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Application of Sonoelastography in Differential Diagnosis of Benign and Malignant Thyroid Nodules

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ABSTRACT

Background: Sonoelastography is a new ultrasound method which could be helpful to determine which thyroid nodule is malignant. We designed this study to evaluate the accuracy of sonoelastography in differentiating of benign and malignant thyroid nodules in Iranian patients.

Methods: Forty thyroid nodules in forty consecutive patients who had been referred for sonography-guided fine-needle aspiration biopsy were evaluated. Gray scale ultrasound and elastosonography by real-time, freehand technique applied for all patients. Elastography findings were classified into four groups. Nodules which were classified as patterns 1 or 2 in elastogram evaluation were classified as benign and probably malignant if elastogram scans were patterns 3 and 4 of elastogram scan.

Results: Mean age ± standard deviation (SD) was 42.2 ± 12.6 years, and mean ± SD thyroid-stimulating hormone level was 1.4 ± 1.9 IU/ml. Thirty-five cases (87.5%) were female and 5 (12.5%) were male. Histological examination indicated 27 (67.5%) benign and 13 (32.5%) malignant nodules. The most elastogram score was 2 (50%) followed by score 3. The cut-off point of 2 considered as the best value to differentiate benign and malignant thyroid nodules with sensitivity and specificity of 61% and 78% (area under the curve = 0.76, 95% confidence interval: 0.6–0.92, $P = 0.007$).

Conclusions: Sonoelastography could help to differentiate benign and malignant thyroid nodules. As our sample size was limited, larger studies are recommended.

Keywords: Iran, nodule, sonoelastography, thyroid

INTRODUCTION

Thyroid nodules are among prevalent endocrine disorders affecting 4–7% of the population in iodine rich areas and more in iodine deficient areas.[1]

The main concerns about thyroid nodules are malignancy and hyperfunction.[2]

Fine-needle aspiration (FNA) is widely used to differentiate malignant and benign thyroid nodules with sensitivity

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and specificity ranging from 60% to 98% and 54% to 90%, respectively.[3,4] Problems associated with FNA are possibility of sampling and analytic errors and potential complications.[5]

Nowadays, ultrasound is widely used for evaluating thyroid nodules. Ultrasound is a useful method for evaluating the size, consistency, microcalcifications, irregular margins, associated lymphadenopathy, and intranodular vascularity of thyroid nodules.[2]

Malignant nodules are specified by irregular margins, hypoechogenicity, blurred or spiculated margins, spot microcalcification, and intranodular vascularity but the accuracy of these signs to differentiate benign and malignant nodules are not very high.[6,7] Hence, there is a need for an accurate method to decide which nodule is more suspicious should be aspirated and evaluated more.

Sonoelastography is a new ultrasound method which reflects tissue deformation in response to tissue compression.[8] The principle of elastography is less compressibility of hard tissues than soft tissues.[8] Information regarding tissue compressibility is shown in color. It is used for different tissues.[9]

In literature, there are reports that evaluate the accuracy of sonoelastography for differentiation of benign and malignant thyroid nodules,[5,8,10,11] but up to now, there is no report from Iranian population. We designed this study to evaluate the accuracy of sonoelastography in differentiating of benign and malignant thyroid nodules in Iranian patients.

METHODS

In this study, which conducted in the Imam Hospital (Affiliated Hospital of Tehran University of Medical Sciences) between February 2012 and August 2013, forty thyroid nodules in forty consecutive patients who had been referred for sonography-guided FNA biopsy were evaluated (project number: 92-01-85-20775).

All patients were asked to fill informed consent forms before study entrance.

Procedures and variables assessment

We performed gray scale ultrasound and elastosonography by real-time, freehand technique using MYLAB 70 XVG (Esaote Company, Jenoa, Italy) with a 5–13-MHz transducer in supine position with hyperextend neck.

A light compression was applied on the thyroid nodule to see elastogram scan. A rectangular region of interest of sufficient dimension was selected, which included entire nodule and enough surrounding tissue. We used a two panel image frame with gray scale on the left and elastogram image on the right. After a consistent level of compression is achieved, the images were recorded. We used four scale elastography scoring system.

Elastography findings were classified into four groups [Figure 1].

Patterns 1 or 2 of elastogram scan were considered as benign and patterns 3 and 4 considered as malignant [Figure 2].

The histopathological results from sonographically-guided FNA were used as a reference standard. The samples studied in pathology ward of the Imam Khomeini Hospital by an expert pathologist.

A structured questionnaire was used to collect information regarding age, sex, history of prior radiation, surgery and family history, size and location of nodule, gray scale, and elsatogram findings along with pathology result.

Statistical analysis

SPSS version 18 was used for data analysis (SPSS Inc., Chicago, IL, USA). Quantitative data are presented in mean ± standard deviation and qualitative as frequencies. In comparison with pathologic findings, sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Receiver operating characteristic (ROC) curve was used to determine optimal cut-off values to differentiate benign and malignant nodules.

$P < 0.05$ was considered statistically significant.

RESULTS

In this study, forty nodules in forty patients with mean age of 42.2 ± 12.6 years and mean thyroid-stimulating hormone level of 1.4 ± 1.9 IU/ml evaluated. All cases were euthyroid at the time of investigation. Thirty-five cases (87.5%) were female and 5 (12.5%) were male. Two patients (5%) had a previous history of radiation and 6 (15%) has a family history of thyroid nodules. Rapid growth of nodule size reported by 8 (20%) of patients while pain reported by 2 (10%).

Histological examination indicated 27 (67.5%) benign and 13 (32.5%) malignant nodules [Table 2].

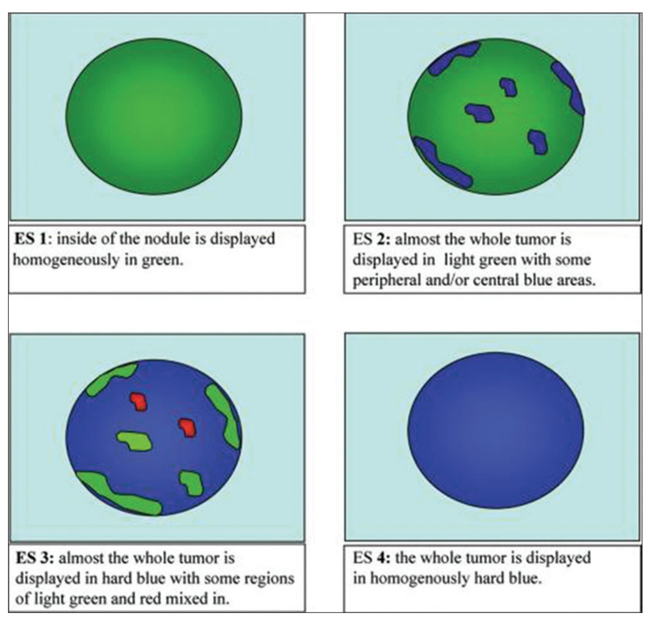

Figure 1: Classification of elastography patterns

Characteristics of nodules are summarized in Table 1.

The most benign pathology of nodules was benign follicular nodule, and the most malignant pathologies were papillary carcinoma and medullary carcinoma.

Among radiologic findings, lack of halo sign had higher sensitivity and specificity [Table 3].

The most elastogram score was 2 followed by score 3 [Table 4].

Using the ROC analysis [Figure 3], the best cut-off point obtained using elastogram scans to differentiate benign and malignant thyroid nodules were 2 with sensitivity and specificity of 61% and 78% (area under the curve = 0.76, 95% confidence interval: 0.6–0.92, P = 0.007).

Table 1: Characteristics of all nodules

Variables	*n* (%)
Lobe	
Right	22 (55)
Left	15 (37.5)
Ismuth	3 (7.5)
Echogenicity	
Hypoecho	16 (40)
Hyperecho	10 (25)
Isoecho	14 (35)
Calcification	
Present	16 (40)
Absent	24 (60)
Comet tail	
Present	4 (10)
Absent	36 (30)
Halo sign	
Present	17 (42.5)
Absent	23 (57.5)
Margin	
Well defined	27 (67.5)
Speculated	13 (32.5)

Table 2: Pathology of nodules

Type of nodules	*n* (%)
Benign nodules	
Benign follicular nodule	24 (60)
Adenomatoid nodule	3 (7)
Malignant nodules	
Papillary carcinoma	5 (12.5)
Medullary carcinoma	5 (12.5)
Lymphoma	3 (7)

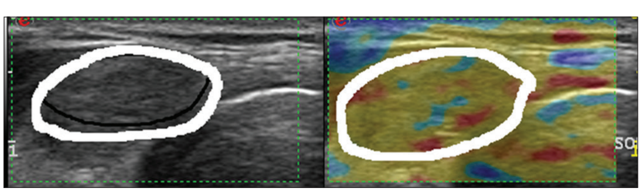

Figure 2: Gray scale and sonoelastography of the nodule in a women. The elastography score is 2

DISCUSSION

Result of the current study showed that sonoelastography to differentiate benign and malignant thyroid nodules had moderate sensitivity and specificity. The best point to differentiate benign and malignant thyroid nodules was 2 with sensitivity and specificity of 61% and 78%. Our finding is compatible with some previous studies. Asteria *et al*. evaluated 86 nodules in 66 patients. They reported the cut-off point between 2 and 3 the best cut-off point to differentiate benign and malignant thyroid nodules with sensitivity and specificity as 94% and 81%.[5] In another study, Kagoya *et al*. assessed 47 nodules in 44 patients by means of sonoelastography and found that patterns 3 and 4 of elastogram scan could be considered as prognostic values of malignancy with sensitivity and specificity of 73% and 64%.[12] In this study, we used four scale scoring system while in some previous studies authors applied 5 scale scoring system. Rago *et al*. applied 5 scale scoring system and investigated that elasticity scores 4–5 were highly predictive of malignancy with sensitivity and specificity of 97% and 100%.[13]

Gietka-Czernel *et al*. used 5 scale scoring to differentiate benign and malignant thyroid nodules in 52 patients. ES scores of 4 or 5 were highly predictive of malignancy with sensitivity and specificity of 86% and 97%.[14]

We also found that lack of halo sign had higher sensitivity and specificity than calcification and hypoechogenicity. In the study conducted by Friedrich-Rust *et al*., calcification and hypoechogenicity had a similar sensitivity (43%) while absent halo sign had higher sensitivity (57%).[15]

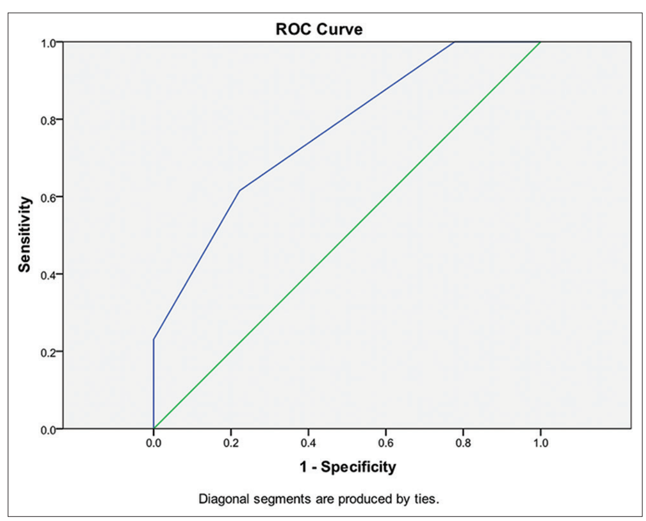

Figure 3: ROC curve of scores

Table 3: Diagnostic accuracy of different signs

Sonographic findings	Benign (%)	Malignant (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Calcification present	12 (44.4)	4 (30.7)	30.7	55.5	68.9	78.9
Lack of halo sign	8 (29.6)	9 (69.2)	69.2	70.3	52.9	82.6
Hypoechogenicity	9 (33.3)	7 (53.8)	52.3	66	43.7	75

Table 4: Number of patients with elastography score and pathology findings

Elasto score	Malignant nodules (%)	Benign nodules (%)
1	0	6 (22.2)
2	5 (38.4)	15 (55.5)
3	5 (38.4)	6 (22.3)
4	3 (23)	0

Prevalence of thyroid nodules reported in 4–7% of the general population while most of these nodules are benign.[1] Near 5% of thyroid nodules are malignant. Accurate differentiation of malignant and benign thyroid nodules is needed.[5]

Although FNA is widely used to differentiate benign and malignant nodules, it is prone to sampling errors, particularly in nodules <1 cm or >4 cm, hemorrhagic lesions, and in multinodular goiter.

On the other hand, near 30% of FNA samples from thyroid nodules are not conclusive. Furthermore, in some samples with adequate cells, differentiating benign and malignant is impossible.[13]

Microcalcifications, hypoechogenicity, irregular margins or lack of "halo" sign, and solid components are characteristics of malignant nodules in conventional ultrasound, but sensitivity and specificity of these characteristics are low (sensitivity 17–87% and specificity 40–95%).[16,17]

Elastography is a new sonographic method which evaluates the degree of distortion of a tissue by means of outside power.[13] Softer part of the tissue moves easier than the harder part. In thyroid, stiffness of malignant nodules is 10-fold greater than the normal tissue.[5] In this study, 5 malignant nodules had a score of 3 and 3 had a score of 4 while 6 benign nodules had a score of 1 and 15 had a score of 2.

This study had some limitations. First, it conducted in a tertiary hospital and number of cases was limited. Multi centric studies with larger sample sizes are recommended.

CONCLUSIONS

Sonoelastography could help to differentiate benign and malignant thyroid nodules, although its diagnostic performance is not ideal. As our sample size was limited, larger studies are recommended.

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Conflicts of interest

There are no conflicts of interest.

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