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ORIGINAL ARTICLE

The clinical value of ultrasound elastography in predicting malignant thyroid nodules

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Ultrasound;
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Abstract *Objective:* This study aims to evaluate the clinical value of ultrasound elastography (USE) in providing information on the nature of the thyroid nodules. This was performed using the elastography score and strain ratio in differentiating thyroid benign and malignant nodules and the histopathological examination was used as the diagnostic standard of reference.

Methods: We examined 84 thyroid nodules in 62 patients with ultrasound elastography. Elastography score was assigned based on a four-point scale according to the classification proposed by Itoh et al. with a score of 1 (low stiffness over the entire nodule) to a score of 4 (high stiffness over the entire nodule). Thyroid strain ratio (normal tissue to lesion strain ratio) was calculated. Histopathological results were the standard reference. The area under the curve (AUC) and the best cut-off point were both obtained using receiver-operating characteristic (ROC) curve analysis. The sensitivity, specificity, and accuracy of both techniques were calculated.

Results: Fifty-four of the 84 nodules had scores of 1 and 2, and 50 of these nodules were diagnosed histopathologically as benign. Thirty of the 84 nodules had a score of 3 and 4, and 21 of these nodules were diagnosed histopathologically as malignant. The scores of 1 and 2 with Itoh criteria were significantly seen in benign nodules, whereas, scores of 3 and 4 were significantly seen in malignant nodules ($p < 0.05$) with sensitivity 84%, specificity 84.7%, PPV 70%, NPV 92.6% and accuracy 84.5%. The mean SR for the benign nodules and malignant ones was significantly different (2.92 ± 0.96 vs. 4.53 ± 0.82, $p < 0.001$). With ROC analysis, the best cut-off strain ratio point

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was 3.5 for differentiating benign and malignant nodules with area under the curve (AUC) = 0.87 (0.8–0.95). The sensitivity of the strain ratio was 88%, while the specificity was 86.4%, PPV = 73.3%, NPV = 94.4% and accuracy = 86.9%.

Conclusions: Both the elastographic score and strain ratio are higher in malignant nodules than those in benign ones. Ultrasound elastography can provide quantitative information on thyroid nodule helping in differentiating benign and malignant ones.

1. Introduction

A thyroid nodule is an abnormal growth of cells within the thyroid gland that represents a commonly encountered medical problem in about 4–8% of adults by palpation and about 41% by ultrasound while may be in about 50% of the population at autopsy studies (1–3).

Additionally, the percentage of malignancy generally accounts for 5% of thyroid nodules (4). Nevertheless, it is of clinical importance to diagnose malignant nodules from benign which do not require surgery and the challenge is to evaluate the thyroid nodule and decide which patient should proceed to biopsy (5–8). Ultrasound elastography was developed to non-invasively evaluate the tissue stiffness of the by measuring its deformation degree in response to stress. The core principle is that on application of compression, the softer parts of tissues deform easier than the harder ones and thus tissue stiffness can be determined objectively (7,9–13). Several studies have used ultrasound elastography for thyroid evaluation (14–18).

We propose a prospective study to evaluate the role of US elastography in predicting the malignancy of thyroid nodules and to define an optimal strain ratio cut-off point that correlated with a histopathologic reference standard.

2. Patients and methods

2.1. Patients

A total of 84 nodules in 62 patients were involved in this study. The study was conducted from January 2013 to January 2014 at hospitals of Cairo university The inclusion criterion was the presence of solid nodule in one thyroid lobe while exclusion criteria were (1) cystic component >15% of the nodule volume, (2) Large nodules occupying >75% of thyroid lobe volume because insufficient surrounding normal thyroid tissue to be used as reference and (3) nodules with peripheral calcifications. The study was approved by the Institutional Review Board at our institution. Before enrollment, an informed consent was obtained from each participant.

2.2. Real time ultrasound elastography

The patient lied in a supine position with his neck slightly extended. A considerable amount of ultrasound gel was applied to the patients' neck as a standoff pad using a linear probe (5–12 MHz) (GE Voluson E8). The probe was positioned slightly in contact with the skin. The ultrasound examination started with B-mode imaging to assess nodular size and presence of sufficient surrounding reference tissue, nodules larger than 4 cm diameter were excluded because of absent of sufficient surrounding reference tissue. Cystic component and egg shell calcifications as the posterior enhancement or posterior shadow artifacts interfere with color-coding process. The region of interest (ROI) was centered on the lesion, including sufficient surrounding thyroid tissue. The great cervical vessels were avoided as much as possible to avoid its pulsation compressive effect. The patient was asked to avoid swallowing and hold their breath during the examination to minimize the motion of thyroid gland. Strong initial compression is avoided as it may increase the possibility of false negative results. An appropriate pressure was defined as a pressure which can sustain the number of the scale between 2 and 4 for at least 3 s. Multiple frames were acquired and many elasticity images were generated by comparing two adjacent frames during compression–relaxation cycles. The deformity was represented by color scale over the B-mode image that ranged from red (i.e., softest components with the greatest elastic strain) to blue (i.e., hardest components with no strain). The images were displayed in a split-screen mode with gray-scale images on the left and images of the ultrasound elastogram on the right.

The best-fit 2D sonogram–elastogram image pairs should fulfill the following requirement (19): (1) Surrounding thyroid tissue displays homogenous green color. (2) The thyroid capsule and surrounding connective tissue display red ribbon. (3) The related cervical muscles display homogenous green color.

2.3. Evaluation based on elastography scores

Each nodule was assigned an elastography score based on a four-point scale according to the classification proposed by Itoh et al. (20).

- Score 1: Low stiffness over the entire nodules (entirely green).
- Score 2: Low stiffness over most of the nodule (almost green with blue spots).
- Score 3: High stiffness over most of the nodule (almost blue with green spots).
- Score 4: High stiffness over the entire nodule (entirely blue).

2.4. Evaluation based on strain ratio

The strain ratio (normal tissue to lesion strain ratio) of each nodule was calculated by dividing the strain value (SV) of the normal tissue by that of the nodule (19). The borderline of the lesion was manually traced and the homogenous adjacent thyroid tissue is used as a reference to calculate strain ratio (SR) automatically using a dedicated software connected to the ultrasound machine. Each lesion was assessed