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The value of ultrasound elastography in differentiation of malignancy in thyroid nodules

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ABSTRACT

We aimed to determine the value of ultrasound elastography (US-E) using carotid artery pulsation in differentiation of malignant and benign thyroid nodules. One hundred ten nodules were evaluated by US-E, and stiffness scores were compared to biopsy results. When cutoff for malignancy was determined as score 4, sensitivity, specificity, positive predictive value, and negative predictive value were 100%, 95%, 40%, and 100%, respectively. We suggest fine needle aspiration biopsy to be performed in all score 4 nodules, while biopsy may be unnecessary in score 1 nodules. Benign biopsy result in a score 4 nodule should suggest radiological–pathological disagreement, and repeat biopsy should be recommended.

1. Introduction

Thyroid gland nodules are common, and palpable nodules are found in between 4% and 7% of the adult population [1,2]. Widespread use of ultrasound (US) imaging and development of high-resolution scanners have significantly improved the detection of thyroid nodules [2]. According to US imaging and autopsy results, the incidence of thyroid nodules may increase up to 50% of population [3–5]. The rate of malignancy among thyroid nodules range between 5% and 15% [6,7]. US imaging is a definitive method for detection of thyroid nodules; however, the predictive value of US in differentiation of malignant nodules is limited [8,9]. Currently, the best available method for discrimination of malignant from benign thyroid nodules is fine needle aspiration biopsy (FNAB) [10–12]. Despite its high sensitivity and specificity, FNAB is an invasive procedure and may give nondiagnostic results in 10% to 20% of biopsies [6].

Palpation is clinically used to evaluate the stiffness of a thyroid nodule; however, it is a subjective method, and findings depend on the size and location of the nodule as well as the examiner's skill [13]. Elastography is a recently introduced noninvasive technique which estimates the stiffness of tissues by assessing distortion under compression [14,15]. US elastography has been successfully applied in the breast and more recently in the prostate gland [16]. Previous ex vivo and in vivo studies have documented significant differences in stiffness of normal thyroid tissue and tumors of the thyroid gland [17,18]. However, out-of-plane motion of the nodule during external compression and compression of the thyroid gland due to pulsation of the carotid artery may limit this technique [17]. Carotid pulsation has also been used as a source of compression for elastography of the thyroid gland [19,20].

In this study, we aimed to determine the diagnostic value of US elastography in the differentiation of malignant and benign thyroid nodules using carotid artery pulsation as the source of compression.

2. Materials and methods

2.1. Patients

The study protocol was approved by the institutional ethical committee, and informed consent was obtained from the patients. The patients who were diagnosed with a thyroid nodule and had an indication for an FNAB were included into the study. The patients were selected prospectively and consecutively. The patients who did not have a final histopathological or cytological diagnosis were excluded from the study.

2.2. Lesion evaluation

US elastography examinations were performed using a 5–13-MHz linear transducer (Acuson Antares, Siemens, Erlangen, Germany). All examinations were performed by the first radiologist. Baseline US

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data were collected from these studies, and related strain images were recorded in the US system as static images and also as short videos. Two radiologists evaluated the images separately and blinded. The first radiologist scored the lesions during real-time examination. Dynamic US elastographic evaluation by the first radiologist took approximately 5–10 min. The second radiologist scored the lesions on the recorded video clips separately from the first radiologist.

Elastography was performed by freehand technique, and carotid pulsation was used to obtain elastography images. A rectangular region of interest was positioned to examine the targeted nodule. Images were displayed in a split screen mode where grayscale images were positioned on the right and the translucent color scale elastography images were shown superimposed on B-mode images. The color scale ranged from red showing the stiffness of the tissue to blue showing the softness. Elastography images were classified according to the scores defined by Asteria et al. [20]. This elasticity scoring originated from the elastography by Itoh et al. [21] which classifies the elastography scores on a scale of 1 to 4. Score 1 indicated elasticity in the whole nodule, score 2 elasticity in a large part of the nodule, score 3 elasticity in a small part of the nodule, and score 4 no elasticity in the nodule [20].

2.3. Histopathological diagnosis

After performing US elastography, US-guided FNAB was performed. The patient's neck was extended by placing a pillow under the shoulder [22]. The skin was sterilized using iodine solution followed by an alcohol swipe. Local anesthesia was not routinely used. Aspiration was performed manually using a 22-gauge needle attached to a 10-cc syringe. The needle was advanced into the nodule under US guidance. Then, the needle was moved to and fro inside the nodule by applying suction and removed from the nodule. The material was handled by the pathologist present on site for preliminary cytological analysis. The procedure was repeated until sufficient material for diagnosis was obtained or up to five needle punctures.

Cytological results were divided into three groups for statistical evaluation: benign, malignant, and insufficient material. Patients with insufficient cytological results underwent repeat biopsy in 3 months after the first procedure. The patients who had an insufficient result for the second time were excluded from the study. The patients who were diagnosed with FNAB as malignant, suspicious, or follicular adenoma underwent thyroidectomy. The histopathological findings of these patients were accepted as gold standard. Patients who were not operated and with FNAB results suspicious for malignancy or insufficient material were excluded from the study. All nodules that were diagnosed benign with FNAB were accepted as benign.

2.4. Statistical analysis

χ^2 test was performed in order to compare the strain scores between benign and malignant nodules. In order to determine the diagnostic accuracy of US elastography for the first and second radiologists compared to histopathological or cytological results, cross-table tests were performed. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Kappa coefficient was used to test the interobserver concordance.

3. Results

A total of 110 thyroid nodules of 99 patients were included in the study. Five nodules from five patients were excluded from the study because of insufficient material as the final cytological result. Two nodules from one patient were also excluded because the patient was lost after a diagnosis of suspicious findings for malignancy with FNAB. A total of 103 nodules from 93 patients (24 men, 69 women) were analyzed in the study. The mean age of the patients was 52.8± 12.5 years (ranging between 24 and 84 years). FNAB was performed on two nodules in eight patients, three nodules in one patient, and solitary nodules in the remaining patients. The longest dimension of the nodules ranged between 4.2 mm and 45 mm (mean 19.88± 9.4 mm). Cytological results were benign in 93 (90.3%) and malignant in 10 (9.7%) nodules. Histopathological examination revealed 6 papillary carcinomas, 3 follicular carcinomas, and 1 anaplastic carcinoma among the 10 malignant nodules.

US elasticity scores and histopathological or cytological results are summarized in Table 1. All lesions scored 1 by the first radiologist and the second radiologist were diagnosed to be benign by cytology. All four score 4 lesions by the first radiologist, while three of score 4 lesions of the second radiologist, were malignant.

Diagnostic accuracy of US elastography in differentiation of malignant and benign nodules was tested at different cutoff levels according to elastographic scores (Table 2). According to the first radiologist's classification, when nodules with an elasticity score of 1, 2, and 3 were accepted benign and score 4 was accepted malignant, US elastography showed a sensitivity, specificity, PPV, and NPV of 100%, 93%, 40%, and 100%, respectively.

The distribution of malignant nodules according to their elastography scores was summarized in Table 3. Three papillary carcinomas were given a score of 4 by both radiologists. One nodule with papillary carcinoma was score 2 and another papillary carcinoma was score 3 in the first and second radiologists' classifications. One papillary carcinoma was given a score of 4 by the first radiologist and 3 by the second radiologist. One nodule with anaplastic carcinoma had a score of 2 by the first and second radiologists, separately. One nodule with follicular carcinoma was given a score of 3 by the first radiologist and a score of 2 by the second radiologist. The remaining two nodules with follicular carcinoma had a score of 3 by the first and second radiologists, separately.

Statistically significant correlation was found among the first radiologist's assessment and the second radiologist's assessment ($P<.001$) (Table 4). Moderate concordance was present between the first and the second radiologist's assessments (kappa: 0.51).

4. Discussion

Advances in imaging techniques have increased the number of documented thyroid nodules considerably; however, characterization of the lesion accurately is not always possible [23,24]. In determination of the malignant lesion, presence of microcalcifications, irregular margins, and intranodular (type III) vascularization are reported to have a high specificity but low sensitivity [25,26]. Despite its advantages, US-guided FNAB is an invasive procedure which may cause sampling errors, especially in hemorrhagic lesions, multinodular goiter, and extreme nodule sizes (smaller than 1 cm or larger than 4 cm). In cytological examination, diagnosis depends predominantly on nuclear features, which are usually unreliable predictors of the malignant potential of endocrine cells [27]. False-negative results

Table 1
US elasticity scores and histopathological and/or cytological results of the nodules

	Score 1	Score 2	Score 3	Score 4	Total
First radiologist					
Benign	27	44	22	0	93
Malignant	0	1	5	4	10
Total	27	45	27	4	103
Second radiologist					
Benign	18	42	30	3	93
Malignant	0	2	6	2	10
Total	18	44	36	5	103