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The predictive value of elastography in thyroid nodules and its comparison with fine-needle aspiration biopsy results

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ABSTRACT

Objective: We aimed to evaluate the predictive value of elastography in determining malignancy during preoperative investigation of thyroid nodules and to compare its results with preoperative fine-needle aspiration biopsy (FNA) and postoperative histopathology results.

Material and Methods: Among the group of patients who had indications for thyroidectomy between January 2013 - September 2013 in the department of general surgery 86 euthyroid patients were prospectively included in the study. Informed consent was obtained from all patients. All patients received simultaneous thyroid ultrasonography and elastography by an experienced radiologist. The patients were classified into five scores according to Tsukuba scoring. Score 1 and 2 were evaluated as soft nodules (benign), score 3 as medium consistency (usually benign), and scores 4 and 5 as hard nodules (malignant). For statistical purposes, the FNA results were classified as benign, probably benign or malignant. The histopathological results were classified as benign or malignant. The results were compared with FNA and elastography findings.

Results: The fine-needle aspiration biopsy of the nodules revealed 60.5% benign, 17.4% high probability of benign, and 22.1% malignant cases; and the elastography diagnosed 38.4% benign, 23.3% high probability of benign, and 38.4% malignant nodules. The postoperative pathology evaluation diagnosed 67.4% of patients as benign, and 32.6% as malignant. The rate of detection of thyroid cancer cases (sensitivity) by elastography was 67.9%, the ability to distinguish healthy individuals (specificity) was 75.9%, and the overall adequacy of the method (accuracy) was determined as 73.3%.

Conclusion: Elastography overlaps with especially benign cytology-pathology at a high rate, and provides definite diagnosis in 58% of malignant cases. In our study, elastography provided more reliable results than FNA, in terms of diagnosing malignancy.

Key Words: Thyroid, nodule, elastography

INTRODUCTION

Thyroid nodules are common thyroid pathologies. Thyroid nodule detection rate is 5% by palpation during screening, 19-67% by high resolution ultrasonography, and 50% in autopsy series (1).

Although thyroid function tests, scintigraphy and ultrasound provide important information for malignancy in the diagnosis of thyroid nodules, which are known to be mostly benign, they cannot differentiate benign and malignant lesions with certainty. Ultrasonographic features like hypoechogenity, border irregularity, microcalcifications, unusual blood supply within the nodule and absence of halo suggest the risk of malignancy; however, FNA is required in many patients since their specificity and sensitivity are not sufficient (2). FNA is often used as the most reliable method in the evaluation of thyroid nodules in recent years. Nevertheless, FNA is an invasive procedure with false-negative results in 15% of patients with cancer (3), and is non-diagnostic in 20% of all patients (4, 5). In addition, requirement for repetition of the procedure in case of insufficient or suspicious FNA results is another disadvantage of this method.

Elastography is a newly developed ultrasonography method in the evaluation of thyroid nodules. Tissue elasticity is measured by application of compression on the tissue. In elastography, the displacement in the longitudinal plane of stiff tissues and adjacent soft tissues with the applied mechanical pressure is measured with the intent to have an idea about their stiffness. In average, benign thyroid nodules are 1.7 times harder than the surrounding thyroid tissue, and malignant thyroid nodules are 5 times harder (6).

In this study, we aimed to evaluate the specificity, sensitivity and accuracy of elastography, which is a non-invasive method, in determining malignancy during preoperative investigation of thyroid nodules and to compare its results with preoperative fine-needle aspiration biopsy (FNA) and postoperative histopathology results.

MATERIAL AND METHODS

Among the group of patients who were admitted to the Department of General Surgery between January-September 2013, 86 patients who had an indication for surgery due to thyroid nodule with normal

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thyroid function tests and who did not have previous thyroid surgery were prospectively evaluated. Informed consent was obtained from all patients. Ethical board review was obtained from the Ministry of Health Haseki Training and Research Hospital Non-Drug Clinical Research Ethics Committee. Informed consent was obtained from all patients.

All patients received simultaneous thyroid ultrasonography and elastography by an experienced radiologist at our hospital's radiology clinic. The investigations were performed with HITACHI HIVISIONTM 7500 (USA and Europe) elastography device and 14 MHz linear transducers. The patient was placed in the supine position. The lesion was centralized, and rhythmic compression-decompression maneuvers were performed with the ultrasound probe perpendicular to the skin, lesion and neck. The color scales visualized as a result of signals that were obtained before and after compression were evaluated by Tsukuba scoring and were divided into five scores. Score 1 and 2 were evaluated as soft nodules (benign), score 3 as medium hardness (usually benign) and scores 4 and 5 as hard nodules (malignant) (Figure 1).

Tsukuba Scoring
Score 1: Lesions with similar elasticity to surrounding thyroid parenchyma, predominantly green coded.
Score 2: Lesions with non-homogeneous elasticity, including areas of blue and green.
Score 3: Lesions coded green at the periphery, blue at the center.
Score 4: Lesions coded blue, without surrounding echogenic halo.
Score 5: Lesions coded blue, with surrounding echogenic halo (the elasticity of the surrounding tissue is also lost).

The FNA was performed under ultrasonographic guidance by using a 21 G- 10 cc syringe in the radiology clinics. The obtained materials were fixed by placing inside containers of 95% of ethyl alcohol and were assessed by pathology clinics after staining with hematoxylin-eosin method. The FNA was performed again in cases with inadequate and suspicious findings. Results of our study were classified as benign, high probability of being benign and malignant in order to obtain accurate statistics results.

The surgical method was total thyroidectomy in 70 patients, and lobectomy in 16 cases. The histopathological results were classified as benign and malignant. The FNA and elastography results were compared.

Statistical Analysis
Statistical Package for the Social Sciences, (SPSS, Inc., Chicago, IL, USA) 15.0 for Windows program was used for analysis. Descriptive statistics were stated as number and percentage for categorical variables, and mean, standard deviation, minimum, maximum for numeric variables. Sensitivity was defined as identification of individuals with health problems among individuals actually with health problems, and specificity as identification of healthy individuals within actually healthy individuals. Positive predictive value was accepted as the percentage of individuals actually with health problems among individuals the test concluded to have health problems, and negative predictive value was the percentage of actually healthy individuals among those the test identified as healthy. The overall strength of the test (accuracy) was defined as the ability to make an accurate diagnosis.

RESULTS
Eighty-six patients who were scheduled for surgery due to thyroid nodules, with a mean age of 47.1±12.0 years, consisting of 67 men and 19 women were included in the study. Table 1 summarizes nodule characteristics.

The FNA results of the nodules were interpreted as benign in 60.5%, likely benign in 17.4%, and malignant in 22.1%. Elastography results showed 38.4% benign, 23.3% likely benign and 38.4% malignant lesions. The postoperative pathology evaluation revealed 67.4% of cases as benign, whereas 32.6% were diagnosed as malignant (Table 2, Figure 2).

Within the group of patients who were diagnosed as benign by FNA, malignancy was detected in 19.2%, and out of the patients who were diagnosed as probably benign by FNA, malignancy was detected in 53,3%. 47.4% of nodules with a diagnosis of malignancy were benign (Table 3, Figure 3).

The pathologic evaluation of patients diagnosed with a benign pathology by elastography revealed malignancy in 27.3%, and all lesions that were diagnosed as probably benign were diagnosed as benign. 42.4% of patients with a malignancy diagnosis were benign (Table 4, Figure 4).

Statistically, there was no correlation between FNA and elastography results (kappa=0.240) (Table 5).

In our study, the rate of detecting patients with thyroid cancer (sensitivity) was calculated as 35.7%, the rate of distinguishing healthy individuals (specificity) was 84.5%, and the overall adequacy (accuracy) was 68.6% for FNA (Table 6).

FNA
Sensitivity=35.7%
Specificity=84.5%
Positive predictive value=52.6%
Negative predictive value=73.1%
Accuracy=68.6%

The rate of detecting patients with thyroid cancer (sensitivity) was calculated as 67.9%, the rate of distinguishing healthy individuals (specificity) was 75.9%, and the overall adequacy (accuracy) was 73.3% for elastography (Table 7).

Figure 1. Ultrasonographic elastography scoring of nodules

Table 1. Nodule characteristics on thyroid ultrasonography

Age (years) mean±SD (min-max)		47.1±12.0 (20-72)
Gender, n (%)	Female	67 (77.9)
	Male	19 (22.1)
Nodule size (mm) Mean±SD (min-max)		25.6±11.1 (4-42)
Nodule location, n (%)	Bilateral-except isthmus	20 (23.3)
	Left	20 (23.3)
	Right	19 (22.1)
	Dominant-left	10 (11.6)
	Dominant-right	7 (8.1)
	Dominant-isthmus	5 (5.8)
	Complete thyroid tissue	5 (5.8)
Preoperative diagnosis, n (%)	MNG	58 (69)
	Suspicious thyroid malignancy	14 (16.7)
	Nodular goiter	12 (14.3)
Nodule border	Regular	67 (77.9)
	Irregular	19 (22.1)
Component	Solid	62 (72.1)
	Solid+cystic	24 (27.9)
Echogenity	Isoechoic	50 (58.1)
	Hypoechoic	36 (41.9)
Hipoechoic halo		54 (62.8)
Vascularity		58 (67.4)
Calcification	None	38 (44.2)
	Micro+	31 (36.0)
	Micro+Macro+	9 (10.5)
	Macro+	8 (9.3)

Mean±SD: standard deviation; MNG: multinodular goiter

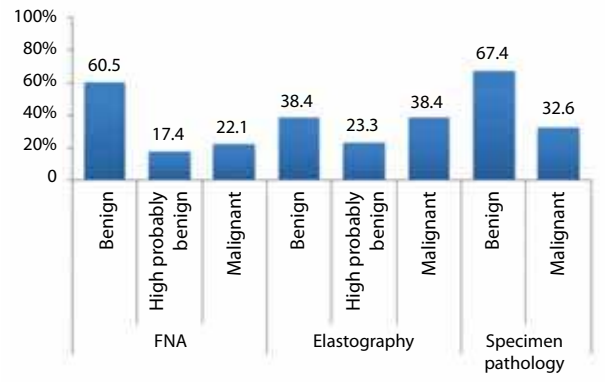

Figure 2. Nodule characteristics according to FNA, elastography and pathology results

FNA: fine needle aspiration

Elastography

Sensitivity=67.9%

Specificity=75.9%

Positive predictive value=57.6%

Table 2. Nodule characteristics according to FNA, elastography and specimen pathology results

		n (%)
FNA	Benign	52 (60.5)
	High probably benign	15 (17.4)
	Malignant	19 (22.1)
Elastography	Benign	33 (38.4)
	High probably benign	20 (23.3)
	Malignant	33 (38.4)
Pathology result	Benign	58 (67.4)
	Malignant	28 (32.6)

FNA: fine needle aspiration biopsy

Table 3. Comparison of FNA and pathology results

		Patholgy result	
		Benign, n (%)	Malignant, n (%)
FNA	Benign	42 (80.8)	10 (19.2)
	High probably benign	7 (46.7)	8 (53.3)
	Malignant	9 (47.4)	10 (52.6)

FNA: fine needle aspiation biopsy

Table 4. Comparison of elastography and patholgy results

		Pathology result	
		Benign, n (%)	Malignant, n (%)
Elastography	Benign	24 (72.7)	9 (27.3)
	High probably benign	20 (100.0)	0 (0.0)
	Malignant	14 (42.4)	19 (57.6)

Negative predictive value=83.0%

Accuracy=73.3%

DISCUSSION

Thyroid cancer accounts for approximately 1% of all cancers, and 90% of endocrine malignancies, and is responsible for 0.4% of cancer deaths (7). The female/male ratio is 4: 1. A large part of these tumors are well-differentiated tumors originating from follicular cells, and has a good prognosis (8, 9). Its significance is not related to its incidence, but rather is due to its occurrence in young adults (10). Although FNA is a method that provides helpful information at a high rate in the diagnosis of thyroid neoplasms, distinguishing between benign and malignant lesions can sometimes be quite difficult. FNA is especially insufficient in discriminating follicular carcinomas from follicular adenomas, which are more common (11). The final postoperative pathology report may be required for definitive diagnosis. Therefore, additional markers are required for accurate diagnosis of thyroid malignancies. One of these is elastography, which is a preoperative radiological diagnostic method.

Differentiation between benign/malignant nodules can not be made with certainty by the usually applied thyroid function tests, scintigraphy and ultrasonography. Preoperatively,

Table 5. Comparison of FNA and elastography results

		FNA			
		Benign	Malignant	High probably benign	Total
Elastography	Benign	29	2	2	33
	High probably benign	12	5	3	20
	Malignant	11	12	10	33
Total		52	19	15	86

FNA: fine needle aspiration biopsy

Table 6. Accuracy of FNA method

			Pathology result	
			Benign	Malignant
FNA	Malignant	Number	10	9
		Column %	35.7	15.5
		Line %	52.6	47.4
	Benign	Number	18	49
		Column %	64.3	84.5
		Line %	26.9	73.1

FNA: fine needle aspiration biopsy

Table 7. Accuracy of elastography method

			Pathology result	
			Benign	Malignant
Elastography	Malignant	Number	19	14
		Column %	67.9	24.1
		Line %	57.6	42.4
	Benign	Number	9	44
		Column %	32.1	75.9
		Line %	17.0	83.0

the most reliable diagnostic method is FNA (12). In contrast, there are studies in the literature that question the reliability of FNA. FNA may be insufficient for diagnosis especially in multinodular goiter, where multiple nodules are present (13).

The sensitivity and specificity of FNA in thyroid malignancies is reported as 65-98% and 72-100%, respectively (14-16).

In our study, the rate of detecting patients with thyroid cancer (sensitivity) was calculated as 35.7%, the rate of distinguishing healthy individuals (specificity) was 84.5%, and the overall adequacy (accuracy) was 68.6% for FNA. In our study, the sensitivity of FNA in detecting cancer was lower than the literature. We think that this discrepancy depends on many factors including radiology, pathology, and the materials used in FNA method, and patients with multiple nodules. Another disadvantage of FNA is its invasive nature. These disadvantages have caused the investigators to search a non-invasive method with fewer variables.

Ophir et al. (17), who have been investigating methods to improve diagnostic accuracy of ultrasonography, presented a new method called elastography in 1991. This method is an ultrasonography technique that detects the stiffness of lesions and accordingly, gives an estimate about the probability of malignancy of the lesion by using ultrasound device (18). Elastography is a newly developed dynamic technique and is a non-invasive evaluation of the degree of tissue stretching under application of an external force that is based on the principle of easier deformation of soft tissue under pressure (19, 20). According to Hooke's law, when an elastic deformity is created by externally applying a force to a substance, the accumulated potential energy provides retrieval of the old shape after decompression. Elastography evaluates distortion that occurs in the tissue by externally applied pressure. It is based on the principle that soft parts of the tissue will sustain greater distortion than stiff parts. It is used to distinguish benign lesions from malignant lesions in the breast, prostate, pancreas, thyroid and lymph nodes (21, 22).

Malignant thyroid nodules are usually harder than benign nodules. Within histological types, this feature is more pronounced in papillary carcinomas. Elastography is performed by comparing the stiffness level of the nodule with that of the surrounding thyroid tissue. Therefore, in cases of thyroiditis that causes stiffness in the surrounding thyroid tissue, and in multinodular patients containing multiple nodules without any healthy surrounding tissue to make a comparison with, elastography may give erroneous results (23, 24). Likewise, calcified nodules and nodules with a more than 20% cystic component can also be misleading (25).

Rago et al. (24), in their study involving 92 patients, detected elastography sensitivity as 97%, and specificity as 100%. However, all of the patients included in the study group were cytologically either suspicious or malignant, and a selected group of patients with large nodule size was included in the study.

In their study of 52 nodules Lyshchik et al. (26), reported the elastography sensitivity as 82%, and specificity as 96%. In this study, it is noteworthy that significant portions of the selected nodules were malignant.

Rubaltelli et al. (27) reported elastography sensitivity as 81.8%, and specificity as 87.5%.

In their study involving 60 patients, Bender et al. (28) stated the sensitivity of elastography as 58.3%, and the specificity as 85.4%. They stated that the reasons why these values were

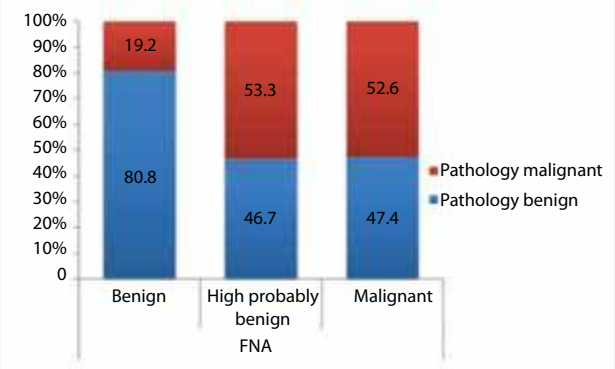

Figure 3. Comparison of FNA and specimen pathology results
FNA: fine needle aspiration biopsy

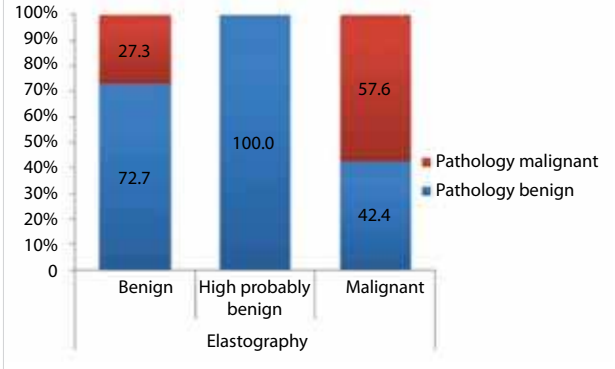

Figure 4. Comparison of elastography and specimen pathology results

lower compared to those in the literature were the limited number of cases and lack of including a selected group of patients.

In our study, for elastography, the rate of detecting patients with thyroid cancer (sensitivity) was calculated as 67.9%, the rate of distinguishing healthy individuals (specificity) was 75.9%, and the overall adequacy (accuracy) was 73.3%. The relatively low rates in our study as compared to the literature are due to the lack of having a selected case group.

In our study, the sensitivity and specificity rates of elastography in the diagnosis of thyroid cancer were higher than FNA.

CONCLUSION

Once a nodule is detected in the thyroid gland, differentiation between benign/malignant nodules should be made with an aim to minimize unnecessary surgical interventions. Therefore, diagnosis of malignancy prior to thyroid operations is important, particularly for the decision to perform total thyroidectomy or neck dissection, if required. At this stage, the diagnosis of malignancy must be confirmed by preoperative imaging techniques and FNA. Elastography is one of the latest developments in ultrasound technology, and is a non-invasive imaging modality that qualitatively and quantitatively evaluates the stiffness of the tissue. It is complementary to gray scale and color Doppler findings and ensures the avoidance of unnecessary FNA at this stage.

Elastography overlaps at a high rate especially with benign cytology-pathology, and can provide a definite diagnosis of malignancy at a rate of 58%. In our study, elastography has yielded more reliable results in the diagnosis of malignancy than FNA.

In the future, FNA perhaps will not be used for the diagnosis of malignancy in patients who are diagnosed with malignancy by elastography.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ministry of Health Haseki Education and Research Hospital Non-Drug Clinical Research Ethics Committee.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2009; 19: 1167-1214. [CrossRef]
2. Lannuccilli JD, Cronan JJ, Monchik JM. Risk for malignancy of thyroid nodules as assessed by sonographic criteria: the need for biopsy. J Ultrasound Med 2004; 23: 1455-1464.
3. Grant CS, Hay ID, Gough IR, McCharthy PM, Goellner JR. Long-term follow-up of patients with benign thyroid fine-needle aspiration cytologic diagnoses. Surgery 1989; 106: 980-985.
4. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med 1993; 118: 282e9.
5. Meko JB, Norton JA. Large cystic/solid thyroid nodules: a potential false-negative fine-needle aspiration. Surgery 1995; 118: 996-1003. [CrossRef]
6. Luo S, Kim EH, Dighe M, Kim Y. Thyroid nodule classification using ultrasound elastography via linear discriminant analysis. Ultrasonics 2011; 51: 425-431. [CrossRef]
7. Sethi K, Sarkar S, Das S, Mohantly B, Mandal M. Biomarkers for the diagnosis of thyroid cancer. J Exp Ther Oncol 2010; 8: 341-352.
8. Maitra A, Abbas AK: The Endocrine System. In Kumar V, Abbas AK, Fausto N (eds). Pathologic Basis of Disease. 7th ed. Philadelphia, Elsevier Saunders; 2005.p.1164-1189.
9. Thompson L DR, Adair C: Non-neoplastic lesions of the thyroid gland, benign neoplasms of the thyroid gland, malignant neoplasms of the thyroid gland. In Goldblum JR (eds). Endocrine Pathology. C L Elsevier;2006.p.1-142.
10. Norris CM, Cady B. Head, neck and thyroid cancer. Clinical Oncology. Edited by Al Holleb, DJ Fink, GP Murphy. Atlanta, American Cancer Society, 1991.pp.306-328.
11. Klonoff DC, Greenspan FC. The thyroid nodule. Adv Intern Med 1982; 27: 101-106.
12. Clark OH. Textbook of Endocrine Surgery, 2nd Edition, Saunders, 2005.

13. Giles Y, Boztepe H, Terzioğlu T, Tezelman S. The advantage of total thyroidectomy to avoid reoperation for incidental thyroid cancer in multinodular goiter. Arch Surg 2004; 139: 179-182. [CrossRef]
14. Supit E, Peiris AN. Cost-effective management of thyroid nodules and nodular thyroid goiters. South Med J 2002; 95: 514-519. [CrossRef]
15. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med 1993; 118: 282-289. [CrossRef]
16. Fletti S, Durante C, Torlontano M. Nonsurgical approaches to the management of thyroid nodules. Nat Clin Pract Endocrinol Metab 2006; 2: 384-394. [CrossRef]
17. Ophir J, Cespedes I, Ponnekanti H, Yazdi Y, Li X. Elastography, a quantitative method for imaging the elasticity of biological tissues. Ultrason Imaging 1991; 13: 111-134. [CrossRef]
18. Hoyt K, Forsberg F, Ophir J. Analysis of a hybrid spectral strain estimation technique in elastography. Phys Med Biol 2006; 51: 197-209. [CrossRef]
19. Lerner RM, Huang SR, Parker KJ. Sonoelasticity images derived from ultrasound signals in mechanically vibrated tissues. Ultrasound Med Biol 1990; 16: 231-239. [CrossRef]
20. Ophir J, Alam SK, Garra B, Kallel F, Konofagou E, Krouskop T, et al. Elastography: ultrasonic estimation and imaging of the elastic properties of tissues. Proc Inst Mech Eng H 1999; 213: 203-233. [CrossRef]
21. Miyanaga N, Akaza H, Yamakawa M. Tissue elasticity imaging for diagnosis of prostate: a preliminary report. Int J Urol 2006; 13: 1514-1518. [CrossRef]
22. Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Hiraoka M, et al. Cervical lymph node metastases: diagnosis at sonoelastography--initial experience. Radiology 2007; 243: 258-267. [CrossRef]
23. Hong Y, Liu X, Li Z, Zhang X, Chen M, Luo Z. Real-time ultrasound elastography in the differential diagnosis of benign and malignant thyroid nodules, J. Ultrasound Med 2009; 28: 861-867.
24. Rago T, Santini F, Scutari M, Pinchera A, Vitti P. Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. J Clin Endocrinol Metab 2007; 92: 2917-2922. [CrossRef]
25. Rago T, Vitti P. Potential value of elastosonography in the diagnosis of malignancy in thyroid nodules. Q J Nucl Med Mol Imaging 2009; 53: 455-464.
26. Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ, et al. Thyroid gland tumor diagnosis at US elastography. Radiology 2005; 237: 202-211. [CrossRef]
27. Rubaltelli L, Corradin S, Dorigo A, Stabilito M, Tregnaghi A, Borsato S, et al. Differential diagnosis of benign and malignant thyroid nodules at elastosonography. Ultraschall Med 2009; 30: 175-179. [CrossRef]
28. Bender Ö, Kılıç Y, Hot S, Ertürk A. The efficacy of elastography in the differential diagnosis of benign-malignant thyroid nodules and its comparison with fine needle aspiration biopsy. Endokrinolojide Diyalog 2012; 9: 103-107.