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The Value of Strain Elastography in the Distinction Between Benign and Malignant Thyroid Nodules in Patients with Hashimoto Thyroiditis

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Abstract

BACKGROUND/AIMS: To assess the value of strain elastography (SE) in the distinction between benign and malignant thyroid nodules in patients with Hashimoto's thyroiditis (HT).

MATERIALS AND METHODS: The study cohort consisted of 74 thyroid nodules in 69 patients with HT. Fine needle aspiration biopsy (FNAB) or surgical excision were used as the reference standards. Gray-scale properties (internal structure, echogenity, presence or absence of hypoechoic halo sign, microcalcifications, "taller than wide" sign), vascularity scores, elasticity scores and strain ratios of all nodules were noted and compared between benign and malignant nodules. Categorical variables were compared using the Pearson chi-square test. Correlation analyses were performed using the Spearman correlation test. The diagnostic performance of the SE was evaluated using receiver operator characteristic (ROC) curves.

RESULTS: Of the included 74 nodules, 67 (90.5%) and 7 nodules (9.5%) were benign and malignant, respectively. There were significant differences in echogenicity (p=0.017), peripheral halo (p=0.003), microcalcifications (p<0.001), and margin and shape (p=0.009) characteristics between benign and malignant nodules. There was a significant association between elasticity scores and histopathological diagnosis of the nodules (p<0.001). A cut-off point of 6.16 for SR value had sensitivity, specificity, PPV and NPV as 71.4%, 100%, 100% and 97.1%, respectively. Area under the ROC curve for the diagnostic performance of SR values in the differentiation of benign and malignant nodules was 0.797 (p=0.01)

CONCLUSION: Our study revealed that SE is an accurate diagnostic tool to characterize thyroid nodules in patients with HT and this may be useful to avoiding unnecessary invasive procedures.

Keywords: Thyroid nodules, Hashimoto thyroiditis, strain elastography

INTRODUCTION

The thyroid nodule is a discrete lesion that is distinguishable from the surrounding parenchyma in the gland.[1] The prevalence of thyroid nodules varies among regions, and people who live in iodine-deficient areas are more prevalent in this glandular abnormality. The widespread usage of ultrasound led a sizable increase in the detection of thyroid nodules. However, only a few percent (<5%) of these lesions were malignant.[2,3]

Hashimoto's thyroiditis (HT) is an autoimmune disease characterized by lymphocytic infiltration of the thyroid gland and it is the most common cause of hypothyroidism.[4-6] HT most commonly occurs in women, and

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it demonstrates the peak incidence in the fourth and fifth decades of the life.[7] Clinically, it is presented as diffuse enlargement of the gland with elevated levels of thyroid autoantibodies.[8,9] Ultrasound may aid in the diagnosis of HT, and heterogeneous hypoechogenic parenchyma with increased vascularity in a diffuse enlarged gland is typical for the sonographic appearance of HT.[10,11] However, despite this well -recognized appearance characterization of existing thyroid nodules on gray-scale sonographic evaluation in patients with HT may be challenging and difficult due to these parenchymal alterations. Furthermore, it has been reported that patients with HT have a higher risk of developing thyroid cancer.[12,13] One study reported that the hazard ratio for developing thyroid cancer in HT patients was 11.8 in comparison to the control group.[13] Therefore, in addition to gray-scale evaluation, utilization of relatively newer ultrasound imaging techniques may contribute to more accurate differentiation of benign and malignant thyroid nodules in patients with HT.

Strain elastography (SE) is an imaging technique that estimates the stiffness of the target tissue in response to applied external forces and provides qualitative and semiquantitative assessments.[14,15] Previous studies have reported that SE may improve the diagnostic accuracy of conventional gray-scale ultrasound evaluation in patients with thyroid nodules.[2,3,16-19] However, limited numbers of studies that evaluate the diagnostic performance of SE in thyroid nodules with concurrent HT patients exist in the current literature.[9,20,21] In this regard, this study aimed to assess the value of SE in the distinction between benign and malignant thyroid nodules in patients with HT.

MATERIALS AND METHODS

This prospective study was approved by the Gazi University Institutional Review Board (approval number: 214, date: 05.23.2012) and written informed consent was provided by the patients. Between January and September 2012, all consecutive patients with HT and coexisting thyroid nodules were included in this study. The diagnosis of HT was made based on the symptoms of the patients and clinical and laboratory findings. The patients lacking histopathological assessment, and the patients with cystic or dense-calcified nodules were excluded. Finally, the study cohort consisted of 74 thyroid nodules in 69 patients with HT. Fine needle aspiration biopsy (FNAB) or surgical excision were used as the reference standards. The age and gender of the included patients were noted.

All patients were examined in the supine position using an ultrasound system (Hitachi EUB 7,500) with a 13-8 MHz linear transducer. The tip of the transducer was covered with a generous amount of ultrasound gel. The thyroid glands of the patients were examined in two orthogonal planes. After gray-scale ultrasound assessment, SE was performed for the detected nodules. During elastographic evaluations, the probe was held in the long axis of the thyroid gland to avoid potential mistracking artifacts that may be caused by lateral displacements originating from pulsations of the adjacent carotid artery. To obtain appropriate elastograms, repetitive external forces were applied perpendicular to the gland. The appropriateness of the elastograms was evaluated due to indicators located at the right lower corner of the screen, and the scores that evaluate the quality of manuel compression equal or higher than 3 was determined as appropriate. For all thyroid nodules at least 3 appropriate elastography images were obtained. Gray-scale ultrasound and elastography images of evaluations were recorded on a digital system, and two experienced radiologists assessed all images in a separate reading session with consensus. The patients were categorized into two subgroups (normal or typical for HT) according to parenchymal patterns of the HT disease. The patients whose thyroid gland did not demonstrate any parenchymal abnormality were considered a normal parenchymal pattern. The largest size of the nodules was measured. The composition, echogenicity, shape, and margin characteristics of the nodules and the presence of a peripheral halo and internal microcalcifications were noted. On color Doppler ultrasound vascularity of the nodules was assessed. A vascularity score was given to all nodules based on the vascularity characteristics of the nodules. Score 1 was given if the nodule did not demonstrate peripheral or internal vascularization. Score 2 was given if the nodule demonstrated only peripheral vascularity (no internal vascularity). Score 3 was given if the nodule demonstrated both minimal peripheral and internal vascularity. Score 4 was given if the nodule demonstrated both extensive peripheral and internal vascularity.

Elasticity scores were given for the thyroid parenchymas of the patients according to color codes on the elastograms. Score 1 was given if the parenchyma demonstrated elasticity (green) in all areas. Score 2 was given if the parenchyma predominantly demonstrated elasticity and includes a few areas with low elasticity (blue). Score 3 was given if the parenchyma demonstrated a mixture of green and blue colors. Score 4 was given if the parenchyma demonstrated only low elasticity. Similarly, elasticity scores were given for the thyroid nodules according to the color-coded elasticity characteristics of the nodules on the elastograms. Furthermore, a region of interest (ROI) that covers the entire nodule was placed in all thyroid nodules on elastograms. A second ROI was drawn on the same elastogram in the thyroid parenchyma adjacent to the nodule. The strain ratio (SR) was calculated automatically for each nodule by dividing the elasticity of the parenchyma to the elasticity of the thyroid nodule (Figure 1, 2).

Statistical Analysis

All statistical analyses were performed using SPSS for Windows version 15.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics of the data consisted of mean ± standard deviation or median (minimum-maximum) values. Mann-Whitney U test was used to compare quantitative variables. Categorical variables were compared using the pearson chi-square test. Correlation analyses were performed using the Spearman correlation test. The diagnostic performance of the SE was evaluated using receiver operator characteristic (ROC) curves. A p-value less than 0.05 was used to determine the statistical significance.

Results

The study cohort consisted of 64 (92.8%) women, and 5 (7.2%) men. The mean age of the patients was 49 years (range: 18 to 74 years). The mean size of the nodules was 16.38±8.38 mm (range: 7 to 60 mm). The histopathological diagnosis of the nodules was obtained using FNAB and post-surgical specimen assessment in 60 (81.1%) and 14 (18.9%) nodules, respectively. Of these 74 nodules, 67 (90.5%) nodules were diagnosed as benign, and 7 (9.5%) nodules were diagnosed as malignant. There were no significant differences in the age (p=0.59) and gender (p=0.375) characteristics between the patients with benign and malignant nodules. There were no significant differences in the mean nodule sizes between the benign (15.46 mm) and malignant (25.14 mm) nodules (p=0.168).

The surrounding parenchymal pattern of the nodules were assessed as normal for 7 (9.5%) nodules and typical for Hashimoto thyroiditis

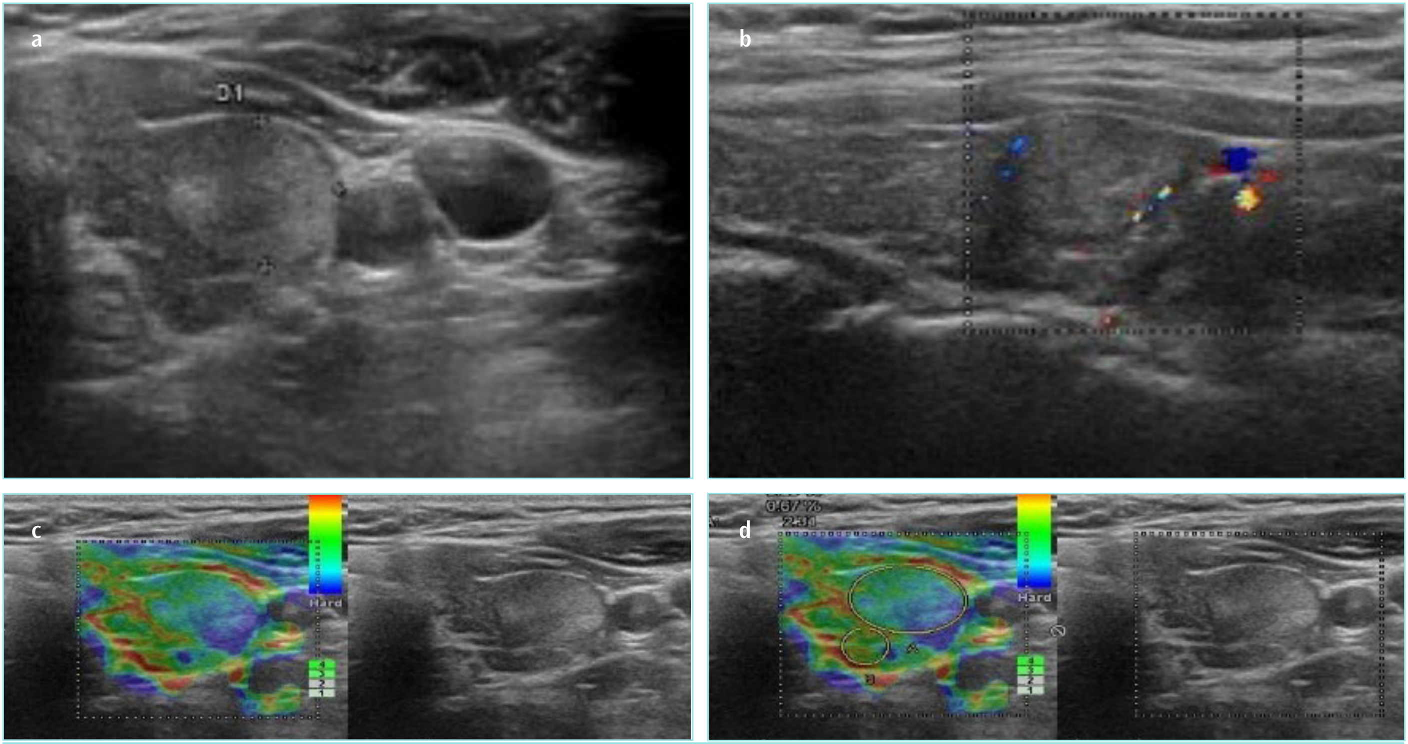

Figure 1. Gray-scale ultrasound (a), color Doppler ultrasound (b), and strain elastography (c, d) images of a 18 year old female patient with Hashimoto thyroiditis demonstrates a round shaped solid nodule with well-defined margin characteristics. The assigned elasticity score was 1, and Strain ratio was calculated as 0.61. Fine needle aspiration biopsy revealed that the nodule was adenomatous nodule.

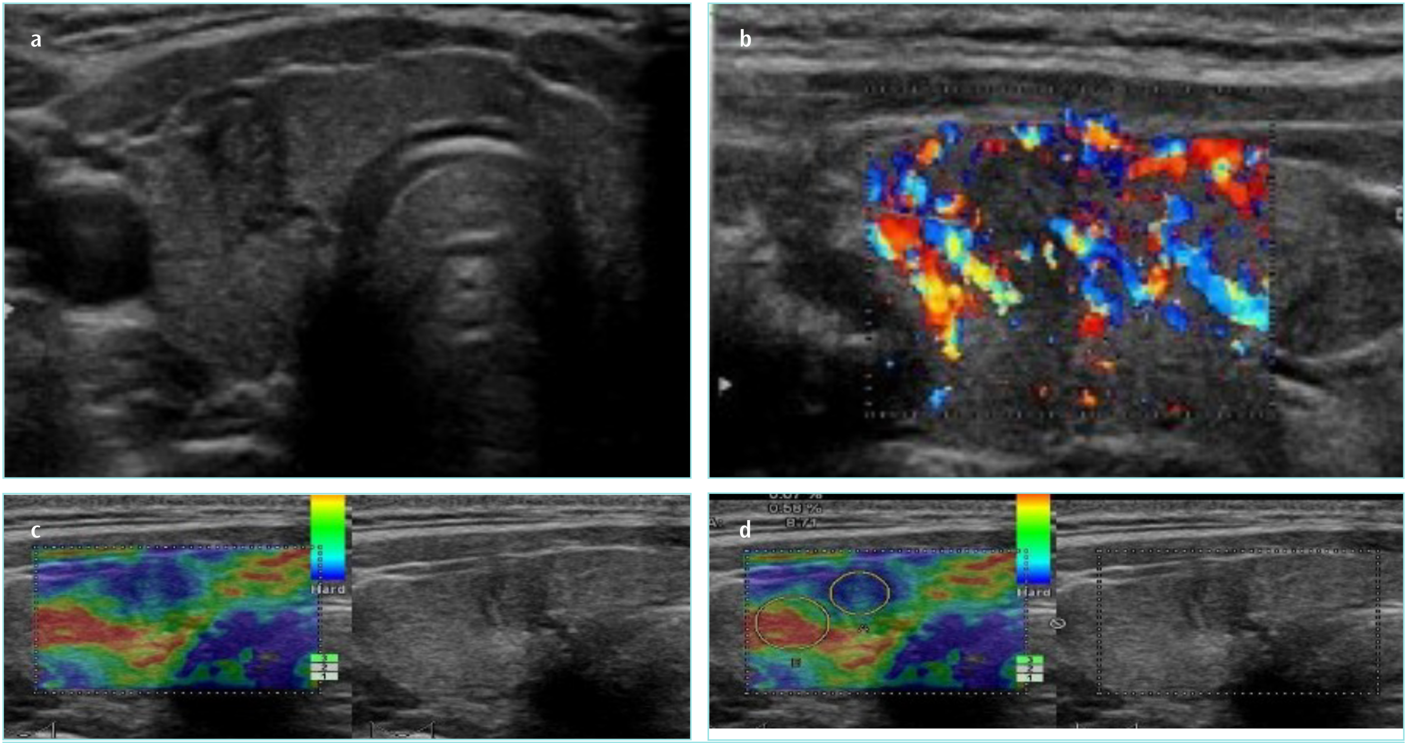

Figure 2. Gray-scale ultrasound (a), color Doppler ultrasound (b), and strain elastography (c, d) images of a 28 year old female patient with Hashimoto thyroiditis demonstrates a hypoechogenic solid nodule with irregular margin characteristics. The assigned elasticity score was 4, and Strain ratio was calculated as 10.5. The histopathological diagnosis was papillary carcinoma.

for 67 (90.5%) nodules. The composition of the nodules were solid and semisolid in 53 (71.6%) and 21 (28.4%) patients, respectively. The echogenicity of the nodules was hypoechogenic in 43 (58.1%) nodules. The margin characteristics were well-defined in 54 (73%) nodules. There were microcalcifications in 10 (13.5%) nodules. There were no statistical significant differences in the sonographic characteristics of the nodules between the parenchymal pattern subgroups (normal and typical for HT) of the patients (p>0.05). There were significant differences in echogenicity (p=0.017), peripheral halo (p=0.003), microcalcifications (p<0.001), and margin and shape (p=0.009) characteristics between benign and malignant nodules. Table 1 represents the distribution of the sonographic characteristics of the benign and malignant nodules. There was a significant difference in vascularity scores between benign and malignant nodules (p<0.001). Table 2 represents the distribution of vascularity characteristics of the benign and malignant nodules.

There was no significant difference in the elasticity scores of the nodules between the parenchymal pattern subgroups (p>0.05). There was a weak correlation between the elasticity scores of the nodules and parenchymas (Spearman's rho: 0.308). Table 3 represents the distribution of elasticity scores for the nodules and parenchymas.

Among the nodules within typical for HT surrounding the parenchyma, 91% (61/67) of the nodules were benign, whereas 9% (6/67) of the nodules were malignant. Among the nodules within the normal surrounding parenchyma, 86% (6/7) of the nodules were benign, whereas 14% (1/7) of the nodules were malignant. There were no significant differences in benign and malignant nodules between the parenchymal pattern subgroups (p=0.517).

On elasticity score assessment, 35 of 67 (52.2%) benign nodules showed score 2 characteristics, whereas 5 of 7 (71.4%) malignant nodules showed score 4 characteristics. There was a significant association between elasticity scores and histopathological diagnosis of the nodules (p<0.001). Table 4 represents the distribution of elasticity scores for the benign and malignant nodules. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of elasticity score 4 in the differentiation of malignant thyroid nodules were 71.4%, 95.5%, 62.5%, and 97% respectively. The area under the ROC curve (AUROC) for the diagnostic performance of the elasticity score in the differentiation of benign and malignant nodules was 0.902 (p<0.001) (Figure 3). The means of SR values for benign and malignant nodules were 1.44±0.86 and 7.46±4.82, respectively. There was a significant difference between SR values of benign and malignant nodules (p=0.01). AUROC for the diagnostic performance of SR values in the differentiation of benign and malignant nodules was 0.797 (p=0.01). If a cut-off point was determined as 6.16 for SR value, the sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 71.4%, 100%, 100% 97.1%, and 97.3%, respectively.

DISCUSSION

The combination of superficial location of the thyroid gland and wide usage of sonography in a clinical setting contributes to detection of a large number of thyroid nodules in daily practice. Although malignant transformation of thyroid nodules is rare, it constitutes a diagnostic challenge. This challenge may become more complicated when thyroid nodules occur in patients with HT. The current study revealed that qualitative and semiquantitative assessments depending on SE can

Table 1. The distribution of sonographic characteristics of the benign and malignant nodules

Characteristics of the nodules		% (number of nodules/total)			p
		Benign	Malignant	Total	
Composition of nodule	Solid	68.7 (46/67)	100 (7/7)	71.6 (53/74)	0.181
	Semisolid	31.3 (21/67)	0 (0/7)	28.4 (21/74)	
Echogenicity	Hyperechogenic	19.4 (13/67)	0 (0/7)	17.6 (13/74)	0.017
	Isoechogenic	26.9 (18/67)	0 (0/7)	24.3 (18/74)	
	Hypoechogenic	53.7 (36/67)	100 (7/7)	58.1 (43/74)	
Peripheral halo	Present	59.7 (40/67)	0 (0/7)	54.1 (46/74)	0.003
	Absent	40.3 (27/67)	100 (7/7)	45.9 (34/74)	
Microcalcifications	Present	7.5 (5/67)	71.4 (5/7)	13.5 (10/74)	<0.001
	Absent	92.5 (62/67)	28.6 (2/7)	86.5 (64/74)	
The margin characteristics	Well-defined	79.1 (53/67)	14.3 (1/7)	73 (54/74)	0.001
	Irregular	20.9 (14/67)	85.7 (6/7)	27 (20/74)	
"Taller than wide" sign	Yes	4.5 (3/67)	42.9 (3/7)	8.1 (6/74)	0.009
	No	95.5 (64/67)	57.1 (4/7)	91.9 (68/74)	

Table 2. The distribution of vascularity characteristics of the benign and malignant nodules

Vascularity scores	Benign	Malignant	Total
1	10 (14.9%)	2 (28.6%)	12 (16.2%)
2	25 (37.3%)	0 (0%)	25 (33.8%)
3	29 (43.3%)	0 (0%)	29 (39.2%)
4	3 (4.5%)	5 (71.4%)	8 (10.8%)
Total	67 (100%)	7 (100%)	74 (100%)

successfully differentiate benign and malignant nodules in patients with HT and this may be helpful in reduce unnecessary invasive procedures for thyroid nodules in HT patients.

Anderson et al.[11] analyzed the sonographic appearances of nodular HT patients, and the authors concluded that the sonographic and vascularity features of nodular HT show wide variations. The authors found that the nodules in patients with HT were most commonly hypoechogenic (47%), and showed well-defined (60%) margin characteristics. In their study, 20% of the nodules had calcifications. The current study revealed that 58.1% of the nodules were hypoechogenic; 73% of the nodules had well-defined margin characteristics, and microcalcifications were present in 13.5% of the nodules. These findings may be considered in accordance with the aforementioned study. Conversely, in that study, Anderson et al.[11] found that 45% (29/64) of cases occurred within normal thyroid parenchymal features, whereas 55% (35/64) of cases occurred within the parenchyma that has typical sonographic features of HT. In the current study, only 10% (7/69) patients demonstrated normal thyroid parenchymal features on sonography. Moreover, Anderson et al.[11] also found that 35% of the nodules were hypervascular, while 29% of the nodules were avascular. In our study, we found that 16.2% (12/74) and 50% (37/74, both score 3 and 4) of the nodules were avascular and hypervascular, respectively. The differences in sonographic and vascularity features of the nodules between the studies are more likely due to potential regional variabilities in nodular HT characteristics.

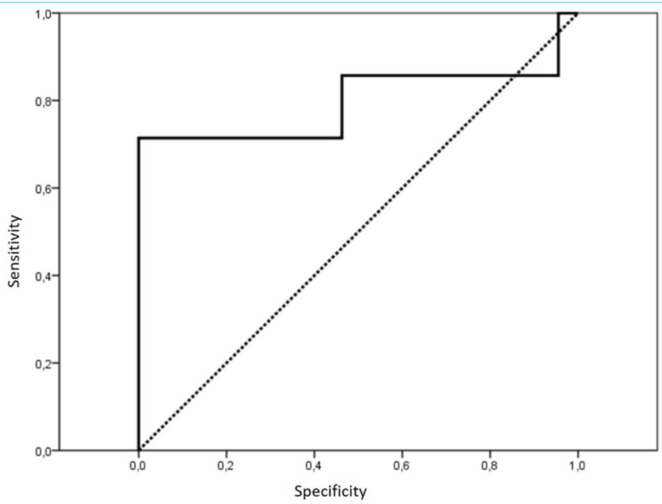

Figure 3. Receiver operating characteristic curve of strain ratio for diagnosis of benign and malignant thyroid nodules.

Cappelli et al.[9] investigated the predictive value of SE in benign thyroid nodules in patiens with co-existing HT. In their study cohort, of the included 242 nodules, 230 (95%) nodules were benign. On elastograms, they found that 79.1% of benign nodules demonstrated elasticity (score 1) in the whole nodule. However, when they categorized the nodules into two subgroups according to parenchymal patterns (mild/moderate versus severe hypoechogenicity) of the gland, they found that the sensitivity of score 1 elasticity on nodules decreased from 75% to 50% in the severe hypoechogenic group. In our study, the distribution of benign (90.5%) and malignant (9.5%) nodules in HT patients was similar to the study cohort of Cappelli et al.[9] We found that 80.6% (54/67) of benign nodules demonstrated score 1 and 2 features on elastograms and this may be considered as in line with the findings of Cappelli et al.[9]

We found a weak correlation between the elasticity scores of the nodules and the gland parenchymas. As lymphocytic infiltration and fibrosis occur in the gland parenchyma of patients with HT, it causes hard tissue characteristics in the gland. This also has the potential to affect the nodule elasticity as the elasticity of the background parenchyma of the nodule may contribute to its elasticity.

Şahin et al.[20] investigated the role of SE in distinguishing benign and malignant thyroid nodules in patients with HT. Their study chort consisted of 267 (92.1%) benign and 23 (7.9%) malignant nodules. The distribution of benign and malignant nodules in their study was quite similar to the current study. They reported that the elasticity score equal or higher than 3 had 82.6% and 50.9% sensitivity and specificity, respectively, for detecting malignant nodules. In the current study, the sensitivity and specificity values for elasticity score 4 in detecting malignant thyroid nodules were 71.4% and 95.5%, respectively. Moreover, Şahin et al.[20] found that a value of 2.45 for the strain index

Table 3. The distribution of elasticity scores for the nodules and parenchymas

Elasticity scores of the nodules	Elasticity scores of parenchymas				
	1	2	3	4	Total
1	13 (68.4%)	2 (10.5%)	4 (21.1%)	0 (0%)	19 (100%)
2	4 (11.1%)	29 (80.6%)	3 (8.3%)	0 (0%)	36 (100%)
3	2 (18.2%)	4 (36.4%)	4 (36.4%)	1 (9,1%)	11 (100%)
4	2 (25%)	5 (62.5%)	1 (12.5%)	0 (0%)	8 (100%)
Total	21 (28.4%)	40 (54.1%)	12 (16.2%)	1 (1,4%)	74 (100%)

Table 4. The distribution of elasticity scores for the benign and malignant nodules

Elasticity scores	Benign	Malignant	Total
1	19 (100%)	0 (0%)	19 (100%)
2	35 (97.2%)	1 (2.8%)	36 (100%)
3	10 (90.9%)	1 (9.1%)	11 (100%)
4	3 (37.5%)	5 (62.5%)	8 (100%)
Total	67 (90.5%)	7 (9.5%)	74 (100%)

had 73.9% and 73% sensitivity and specificity, respectively, for detecting malignant nodules. On the other hand, Wang et al.[21] reported that 5.03 (sensitivity 75%, specificity 92.1%) was the best cut-off point for differentiating benign and malignant thyroid nodules in patients with HT. In our study, a value of 6.16 for SR had 71.4% and 100% sensitivity and specificity, respectively. Differences in the ROI selection criteria and potential reader variabilities may lead to these discordant results between the studies. Moreover, Dietrich et al.[22] reported that for determining benign and malignant thyroid nodules by using SR values, there is no agreement on the best cut-off point.

To maintain the quality of patient care, it is desirable to avoid unnecessary invasive procedures. In a systematic review and meta-analysis,[3] it has been concluded that sonoelastography is an accurate adjunctive technique for evaluating thyroid nodules and it may be helpful to decrease the number of FNAB. Among the 55 nodules that demonstrated elasticity score 1 or 2 features in this study, only 1 (1.8%) nodule had a malignant diagnosis. In this context, in patients with HT, if a nodule has an elasticity score 1 or 2 characteristics on elastograms, to reduce the number of unnecessary biopsies follow-up may be preferrable rather than FNAB.

Study Limitations

The current study has limitations. First, the number of included nodules was small. Second, this study did not evaluate inter- and intraobserver variabilities, which have the potential to lead to wide variations in diagnostic performance of SE. Therefore, future studies with a larger number of nodules that additionally evaluates inter- and intraobserver variabilities will be more impactful.

CONCLUSION

Our study revealed that SE is an accurate diagnostic tool to characterize thyroid nodules in patients with HT and this may be useful to avoid unnecessary invasive procedures.

MAIN POINTS

- SE can be useful in the distinction between benign and malignant thyroid nodules in patients with Hashimoto thyroiditis.
- SE as an adjunctive tool to ultrasound can reduce the number of benign biopsies in patients with Hashimoto thyroiditis.
- Elasticity scores had a significant association with histopathological diagnosis of the thyroid nodules.

ETHICS

Ethics Committee Approval: This prospective study was approved by the Gazi University Institutional Review Board (approval number: 214, date: 05.23.2012).

Informed Consent: Written informed consent was provided by the patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: E.P.S., S.Ö.O., C.Y., Design: H.N.Ş., S.Ö.O., Supervision: S.Ö.O., C.Y., Materials: E.P.S., H.N.Ş., M.N.C., Data Collection and/or Processing: E.P.S., H.N.Ş., M.N.C., Analysis and/or Interpretation: E.P.S., H.N.Ş., M.N.C., E.C., Literature Search: E.P.S., Writing: E.P.S., H.N.Ş., Critical Review: E.P.S., H.N.Ş., M.N.C., E.C., S.Ö.O., C.Y.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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