Original Article

A analysis of preoperative sonographic findings and fine needle aspiration biopsy results of thyroidectomy cases

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ABSTRACT

Objectives: The aim of present study is to compare the preoperative sonographic findings, fine-needle aspiration biopsy (FNAB) and postoperative histopathological results in patients who underwent total thyroidectomy.

Patients and Methods: A total of 884 patients (685 females 199 males; average age 46.84±12.73; range, 16 to 82 years) who underwent total thyroidectomy were included in this study. Thyroid ultrasonography was performed in all of patients with an initial diagnosis of thyroid nodules. Sonographic findings of thyroid nodules were evaluated. The sonographic characteristics were the number of nodules and sizes, having microcalciŞcations, having irregular margins and echogenicity. Sonographic malignancy scores were calculated due to sonographic findings. All thyroidectomy specimens were sent for pathological evaluation. The specimens were divided into two groups, benign and malign group, due to pathological evaluation. Each groups were compared in terms of preoperative sonographic findings, FNAB and postoperative histopathological results.

Results: The sonographic malignancy scores were statistically higher in malignancy group than in benign group (p=0.000). Nodule size was smaller in malignancy group than in benign group (p=0.000). Capsule irregularity rate was statistically higher in malignancy group than in benign group (p=0.000). Hypoechogenicity rate was statistically higher in malignancy group than in benign group (p=0.000). There was statistically significant consistency between pathology and FNAB results (kappa= 0.478, p=0.000). The sensivity, specificity, positive predictive and negatif predictive values of FNAB were %55.7, %92.4, %72.5 and %82.9, respectively.

Conclusion: Although the thyroid FNAB has an acceptable sensitivity and specificity, it is not effective alone in the decision of operation. Risk factors of thyroid malignancy should also be considered when assessing FNAB results, which are accepted as the gold standard in approach to thyroid nodules.

Keywords: Biopsy; consistency; malignancy; nodule; thyroid; ultrasonography.

Thyroid nodules are the most common diseases of the thyroid gland. With palpation, only 4-7% of thyroid nodules are diagnosed, while in autopsy series these rates are reported as 50-60%.[1-5] Since most of the thyroid nodules do not show any clinical findings and most of them do not reach the size to be examined by palpation, in epidemiological studies, the rates of thyroid nodules differ.[5]

Epidemiological studies report the prevalence of palpable thyroid nodules as 5% for women and 1% for men in iodine deficient areas.[6]

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In high-resolution ultrasonography imaging (USG), this rate is reported to vary between 19% and 68%.[6,7] The clinical significance of thyroid nodules is the risk of malignancy. For a clinician, exclusion of malignancy is a necessity for cases with thyroid nodules. Depending on factors such as age, gender, radiation exposure, geographic region, family history and genetics; malignancy may be detected in 7 to 15% of thyroid nodules.[8] In the United States, 37,200 cases were diagnosed with new thyroid cancer in 2009, while in 2014, 63,000 cases were diagnosed with thyroid cancer. The frequency of the thyroid cancer increased about 3 times from 1975 to 2009.[8,9] However, the rate of thyroid cancer diagnose in below 1 cm thyroid nodules was 25% in 1988-1989, this rate increased to 39% in 2008-2009.[9] As a result of fine needle aspiration biopsies (FNAB) performed on thyroid nodules, the incidence of thyroid cancer has almost tripled in the last three decades. However no increase in the rate of death was observed due to thyroid cancer at the same period.[10,11]

The presence of many findings that left clinicians in the dilemma in the evaluation of thyroid nodules necessitated the standard application for the approach to thyroid nodules.[4] According to The American Thyroid Society (ATD) recommendation FNAB is the first line FNAB in the thyroid nodules approach.[4] Thyroid FNAB is a safe, easy and minimally invasive procedure that can be performed in outpatient setting. According to FNAB results, follow-up and treatment can be routed. Thyroid FNAB sensitivity was reported between 65-98% and specificity was 70-98%.[12-16] However, thyroid FNAB will not always able to rule out malignancy and may lead to unnecessary surgical interventions.[17]

In this study, preoperative USG findings, thyroid FNAB and histopathological examination of the total thyroidectomy specimens in our hospital were evaluated.

PATIENTS AND METHODS

Between February 2007 and February 2017, patients who underwent total thyroidectomy in our otolaryngology and general surgery clinics were included in this retrospective clinical study. The study was approved by the ethics committee of the same hospital (Ethics committee no: 2017/356). The study was conducted in accordance with the guidelines of the Helsinki Declaration and Good clinical practice. Demographic data of the patients were obtained by scanning the patients' files in the hospital registry system.

A complete ear nose throat examination was performed in all patients who were referred to our clinic with a preliminary diagnosis of thyroid nodule. All patients underwent thyroid USG. Sonographic records of the nodules were examined. Thyroid FNAB was applied to the patients according to sonographic findings. Thyroid FNAB was performed by an expert radiologist in the interventional radiology clinic with a 25 gauge (0.46 mm) needle under USG. The pathological materials taken with FNAB were sent to the pathology clinic for evaluation.

Sonographic characteristics, nodule size and number, presence of capsule irregularity, presence of microcalcifications, and presence of echogenicity were recorded. A malignancy score was established according to sonographic features.

Sonographic malignancy score was calculated according to the following scoring system;

1- Nodule size;

- 0; diameter of largest thyroid nodule was under 1.5 cm,
- 1; diameter of largest thyroid nodule was over 1.5 cm

2- Nodule number;

- 0; multinodular thyroid disease
- 1; isolated thyroid nodule

3- Capsule irregularity;

- 0; absent
- 1; present

4- Microcalcification;

- 0; absent
- 1; present

5- Hypoechogenity

- 0; absent
- 1; present

A total malignancy score was calculating by adding the age off all patients. For age score 1 point were given under 20 years of age or older than 45 years.

Total thyroidectomy was performed by obtaining the consent of the patients. Patients with cosmetic deformity and patients with airway compromise underwent surgery without FNAB. All other cases underwent total thyroidectomy according to the pathology results. The specimens of total thyroidectomy patients were sent to histopathological examination. According to histopathological evaluation, patients were divided into two groups as benign and malignant. The findings of the two groups were compared for USG score-final histopathology consistency and FNAB-final histopathology consistency.

Statistical analysis

For statistical analysis, NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used. In the descriptive statistics of the data, mean, standard deviation, median lowest, highest, frequency and ratio values were used. The distribution of variables was measured with Kolmogorov Smirnov test. Mann-Whitney U test was used to analyze the quantitative independent data. Chi-square test was used for the analysis of qualitative

Table 1. Demographic data of patients

	n	%	Mean±SD	Range
Age (year)				
≤45	364	41.2		
>45	520	58.8		
Gender				
Female	685	77.5		
Male	199	22.5		
Pathologic examination				
Benign	645	73.0		
Malign	239	27.0		
FNAB				
Benign	648	80.1		
Malign	160	18.9		
Nodule size (cm)				
>1.5	265	30.0		
≥1.5	619	70.0		
Capsule irregularity				
(-)	815	92.2		
(+)	69	7.8		
Number of nodules				
Single	577	65.3		
Multipl	307	34.7		
Microcalcification				
(-)	734	83.0		
(+)	150	17.0		
Echogenicity				
Hyperecogene	156	17.6		
Hypoechogene	360	40.7		
Isoechogene	178	20.1		
Mixt	190	21.5		
Total malignancy score			2.4±1.2	0.0-6.0
USG malignancy score			1.8±1.1	0.0-5.0
Nodule size (mm)			25.9±15.5	0.0-90.0

SD: Standard deviation; FNAB: Fine needle aspiration biopsies.

Table 2. Histopathological evaluation of patients underwent total thyroidectomy

Histopathological evaluation		
Benign	645	100
Follicular nodule	254	39.4
Degenerated nodule	115	17.8
Cystic nodule	82	12.7
Colloidal nodule	64	10.0
Lymphocytic nodule	17	2.6
Chronic thyroiditis	16	2.5
Follicular adenoma	73	11.3
Hurtle cell adenoma	24	3.7
Malign	239	100
Papillary thyroid carcinoma	138	57.8
Follicular cell carcinoma	89	37.2
Hurtle cell carcinoma	12	5.0

independent data and Fischer test was used when the chi-square test conditions were not met. Kappa fit test was used for compliance analysis. Statistical significance was assessed at $p<0.05$.

RESULTS

A total of 884 cases (685 females, 199 males; mean age 46.84 ± 12.73 years, range, 14 to 82 years) were included in the study. The demographic characteristics of the patients included in the study are summarized in Table 1. Of the patients included in the study, 808 (91.40%) underwent total thyroidectomy with FNAB and 76 (8.60%) underwent total thyroidectomy without FNAB. Histopathology results are summarized in Table 2.

Table 3. Comparison of groups according to pathological evaluation

	Benign			Malign			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			47.2±12.6			45.8±13.2	0.160*
Age (year)							0.140**
≤45	256	39.7		108	45.2		
>45	389	60.3		131	54.8		
Gender							0.293**
Female	494	76.6		191	79.9		
Male	151	23.4		48	20.1		
Total malignancy score			2.2±1.1			3.0±1.3	0.000*
USG malignancy score			1.6±0.9			2.4±1.2	0.000*
Nodule size (mm)			27.9±15.7			20.4±13.5	0.000*
Nodule size (cm)							0.000**
>1.5	159	24.7		106	44.4		
≥1.5	486	75.3		133	55.6		
Capsule irregularity							0.000**
(-)	621	96.3		194	81.2		
(+)	24	3.7		45	18.8		
Number of nodules							0.000**
Isolated	443	68.7		134	56.1		
Multiple	202	31.3		105	43.9		
Microcalcification							0.000**
(-)	559	86.7		175	73.2		
(+)	86	13.3		64	26.8		
Echogenity							
Hyperechogene	130	20.2		26	10.9		0.001**
Hypoechogene	208	32.2		152	63.6		0.000**
Isoechogene	151	23.4		27	11.3		0.000**
Mixt	156	24.2		34	14.2		0.001**

* Mann-Whitney U test; ** Chi-square-test.

Table 4. Diagnostic value of fine needle aspiration biopsies

	Benign		Malign				Sensitivity	Positive predictive value	Specifity	Negative predictive value	
	n	%	n	%	Kappa	*p*	%	%	%	%	*p*
FNAB											
Benign	537	83.3	111	46.4	0.478	0.000*	55.1	72.5	92.4	82.9	0.000**
Malign	44	6.8	116	48.5							

FNAB: Fine needle aspiration biopsies; * Kappa test; ** Chi-square test.

There were no statistically significant differences in the age and sex distribution of the patients between benign and malignant groups (p=0.160, p=0.293). Capsular irregularity rate, hypoechogenicity rate, multiple nodule presence, USG malignancy score and total

Table 5. Comparison of FNAB results between FNAB consistent and FNAB inconsistent groups

	Benign			Malign			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			47.1±12.4			45.8±13.5	0.703*
Age (year)							0.984**
≤45	266	40.7		63	40.6		
>45	387	59.3		92	59.4		
Gender							0.406**
Female	513	78.6		117	75.5		
Male	140	21.4		38	24.5		
Total malignancy score			2.4±1.2			2.6±1.1	0.000*
USG malignancy score			1.8±1.1			2.0±1.1	0.000*
FNAB results							0.003**
Benign	537	82.2		111	71.6		
Malign	116	17.8		44	28.4		
Nodule size (mm)			26.5±15.6			23.0±15.3	0.000*
Nodule size (cm)							0.030**
<1.5	190	29.1		59	38.1		
≥1.5	463	70.9		96	61.9		
Capsule irregularity							0.523**
(-)	604	92.5		141	91.0		
(+)	49	7.5		14	9.0		
Number of nodules							0.058**
Isolated	424	64.9		88	56.8		
Multiple	229	35.1		67	43.2		
Microcalcification							0.618**
(-)	541	82.8		131	84.5		
(+)	112	17.2		24	15.5		
Echogenity							
Hyperechogene	126	19.3		25	16.1		0.363**
Hypoechogene	255	39.1		87	56.1		0.000**
Isoechogene	131	20.1		17	11.0		0.009**
Mixt	141	21.6		26	16.8		0.183**

FNAB: Fine needle aspiration biopsies; * Mann-Whitney U test; ** Chi-square-test.

malignancy score were significantly higher in the malignant group than the benign group (all p<0.05). In the malignant group, nodule size, hyperechogenicity rate, isoecogenicity ratio, mixed echogenicity ratio were significantly lower than the benign group (p values; p=0.000, p=0.001, p=0.000 and p=0.001, respectively) (Table 3).

There was a statistically significant correlation between pathology and FNAB results (kappa= 0.478, p=0.000). The sensitivity of FNAB was 55.7%, positive predictive value was 72.5%, specificity was 92.4% and negative predictive value was 82.9% (Table 4).

No significant difference was found in terms of age and gender distribution (p values; 0.703, 0.984 and 0.406, respectively) between FNAB consistent and inconsistent groups. The nodule size, isoecogenicity rate, total malignancy score, and USG malignancy score were significantly lower in the FNAB consistent group than FNAB inconsistent group (for all comparisons, p=0.000). The rate of hypoechogenicity, FNAB malignancy predictive rate, were significantly higher in FNAB consistent group (p values; 0.000 and 0.003, respectively). There was no significant difference in terms of the number of capsular irregularities, number of nodules and microcalcification rates FNAB consistent and inconsistent groups (p=0.523, p=0.058 and p=0.618, respectively) (Table 5).

DISCUSSION

The usage of FNAB in thyroid diseases was first reported in the 1930s by researchers named Martin and Ellis. It was then used to rule out the possibility of malignancy according to the sonographic findings.[18,19]

Fine needle aspiration biopsy has acceptable specificity and sensitivity for thyroid cancers.[17] With the usage of thyroid FNAB, the diagnosis of thyroid cancer has increased twice in the last five decades. Cibas and Ali reported that the routine usage of thyroid FNAB leads to an increase in the rate of detection of cancer in thyroid nodules.[20] Thyroid FNAB cannot always rule out the diagnosis of malignancy, and may also delay the diagnosis of malignancy due to false negative results. Yeh et al. reported that false negative results delay the surgical operation time in patients with perivascular and capsular invasion for two years. In this study, thyroid FNAB sensitivity was 55.7% and specificity was 92.4%.[21]

A gold standard diagnostic method should have high sensitivity and specificity rates as well as high positive and negative predictive rates. The higher the positive and negative predictive rates of a diagnostic test, the more reliable the diagnostic test is. In our study, the FNAB positive predictive value was 72.5% and the negative predictive value was 82.9%. Although the thyroid FNAB has an acceptable level of sensitivity, specificity, positive and negative predictive values, it has some limitations. The necessity of a multidisciplinary approach to thyroid nodules, the need for a well-trained cytopathologist to examine the pathology specimen, the difficulty of using aspiration equipment and the power of the aspiration, may cause different results between different centers.[20,21]

In the studies investigating the compliance of the sonographic findings with the thyroid FNAB, important information was obtained. Akhawan et al. compared the correlation between thyroid sonography findings and FNAB results, and reported that the nodule surface area was the most correlated sonographic finding with malignancy. Irregular nodule boundaries calcification and hypervascularity were the most prominent findings in malignancy in USG.[17] Üçler et al. reported that the size of the nodule had no effect on the correct outcome of FNAB.[22] Samulski et al. reported that sonographic findings such as nodule size, echogenicity and vascularity did not have a significant effect on the diagnosis of malignancy.[23] In their study, Tutuncu et al. reported that nodule size and calcification were effective in the diagnosis of malignancy and that echogenicity and solid form had no effect on the diagnosis of malignancy.[24] Shin et al. reported that the nodule size, nodule borders and microcalcifications were effective in the diagnosis of malignancy.[25] Na et al. reported that isolated macrocalcific thyroid nodules may had a low malignancy potential and should not be considered as a benign lesion.[26]

Studies comparing the diagnostic power of FNAB with sonographic findings indicate that these two diagnostic tests are relatively reliable. All published guidelines recommends thyroid FNAB in cases with suspicion of malignancy. ATD recommends FNAB for nodules larger than 1 cm in patients without a risk factor and if there is no suspicion of malignancy in USG.[4] However, in patients with a first-degree relative thyroid cancer history, in patients with a history of radiation, syndromic cases such as multiple endocrine neoplasia-2 syndrome, or in patients with calcitonin above 100 pg/mL, ATD recommends FNAB for cases larger than 5 mm in size.[4] American Association of Clinical Endocrinologists recommends FNAB in cases with this risk factor regardless of the size of the nodule.[27] In our study, thyroid FNAB recommendations of ATD association were considered. All patients in our study were followed-up with thyroid ultrasonography and below 1 cm size patients without risk factors did not underwent FNAB. In cases with the aforementioned risk factors, if the size of the thyroid nodule was smaller than 5 mm, because of the small size of the nodule, the FNAB was difficult to perform and FNAB was not done. FNAB was recommended for the patients with larger nodules in the case of aforementioned risk factors. In this study, thyroid nodule size was found to be smaller in patients with thyroid malignancy compared to the benign group. We think that our strategy of making FNAB even in the small nodule size in patients with malignancy suspicion resulted with this finding. In this study, the number and size of nodules, capsular irregularity, presence of microcalcifications and echogenicity are the sonographic findings. As the study was retrospective and included a long period of ten years, it was observed that the vascularity of the thyroid USG records was not recorded. The absence of standard thyroid USG records in our hospital and the inclusion of multiple thyroid USG records should be accepted as the limitation of the study. According to the findings of this study, the presence of capsular irregularity, hypoechogenicity and microcalcification in thyroid nodules should induce suspicion of malignancy.

In this study, when the sonographic findings of the patients with thyroid FNAB compatible and incompatible were compared, it was found that the large nodule size and high isoechogenic nodule ratio were higher in the compatible group. No significant difference was found between groups for the other sonographic findings.

Although this study is a valuable study in terms of reporting the sonography and FNAB results of total thyroidectomy cases in a tertiary hospital, there are some limitations. The retrospective nature of the study, thyroid USG records, thyroid FNAB 's made by different physicians and the absence of vascularity in the sonographic record are the main limitations. In addition, in our hospital, the thyroid FNAB reports were not reported according to the Bethesda classification system by the pathology clinic in the study period.

Conclusion

In this study, the files of cases with total thyroidectomy were evaluated retrospectively. Although the thyroid FNAB has an acceptable sensitivity and specificity, it is not effective in the decision of operation alone. When evaluating the results of FNAB, which is accepted as the gold standard in the approach to thyroid nodules, the risk factors of malignancy should be taken into consideration.

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