Evaluation of elastosonography and fine-needle aspiration biopsy results in the diagnosis of thyroid nodules

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Objective
The aim of our study is to investigate the importance of strain sonoelastography (SSE) in the diagnosis of thyroid nodules and in the selection of indications for fine-needle aspiration biopsy (FNAB).
Materials and methods
We included 481 patients who visited our clinic between 2019–2022 with thyroid nodules in the study and used a stepwise diagnostic approach to choose patients to perform surgery on and follow-up. All patients were ranked into 2 groups: Group 1 included 135 (28,1%) patients were assessed as SSE along with traditional examinations. The 2nd group included 346 (71.9%) patients who underwent ultrasound examination using SE, only the hard nodule or hard regions of the nodule detected by SSE were obtained with FNAB. We followed up on nodules with benign FNAB results, and nodules with suspicious or malignant results underwent thyroidectomy. Histopathology results of surgically removed nodules were compared with SSE and FNAB results. AUROC was the primary, while sensitivity, specificity, PPV and NPV were the secondary outcome.
Results
Out of 481 patients, 420 (87.3%) were female, 61 (12.7%) were male, and the age range was 17–83 (CI=45.57±25.9). The mean nodule size was 23.33±16.7 mm. After evaluating elastography results, FNAB was performed on 346 (71.9%) nodules. Surgical treatment was performed in 114 (group 1) (84.4%) of 135 patients, benign tumors were diagnosed in 107 (93.8%), and malignant tumors in 7 (6.2%). Surgical treatment in group 2 was performed in 146 (42.2%) of 346 patients, benign tumors were detected in 105 (71.9%) patients, and malignant in 41 (28.9%). The combined use of the sonoelastography and fine-needle aspiration biopsy contributed to a significant increase in the frequency of detection of thyroid nodules of malignant structure, which amounted to 28.9% in patients of the main group (versus 6.2% in patients of the control group) and a decrease in the frequency of surgical interventions by more than 2 times in patients of the second group.
The area of the ROC curve for SSE was S=0.851±0.029; 95% CI (0.794 to 0.908); *P*=0.000. It is a statistically significant marker in the diagnosis of thyroid nodules. The most important marker in the diagnosis of thyroid nodules was the FNAB test: S=0.874±0.034; 95% CI (0.807 to 0.940); *P* =0.000.
Sensitivity, specificity, PPV, and NPV of elastosonography of the I group were 42.9 ±18.7%, 96.3±1.8%, 42.9%, 96.3; of II group 68.3±7.3%, 87.6±3.2%, 68.3%, 87.6%; FNAB 90.2±4.6%, 90.5±2.9%, 76.2%, 91.3%, respectively.
Conclusion
Combined use of SE and Bethesda system was able to detect malignancy in the early stages and to reduce the number of operations.

Keywords:
bethesda, fine-needle aspiration biopsy, sonoelastography, thyroid cancer, thyroid nodules, TI-RADS

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Introduction

Recently, the increased tendency of nodular pathologies in the general structure of thyroid diseases has drawn attention. Thyroid nodules can be solitary or multiple and form as nodular goitre limited to the thyroid gland or diffusely as diffuse goitre. The malignant transformation risk of all these nodules is the same. Therefore, early diagnosis and identification of the structural characteristics of thyroid nodules are one of the actual problems of thyroidology. Nodular goitre (NG) has been seen in 2–5% of the population with palpation and 19–67% by ultrasonography (US) [1,2]. There is a steady increase in the incidence of thyroid cancer (TC) worldwide, which can also be attributable to improved diagnostic

methods rather than the actual increase in frequency [3]. When diagnosed early and differentiated well pathologically, TC can be easily treatable, and the prognosis is close to perfect [4]. US is the most common imaging method to detect structural disorders of the thyroid gland. US is routinely used in the diagnosis and treatment, starting from the initial identification and diagnosis, in preoperative planning and postoperative follow-up of TC. As 7–15% of nodules have a risk of malignancy, fine-needle aspiration biopsy (FNAB) and cytological examination of suspicious nodules are required [5,6]. However, it is characterized by false negative results in 15% of cancer patients and indeterminate diagnostic results in 20% of all patients [5,7]. On the other hand, when the results of this method are uninformative or doubtful, the need for repeated examinations is considered its shortcomings and defects.

Ultrasound elastography (ES) technique, developed in recent years, is frequently used to evaluate thyroid nodules due to its noninvasiveness and easy application. ES is a noninvasive diagnostic method that measures the hardness and elasticity of tissue. Benign thyroid nodules are 1.7 times, and malignant thyroid nodules are 5 times harder than normal thyroid tissue [8–10]. American Thyroid Association (ATA) guidelines showed that SE could be a helpful method in risk assessment for patients before surgery [11].

Objective: The aim of our study is to investigate the importance of sonoelastography (SE) in the diagnosis of thyroid nodules and in the selection of indications for fine-needle aspiration biopsy (FNAB).

Materials and methods

We included 481 patients who visited our clinic between 2019 and 2022 with thyroid nodules in the study and used a stepwise diagnostic approach to choose patients to perform surgery on and follow-up. All patients were ranked into 2 groups: Group 1 included 135 (28.1%) patients were assessed as SSE along with traditional examinations. The 2nd group included 346 (71.9%) patients who underwent ultrasound examination using SSE, only the hard nodule or hard regions of the nodule detected by SE were obtained with FNAB. We followed up on nodules with benign FNAB results, and nodules with suspicious or malignant results underwent thyroidectomy. Histopathology results of surgically removed nodules were compared with SSE and FNAB results. AUROC was the primary, while sensitivity, specificity, PPV and NPV were the secondary outcome.

US investigation was carried out by an endocrine surgeon using Sonoscape S9 pro 13 to 15- MHZ high linear-array transducers, grey-scale and colour Doppler examinations. Nodules have been initially evaluated by SSE both transversally and longitudinally. We archived examination images digitally.

During SSE the patient was placed on the stretcher in a supine position, and also the neck was brought to a slight extension by placing a pillow under it. After the grey-scale US, a freehand compression elastography examination was performed. In this method, the nodule investigated by the US was centralized; rhythmic cycles of compression-decompression were applied to the nodule and skin vertically with the help of a transducer, and the colour scale formed by signals obtained before and after compression was evaluated according to the Tsukuba elasticity score (TES) consisting of 5 points.

Tsukuba Elasticity Score 1: Nodules that were entirely coded green, having equal elasticity with surrounding thyroid parenchyma

Tsukuba Elasticity Score 2: Nodules with mosaic pattern of blue and green areas, with inhomogeneous elasticity

Tsukuba Elasticity Score 3: Nodules that were coded green in periphery and blue in the centre

Tsukuba Elasticity Score 4: Nodules that were coded blue and does not have an echogenic halo around

Tsukuba Elasticity Score 5: Nodules that were coded blue and have an echogenic halo around

The endocrine surgeon performed FNAB of the cases under US guidance using 5 cc syringes with 21G needles. Obtained cytological samples were sent to the department of pathology, and the results were declared by the cytopathologists in an official report. Indication for surgery was decided by considering the size and malignancy of nodules. We performed a total thyroidectomy on 260 patients. After classifying the pathology results of nodules as benign and malignant, we compared the SSE and FNAB results.

Statistical analysis

In this study, we used mean and standard deviation, frequency and percentage values in the descriptive statistics of data. Sensitivity, specificity, and positive and negative predictive values were used to investigate

Table 1 Comparison of Bethesda categories with the Tsukuba Elasticity Score

	Bethesda 1n	Bethesda 2n	Bethesda 3n	Bethesda 4n	Bethesda 5n	Bethesda 6n
SSE 2	0 (0)	33 (19.1)	1 (5.6)	4 (4.7)	0 (0)	0 (0)
SSE 3	3 (100)	126 (72.8)	14 (77.7)	66 (78.7)	15 (30.6)	3 (15.8)
SSE 4	0 (0)	14 (8.1)	3 (16.7)	14 (16.6)	32 (65.3)	16 (84.2)
SSE 5	0 (0)	0 (0)	0 (0)	0 (0)	2 (4.1)	0 (0)
Total	3 (100)	173 (100)	18 (100)	84 (100)	49 (100)	19 (100)

Note: $\chi 2$=49,77; P<0,001.

diagnostic performance. We used SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) 16 for the Windows programme for statistical analysis.

Results

Among the patients (481 nodules) included in our study, 189 nodules (39.3%) were detected in the right lobe, 137 nodules (28.5%) in the left lobe, both lobe 154 (32.0%) nodules and 1 (0.2%) nodules in the isthmus. According to findings, 135 nodules (33.6%) were smaller than 1.5sm, 132 (32.8%) around 1.5–2.5sm, and 135 (33.6%) larger than 2.5sm.

In I group US elastography, we detected TES 2, TES 3 and TES 4 in 78 (57.8%), 49 (36.3%) and 8 (5.9%) correspondingly. Surgical treatment was performed in 114 (group 1) (84.4%) of 135 patients, benign tumors were diagnosed in 107 (93.8%), malignant tumors in 7 (6.2%).

346 (71.9%) of 481 nodules were biopsied, and 200 nodules with benign findings were taken for monitoring. In the evaluation of FNAB results, we present the comparison of Bethesda categories with the Tsukuba Elasticity Score in Table 1.

Surgical treatment in group İİ was performed in 146 (42.2%) of 346 patients, findings in 105 (71.9%) were benign, and 41 (28.9%) were malignant.

The combined use of the sonoelastography and fine-needle aspiration biopsy contributed to a significant increase in the frequency of detection of thyroid nodules of malignant structure, which amounted to 28.9% in patients of the main group (versus 6.2% in patients of the control group) and a decrease in the frequency of surgical interventions by more than 2 times in patients of the second group.

Area under the curve

The area of the ROC curve for SSE was statistically significant ($p < 0.05$) S = 0.851 ± 0.029; 95% CI (0.794 to 0.908); $p = 0.000$. It is a statistically significant marker in the diagnosis of thyroid nodules in Table 2.

Table 2 Test Result Variable(s): Elastoqrafiya

			Asymptotic 95% Confidence Interval	
Area	Std. Error	Asymptotic Sig.	Lower bound	Upper bound
0.851	0.029	0.000	0.794	0.908

The most important marker in the diagnosis of thyroid nodules was the FNAB test: S=0.874±0.034; 95% CI (0.807–0.940); P=0.000.

Sensitivity, specificity, PPV and NPV of elastosonography of I group were 42.9±18.7%, 96.3 ±1.8%, 42.9%, 96.3; of II group 68.3±7.3%, 87,6±3,2%, 68,3%, 87,6%; FNAB 90,2±4,6%, 90,5±2,9%, 76,2%, 91,3%, respectively.

Discussion

Thyroid cancer constitutes 1% of all malignant tumours and 90% of endocrine cancers [2,4]. Most of these are differentiated tumours originating from follicular cells and have a good prognosis [2,3]. Both TN and TC are seen four times more frequently among females than males. In our study, there were 420 (87.3%) females and 61 (11,2%) males, and the female/male ratio was 6.6, which is consistent with the literature [12,13].

Even though FNAB plays a principal role in the thyroid neoplasms diagnosis, sometimes it is significantly hard to differentiate between benign and malignant tumours. Especially FNAB may not be sufficient for diagnosing multinodular goitre (MNG) [5,6]. The sensitivity of FNAB in thyroid nodules was 65–98% and specificity 72–100% [5–7,14]. In particular, FNAB is insufficient in the differential diagnosis of follicular adenomas and cancers [8,14]. It is necessary to wait for pathology results after the surgery to make a final diagnosis. However, it is the disadvantage that FNAB should be repeated in case of inadequate and non-diagnostic results such as atypical or suspicious [13,14]. Therefore, additional examinations are required to diagnose malignant thyroid tumours. For this

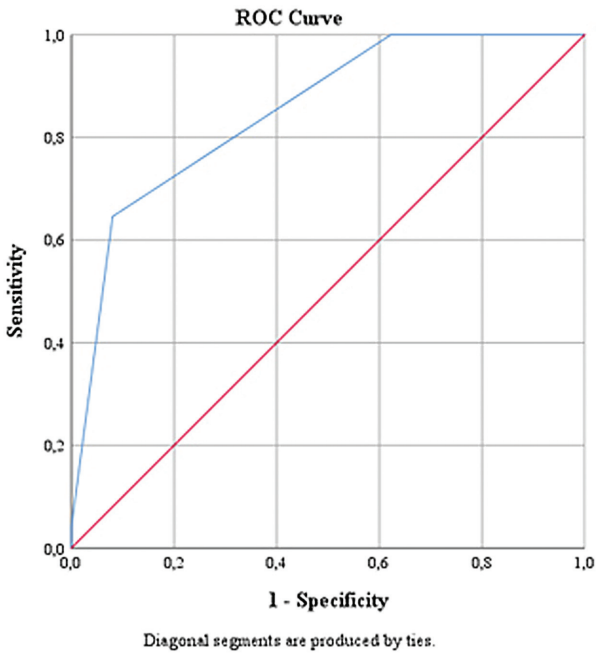
purpose, we use SSE, one of the preoperative radiologic diagnostic methods. It is an echography method that uses an ultrasound device to determine the degree of hardness of the nodule and give information about the possibility of malignancy in that nodule [9,12,15]. Yener N *et al.* detected the accuracy, specificity, sensitivity, negative and positive predicted values of FNAB in the detection of malignancy as 85.0%, 86.2%, 81.8%, 92.59%, 69.23% correspondingly by comparing cytology, histopathology, and ultrasound findings of 284 cases [13]. In our study, because we determined the indication for FNAB of TN after using SSE of the nodule, the values were 90.2%, 90.5%, 76.2%, and 91.3%.

In a study by Rago *et al.* involving 92 patients, the assessed sensitivity of SE was 97% and the specificity 100% [15]. In an original study by A. Lyshchik et al. with 52 nodules, the assessed sensitivity of SE was 82% and the specificity 96% [16]. In that study, most of the selected nodules were found to be malignant. On the contrary, Moon *et al.* evaluated 703 solid tumours, while reporting the sensitivity of grey-scale US to be 91.7%, sensitivity according to Asteria criteria was 65.2% and sensitivity according to Rago criteria 15.7% [17]. When the findings of grey-scale US and SE were evaluated together, sensitivity according to Asteria criteria was 95.2% and specificity 65.7%. According to Rago criteria, the results were a sensitivity of 92.1% and a specificity of 76.9%. Most studies reported that the combined application of conventional US and SE showed higher sensitivity than the US alone. In contrast, Trimboli *et al.* reported that combining grey-scale findings with elastography increased the sensitivity of grey-scale ultrasonography (from 85% to 97%) [18]. In our study, the sensitivity of ES was 68.3%, the specificity 87,6%, the PPV 68,3%, and the NPV 87,6%. The sensitivity and specificity obtained in our study are similar to the studies in the literature [8–10,12].

Strain SE made the detection of highly and moderately suspicious nodules easier. In 2013 EFSUMB (European Federation of Societies for Ultrasound in Medicine and Biology) Guidelines and Recommendations for the clinical use of elastography SE were recommended as an additional method to routine USG. This method is beneficial in the follow-up of thyroid nodules that were previously biopsied and had 'benign' results, but precise criteria have not been reported [17,18]. In our study, 221 nodules were followed up with SE. It is possible to assume that SE will gain wider use and be included in more guidelines in the future, thanks to the technological developments and the works done in the direction of standardization of the SE technique.

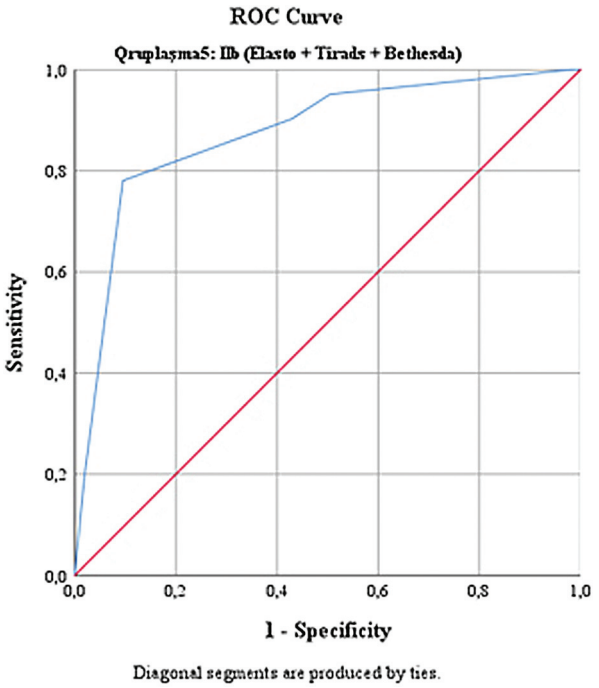
According to current reports, SE is not a substitute for routine nodule biopsy, so it should not be a criterion for

Figure 1



ROC-curve reflecting the predictive capabilities of the integrated use of SSE, 95% confidence interval.

Figure 2



ROC-curve reflecting the predictive capabilities of the integrated use of FNAB, 95% confidence interval.

postponing biopsy in nodules with suspicious grey-scale US symptoms [18]. In a study by Vorlander *et al.*, the accuracy of elastography was reported to be suboptimal in the diagnostics of malignant thyroid nodules [10]. In some cases, the use of elastography is limited. Some limitations also exist in the current study because ultrasound waves do not pass through calcifications, and in nodules with macrocalcifications, the result of the investigation can be faulty. Other than that, as the elasticity of the tissue is largely determined by the liquid part, its application is not appropriate in completely cystic or mixed nodules with the cystic component, as well as in nodules connected to large blood vessels. Even though we obtain very successful results in classic papillary cancer and other types of papillary cancer, there is not enough information about the outcomes of its application in follicular, medullary, secondary metastatic tumours, anaplastic carcinomas and lymphomas [9,12,19].

To reduce the number of unnecessary FNAB, SE can show, which nodule has FNAB indication. SE completes the grey scale and colour Doppler criteria and helps to avoid unnecessary FNAB at this stage. According to C.K. Zhao, the combined use of SE can decrease the FNAB number by 60.8% [20]. In our study, the combined use of SE by 71.9%, and the histopathology result was malignant by 28.9%. The combined use of SE with grey-scale US increases the sensitivity and specificity of the method and may cause a decrease in indications for biopsy.

Conclusion

Combined use of SE and Bethesda system was able to detect malignancy in the early stages and to reduce the number of operations.

Ethics committee permission

This committee permission This study was conducted in accordance with the Declaration of Helsinki and was approved by Azerbaijan Medical University (Prot. No: 23.2022.05.19) (Figs. 1,2).

Conflicts of interest

There are no conflicts of interest.

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