of ultrasonic elastography held by Philips Company and passed the examination. Third, a senior clinical skills training doctor of Philips Company visited our center and provided practical guidance on the clinical procedures of ultrasonic elastography for the sonographers. Finally, the sonographers practiced ultrasonic elastography test and scoring on approximately 300 thyroid nodules in roughly 5 months.

All patients were examined in supine position with extended neck and small bad under the shoulders for better exposure of the lower thyroid margins. Scans of both thyroid lobes and ismuth were obtained in both transverse and longitudinal planes.

2.3. Imaging method

Conventional ultrasound: Conventional ultrasound images of the thyroid were obtained from patients in supine position and with the neck slightly extended. During our conventional examination, we first obtained B-mode images and then performed color Doppler ultrasound. The three-dimensional size, location, morphology, aspect ratio, boundary, echo characteristics, presence or absence of calcifications, and intratumoral and peripheral blood flow of the thyroid nodules were examined. In addition, the lymph nodes of both the central area and bilateral cervical region were recorded.

Elastosonography: Real-time elastosonography was performed after conventional ultrasound. The probe was applied to the thyroid and vertically moved slightly inferior and superior to obtain the elasticity images of nodules. The region of interest used for obtaining elasticity images was set to be larger than twice the area of nodules, avoiding the trachea and neck blood vessels.

Conventional ultrasound and elasticity images were reconstructed offline by using the same radiofrequency echo data acquired during the ultrasound examination (Philips iU22). Images were displayed in a side-by-side format within the individual frames contained in a cine-loop sequence of approximately 100 frames. Observers made their measurements on a single representative image frame personally chosen as best (designated as "own image") from the cine-loop sequence of approximately 100 frames.

2.4. Imaging analysis

All ultrasound elasticity images were evaluated and recorded by two independent sonologists (S.Z; X.J.X), who both had more than 8 years of experience in scanning with B-mode and Doppler, and training in thyroid elastosonography data acquisition. Each sonologist was blinded to the pathology and each other's results based on elasticity scores [10,11]. The final decision was reached by a consensus. If any inconsistency was found in the assigned scores between the two observers, a third radiologist (X.W) was consulted to arrive at a consensus.

The mean strain index of the lesion and surrounding thyroid tissue was also measured. To the extent possible, the surrounding tissue was selected as a reference at the same depth as the nodule. The average strain of the lesion was expressed as A. Then, a corresponding normal region of surrounding thyroid tissue was selected. The average strain was expressed as B (the sizes of A and B were the same). The resultant strain ratio was calculated according to the following equation: strain ratio = B/A, which is correlated with the stiffness ratio of the lesion [12].

2.5. Pathologic diagnosis

All histology diagnoses were made by a pathologist with 15 years of experience in the pathologic analysis of thyroid cancer from surgical samples, all of which obtained according to previously established criteria [13,14]. Lesions were classified as malignant (TMC) or benign and categorized into the two respective groups. The TMC group was further subcategorized as with extracapsular extension (A1 group, 129 nodules) and without extracapsular extension (A2 group, 246 nodules) based on the histological analysis.

2.6. Statistical analysis

All statistical analyses were performed using the SPSS software package (version 16.0; SPSS, Chicago, IL, USA). All measurement data were reported as mean and standard deviation, and their differences were evaluated with the independent sample t-test. The rank-sum test was used to compare the ES values between TMC and benign groups. The chi-squared test was used to compare other numeration data. The differentiation diagnostic threshold and efficiency of ES and SR for benign or malignant micronodules were analyzed by the receiver-operating characteristic (ROC) curve, with the pathological results as the gold standard. Two-tailed P-values of less than 0.05 were considered to indicate statistically significant difference.